 DOI: 10.18231/2455-6807.2016.0010

Evidence of potential threat of microbial drug resistance to commonly used antimicrobials in cases of active tubotympanic CSOM from Raipur, Chhattisgarh, India

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Abstract

Background: To identify the causative aerobic microbial pathogens of active tubotympanic (TT) type Chronic Suppurative Otitis Media (CSOM) and their antimicrobial susceptibility pattern.

Method: A total of 248 clinically diagnosed CSOM patients were investigated for bacterial identification and antimicrobial sensitivity profiling.

Results: Out of 248 cases, 226 cases (91.12%) were found positive and 22(8.87%) negative in culture. *S.aureus* (30.9%) *e*merged as the predominant cause of CSOM followed by *P.aeruginosa* (23.4%), Coagulase Negative Staphylococcus (CONS) (8.4%), Enterobacteriaceae bacilli (8.8%) and others. S.aureus exhibited significant drug resistance to Penicillin, Ciprofloxacin and Cotrimoxazole whereas P.aeruginosa showed 37.8% resistance to Ceftazidime. The Enterobacteriaceae family of bacilli showed significant resistance to Cefotaxime, Amoxyclav and Cotrimoxazole. The meance of drug resistance posed a serious threat of emergence of drug resistance strains that could pose a challenge in subsequent management. TT-CSOM was predominantly caused by monomicrobial (179 cases, 79.2%) followed by polymicrobial(47 cases, 20.7%) aetiological agent. *S.aureus* was found most sensitive to Oxacillin and Clindamycin for Methicillin sensitive *S.aureus* (MSSA) and only Clindamycin for Methicillin Resistant *S.aureus* (MRSA) and CONS among primary antibiotics. In MSSA, MRSA and CONS, most sensitive secondary line of antibiotics included Linezolid and Gentamicin. *P.aeruginosa* showed highest sensitivity to Tobramycin, Piperacillin and Gentamicin among the primary and Piperacillin-Tazobactam, and Amikacin in the secondary line of antimicrobials respectively. The Enterobacteriaceae family of bacilli showed maximum susceptibility to Gentamicin and Amikacin among primary and secondary line of antimicrobials respectively.

Conclusion: Compelling evidence of emergence of drug resistant microbial causative agent of TT-CSOM warrants the utmost need to strictly implement evidence based treatment of all clinical cases of TT-CSOM for better surgical outcome and before it could lead to intractable situation with ever-growing drug resistance.

Keywords: TT-CSOM, *S.aureus*, *P.aeruginosa*.

Introduction

WHO in 1996 defined CSOM as a chronic infection of middle ear cleft, i.e. Eustachian tube, middle ear and mastoid, and in which a non-intact tympanic membrane and discharge (otorrhoea) are present for two weeks or longer.(1) CSOM is classically divided into two types (a) TT affecting the middle ear mucoperiosteum and (b) an attico-antral type which is an active squamous disease within a growth of squamous epithelium into the middle ear cleft.(2) TT-CSOM mainly affects pars tensa while attico-antral CSOM mainly affects pars flaccida of tympanic membrane. Etiology of the CSOM may differ as various microorganism viz., bacteria, viruses or fungi can inflict inflammation of mucosal lining of tympanic membrane leading to reversible/irreversible, slow and insidious pathological changes. Bacterial etiological agents inflict the CSOM infection in majority of cases. The common microorganism reported in the literature are *Pseudomonas aeruginosa (P.aeruginosa)*, *Staphylococcus aureus (S.aureus)*, *Proteus mirabilis (P.mirabilis)*, *Klebsiella pneumonia subspecies pneumoniae (K.pneumoniae)*, *Escherichia coli (E.coli)*, *Aspergillus spp.* and *Candida spp.* but their frequency may vary in various geographical areas.(3,4)

CSOM is a real challenge for health care system due to its profound impact on the society by causing the conductive hearing loss and adverse effects on child development.(4-5) It affects both sexes and all age groups. Positivity rate of 3 to 14.63% by various studies in India warrants the urgent attention for the effective management of this massive public health problem.(3,6-9) However the proper management is adversely affected due to lack of anti-biogram data, implementation of antibiotic policy, regular monitoring of frequency of causative bacterial etiology and more importantly clinician inclination for empirical antibiotic treatment. Negligence of this public health problem is further evidenced by paucity of data of frequency of different microorganism and their respective anti-biogram in Chhattisgarh, a central part of India from where no studies have been reported so far.

All India Institute of Medical Sciences (AIIMS), a tertiary care hospital in Raipur, Chhattisgarh caters to the health needs of natives of Chhattisgarh where majority of the population belongs to tribals living in rural areas. They have low literacy rate, poor socioeconomic status with inadequate medical access. TT-CSOM constitute a major portion of patients presenting with ear discharge

and due to lack of antimicrobial data usually treated with empirical broad spectrum antibiotics as systemic as well as local ear drops. Such indiscriminate usage of broad spectrum antibiotics may seriously precipitate the potential emergence of multiple drug resistant strains which could produce the constant threat of untreatable primary and postoperative infections. Changes in the microbiological flora following the empirical treatment may also lead to change of microbial pathogens of CSOM. Accordingly this study has been conducted to determine the epidemiological trend of microbial etiology of TT-CSOM in Raipur, Chhattisgarh and their anti-biogram pattern to help the clinician to plan effective treatment guideline for medical and surgical management of CSOM patients.

Materials and Methods

A prospective study was conducted in the out-patient department (OPD) of ENT in AIIMS, Raipur from 1st Jan, 2014 to 30th Dec, 2015 to determine etiology of tubo-tympanic CSOM.

A total of 430 patients of ear discharge were screened (Fig. 1). A total of two hundred forty eight [248] patients of all age groups with clinical presentation of TT-CSOM of unilateral or bilateral ear discharge of more than 3 months were enrolled in this study after obtaining their consent and rest of 182 patients were excluded. The right ear was involved in 121(48.79%), left ear in 108[43.54%] and bilateral ear in 19 cases (7.6%). The following inclusion and exclusion criteria were used in the present study.

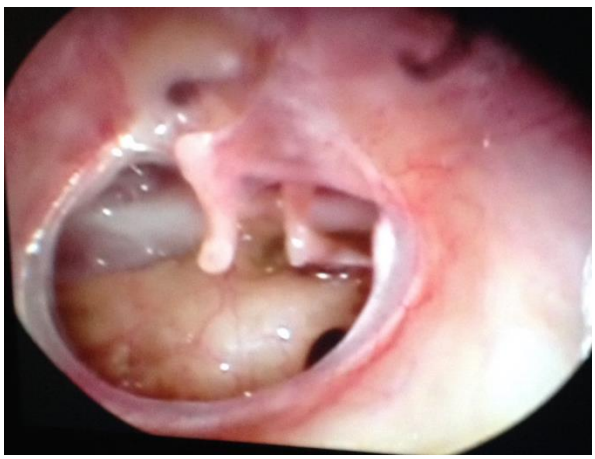

Fig. 1: ***CSOM left TT disease***

Inclusion criteria: All patients with active uni or bilateral ear discharge who have not used any antibiotic medication either topical or systemic for at least 7 days prior to their presentation in ENT OPD irrespective of age and sex. The complete clinical history including age, sex, discharge duration, hearing loss, pain, fever, other associated symptoms and usage of antibiotic therapy was taken. Clinical examination revealed a central perforation of tympanic membrane and a conductive hearing loss ranging from 30dB SPL to 55dB SPL.

Exclusion criteria: All the patients presented with one or more of following features were excluded from the study. (a) Any patient of attico-antral CSOM with attic or posterior marginal perforation who are likely to have anaerobic bacterial etiology as our study did not use anaerobic culture media or (b) Any patient who has been using an antibiotic within 7 days of clinical presentation (c) Any patient who has been clinically diagnosed for CSOM inactive TT disease or (d) Any patients of otitis externa.

Sample collection and processing: Two swabs of ear discharge were collected under aseptic precautions to avoid surface contamination to harvest the middle ear micro flora through the tympanic membrane perforation via aural speculum. The ear discharge swabs were immediately transported to microbiology laboratory for further processing. One swab was utilized for Gram's staining and the other was inoculated on Blood, Chocolate and MacConkey agar and incubated at 37^0C for 24hours. The bacterial growth was identified according to standard microbiological method. Antibiotic sensitivity was tested on Mueller Hinton Agar by Kirby Bauer Disc diffusion method according to Clinical and Laboratory Standard Institute [CLSI] guidelines, 2013.[10] Any fungal element seen in microscopy was isolated on Sabouraud's dextrose agar and identified subsequently.

Statistical analysis: The rate of culture positivity and affected age group were statistically compared by Chi square test (χ^2) using Stata statistical software[release 5.0; Stata Corporation, USA].

Results and Observation

A total of 248 patients comprising of 161(64.9%) male and 87(35.08%) female with male: female ratio of 1.85:1 were included in this study (Table 1). The age range was from 3 to 75 years with mean age of 31.08 years for males and 30.01 for females (data not shown). Most of the patients were from age group between 21-30 years (n=78, 31.45%), followed by 0-10 years (n=59, 23.79%) and 11-20 years (n=49, 19.75%) (Table 1). Out of 248 cases, 226 cases (91.12%) were found positive and 22(8.87%) negative in culture. Among 226 culture positive cases, significant difference was seen in positivity between male (n=154, 68.14%) and female (n=72, 31.85%) ($p<0.05$, $\chi^2 = 7.29$)(Table 1). However we did not found any statistical significant age predilection for culture positive CSOM ($p>0.05$, $\chi^2 = 1.44$).

The frequencies of monomicrobial and polymicrobial pathogens are shown in (Fig. 3&4). Among 226 cases, 179(79.2%) showed the etiology of single organism with their isolated growth in culture

whereas 47 cases (20.7%) showed polymicrobial etiology with growth of more than one organism in culture (Table 2, Fig. 2&3). Among the top 10 predominant organisms, *S.aureus* was identified as most predominant monomicrobial etiological agent in 70 cases (30.97%) and polymicrobial in 19 cases (8.40%) (Table 2, Fig. 4). The second most common organism recovered was *P.aeruginosa* with monomicrobial and polymicrobial positivity of 23.45% (53 cases) and 14.15% (32 cases) respectively. Out of 85 *Pseduomonas* isolates, 7 were identified as *P.stutzeri*. CONS was found in 19 cases (8.40%) as the monomicrobial and in 9 cases (3.09%) as the polymicrobial isolate. *Proteus spp.* was found in 7(3.09%) (6 *P.mirabilis* and 1 *P.vulgaris*) and 9(3.98%) cases as monomicrobial and polymicrobial isolate respectively. *K.pneumoniae, E.coli, Streptococcus pyogenes (S. pyogenes), Enterobacter aerogenes (E.aerogenes), Citrobacter koseri (C.koseri)* and *Aspergillus niger(A.niger)* also accounted for mono and polymicrobial etiological agent with maximum positivity of 6.19 % for *K.pneumoniae* to minimum of 2.21% for *C.koseri* (Table 2).

The antibiogram pattern of *S.aureus*, *P.aeruginosa*, CONS, *Proteus sp*, *K.pneumoniae*, *E.coli, E.aerogenes, C.koseri* and *S.pyogenes* were studied for recommended primary and secondary line of antimicrobial as per the CLSI guidelines, 2013(Table 3&4). On observing the antibiogram it was found that *S.aureus* isolates were resistant maximally to Penicillin (93.2%) followed by Ciprofloxacin (89.8%) and Cotrimoxazole (64%) (Table 3). Nine (09) *S.aureus* isolates were found to be MRSA exhibiting resistance to all currently available β lactam antibiotics except newer Cephalosporins with anti MRSA activity (e.g. ceftaroline). MRSA isolates showed very low sensitivity to Ciprofloxacin, Erythromycin and Cotrimoxazole. *S.pyogenes* too showed low sensitivity to Clindamycin. Among *S.aureus*, MSSA showed maximum sensitivity to Oxacillin sensitive group of antibiotics and Clindamycin in primary line of antimicrobials. MRSA and CONS on the other hand were found most sensitive to Clindamycin among primary line of antibiotics. All *S.aureus* (MSSA, MRSA) and CONS isolate exhibited highest sensitivity to Linezolid followed by Gentamicin in secondary line of antimicrobial. Sensitivity to Oxacillin was interpreted as per the CLSI guidelines as susceptible to penicillinase stable Penicillin, β lactam/β lactamase inhibitor combinations, relevant Cephems and Carbapenems but resistant to penicillinase labile Penicillins. *S.pyogenes* showed high sensitivity of 100% to Ampicllin and Cefotaxime in primary and Linezolid among secondary line of antimicrobials.

P.aeruginosa showed resistance to Ceftazidime in 37.8 % cases. It was found most sensitive to Tobramycin, Piperacillin and Gentamicin among primary and Piperacillin+Tazobactum, Imipenem, and Amikacin among secondary line of antibiotics (Table 4).
Enterobacteriaceae family of bacilli showed significant resistance to Cefotaxime, Amoxyclav and Cotrimoxazole.

Table 1: Age and sex distribution of CSOM (n=248)

Age Group	Total no. of cases	Male		Female	
		Cases	Culture positive	Cases	Culture positive
0-10yrs	59	38	36	21	18
11-20 yrs	49	31	4*+25	18	6*+11
21-30yrs	78	48	47	30	26
31-40yrs	26	21	20	5	3
41-50yrs	20	13	13	7	6
>50yrs	16	10	9	6	2
Total	248	161	154	87	72

*Positive culture in cases less than 16 yrs of age.

Table 2: Positivity of 10 predominant microorganisms in single and mixed polymicrobial capacity

Organism isolated	Causative organism (%)		Combined percentage
	Monomicrobial growth	Polymicrobial (Mixed growth)	
S.aureus	70(30.97%)	19(8.40%)	89(39.38%)
P.aeruginosa and others	53(23.45%)	32(14.15%)	85(37.61%)
CONS	19(8.40%)	9(3.98%)	28(12.38%)
Proteus sp(*P.vulgaris* 01 & *P.mirabilis* 15)	7(3.09%)	9(3.98%)	16(7.07%)
K.pneumonia	4(1.76%)	10(4.42%)	14(6.19%)
E.coli	4(1.76%)	7(3.09%)	11(4.86%)
C.koseri	2(0.88%)	6(2.65%)	8(3.53%)
S.pyogenes	4(1.76%)	3(1.32%)	7(3.09%)

E.aerogenes	3(1.32%)	3(1.32%)	6(2.65%)
Aspergillus niger	4(1.7%)	1(0.004%)	5(2.21%)

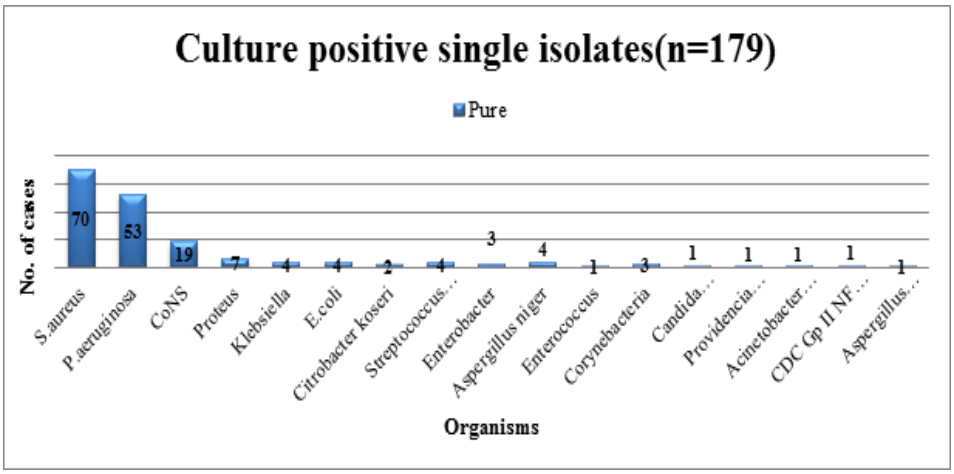

Fig. 2: The frequency of single microbial etiology in TT CSOM

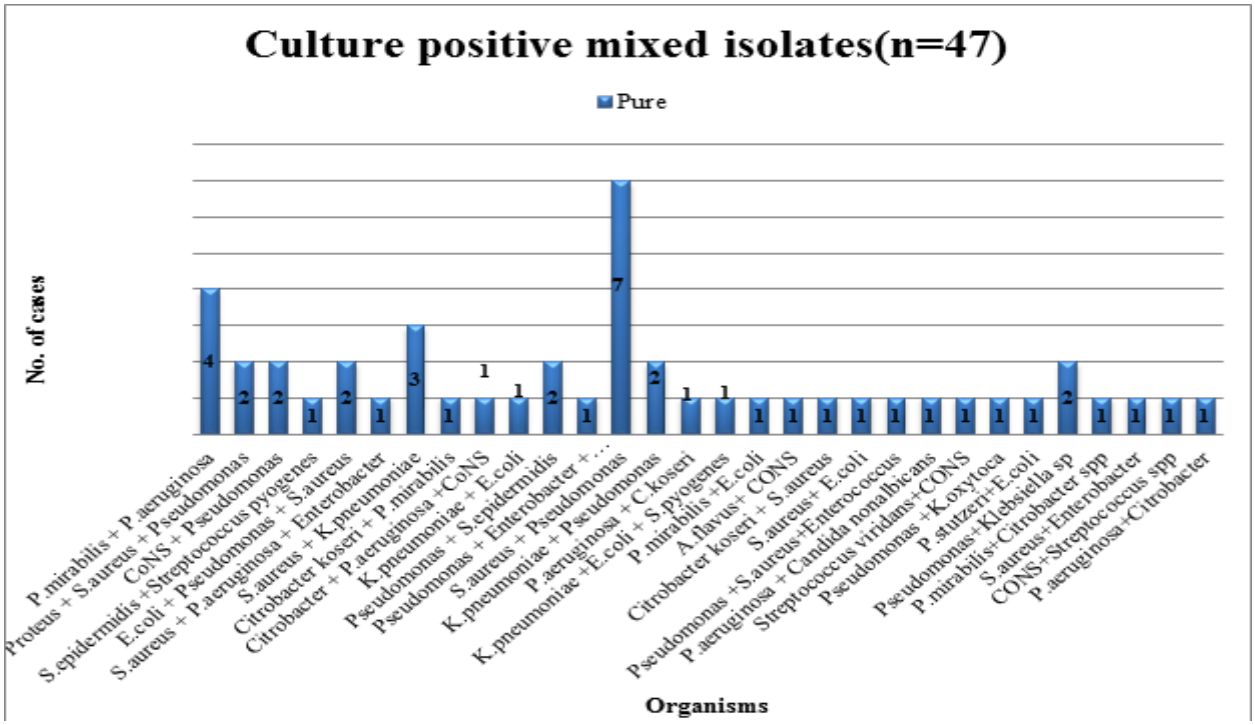

Fig. 3 Frequency of mixed microbial etiology (n=47)

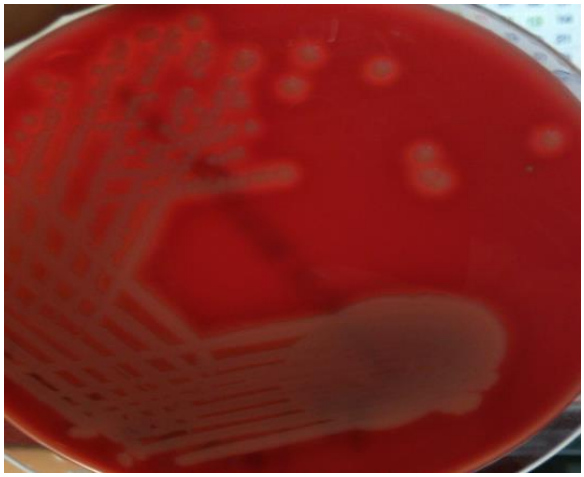

Fig. 4: β Haemolytic colonies of S.aureus

Table 3: Susceptibility pattern of Gram positive aerobic bacterial isolate to various antibiotics with theirtested concentration

Organism (No.)	Antibiotics (Sensitive) (No.) (%)									
	P	**Cx**	**Ci**	**Cd**	**Ct**	**Er**	**Gm**	**Ce**	**Lz**	**Am**
S.aureus (89)	6 (6.7)	80(89.8)	9(10.1)	79(88.7)	32(35.9)	43(48.3)	80(89.8)	-	89(100)	-
CONS (19)	5(26.3)	11(57.8)	14(73.6)	16(84.2)	10(52.6)	11(57.8)	16(84.2)	-	19(100)	-
MRSA (9)	0(0)	0	2(22.2)	7(77.7)	3(33.3)	3(33.3)	9(100)	-	9(100)	-
S.pyogenes (7)	5(71.4)	-	NR	4(57.1)	-	6(85.7)	6(85.7)	7(100)	7(100)	7(100)

Abbreviation used for antimicrobials P = Penicillin (10U), Cx = Cefoxitin(30µg); Ci = Ciprofloxcin (5µg) Cd= Clindamycin (2µg), Ct= Cotrimoxazole (25µg), Er= Erythromycin (15µg), Gm= Gentamicin (10µg), Ce= Cefotaxime(30 µg), Lz=Linezolid(30 µg), Am= Ampicillin(10µg).

Table 4: Susceptibility pattern of Gram negative aerobic bacterial isolates to various antibiotics with their tested concentration

Organism	Am	Ak	Cf	Pi	Gm	Cp	Ci	Az	Tb	Pi+Tz	AC	Ce	Ct	I
P. aeruginosa (85)	-	84(98.8)	53(62.3)	80(94.1)	77(90.5)	72(84.7)	70(82.3)	67(78.8)	84(98.8)	85(100)	-	-	-	85 (100)
Proteus sp (16)	12(75.0)	16(100)	-	-	16(100)	14(87.5)	16(100)	-	-	-	14(87.5)	5(31.2)	6(50.0)	-
K. pneumoniae (14)	11(78.5)	12(85.7)	-	-	7(50.0)	13(92.8)	13(92.8)	-	-	-	7(50.0)	5(35.7)	13(92.8)	-
E.Coli (11)	6(54.5)	11(100)	-	-	9(81.8)	10(90.9)	6(54.5)	-	-	-	6(54.5)	3(27.2)	4(36.3)	-
Enterobacter aerogenes(6)	5(83.3)	6(100)	-	-	6(100)	6(100)	6(100)	-	-	-	5(83.3)	6(100)	3(50.0)	-
Citrobacter koseri(8)	2(25.0)	8(100)	-	-	8(100)	8(100)	8(100)	-	-	-	7(87.5)	8(100)	6(75)	-

Abbreviation used for antimicrobials Am=Ampicillin (10µg), Ak = Amikacin (30 µg) Cf = Ceftazidime (30µg), Pi=Piperacillin (100 µg), Gm=Gentamicin (10 µg), Cp=Cefepime(30 µg), Ci=Ciprofloxacin(5µg), Az=Aztreonam(30µg), Tb=Tobramycin(10µg), Pi+Tz= Piperacillin + Tazobactum (100/10 µg), Ac=Amoxyclav(30 µg), Ce=Cefotaxime(30 µg), Ct=Cotrimoxazole (25 µg), I= Imipeneum (10µg).

Discussion

CSOM and its complications are one of the most common ear diseases which have been frequently encountered in OPD of Otolaryngologist, pediatrician and general practitioners. It imposes great risk of causing irreversible local destruction of middle ear structures and also the dreadful intracranial complications. Poorly treated or untreated CSOM can lead to many complications like mastoiditis, meningitis and brain abscess. Medical treatment includes aural toilet and the provision of topical or/and systemic antibiotics, steroids and antifungals. Surgical treatment includes tympanoplasty and mastoidectomy or both. Hence, early identification of microorganisms along with their antibiogram pattern is important for proper management as a wide range of organisms can inflict CSOM with ever-changing antimicrobial sensitivity pattern.

In our study, CSOM was found most prevalent in the young adults of 21-30 years age group followed by 0-10 and 11-20years age groups. This observation was found in tandem with earlier observation of Vishwanath *et al.*[11] Various published studies showed varied prevalence of CSOM according to age group with some studies documented high prevalence in children and young adults less than 20years of age while others observed age group of 31-40 years more affected.[4,12-17] In our study males (64.91%) were more affected than females (35%) and significant difference was found between the two($P<0.01$) without significant difference in age predilection($P>0.01$). Similar observation were also published by earlier studies of Shrestha *et al.*, Vishwanath *et al.*, Poorey *et al.*, Ghosh *et al.*, and Moorthy *et al.*[4,11,12,14,18] However contrary to our observation, some studies showed more prevalence in females which could probably be due to geographical and social reasons.[4,15-16]

Our study showed the culture positivity of 91.26% with monomicrobial and polymicrobial growth in 79.20% (179) and 20.7% (47) cases respectively. Previous studies done by Khanna *et al.*, Poorey *et al.*, Deb *et al.*, Nikakhalgh *et al.*, Ghosh *et al.*, Prakash *et al.*, showed the culture positivity rate of 84%, 92%, 53%, 82%, 96.29% and 93.75% respectively (Table 5).[12,14,16,19-21] Polymicrobial growth rate of 39% and 10% was reported by earlier studies of Khanna *et al.*, and Poorey *et al.*, respectively.[12,19]

The ten(10) most predominant etiological agents of TT-CSOM recognized in our study in chronological order included *S.aureus* followed by *P.aeruginosa*, CONS, *Proteus spp*, *K.pneumoniae*, *E.coli*, *C.koseri*, *S.pyogenes*, *E.aerogenes*, *A.niger* and others. Our observation was also corroborated with earlier findings of Nikakhlagh *et al.*, from Iran, Shreshta *et al.*, from Kathmandu, Nepal, Prakash R *et al.*, from Uttrakhand, Loy *et al.*, from Singapore, Taneja *et al.*, from Muzaffarnagar, UP but differ from some studies which showed *P.aeruginosa* as the most frequent organism isolated (Moorthy *et al.*, in Hyderabad, Sharma *et al.*, Eastern Nepal and Yeo *et al.*, from Korea, Khanna *et al.*, from Chandigarh, Poorey *et al.*, from Rewa, MP)(Table 5).[4,12,16-19,21-24] This variation could be due to difference in climatic conditions, occupation of the inhabitants, social customs and the distribution of microorganisms in the environment. *P.aeruginosa* is known to reside in the moist environment of the external auditory canal, whereas *S.aureus* is universally harbored within human nares. The proximity of these bacteria aptly reflects the likelihood of their eventual presence within middle ear, either as contaminants or bonafide pathogens. CONS was the next most common organisms isolated with a positivity rate of 12.38%. Although considered as commensal organism of the skin, CONS etiology of CSOM has been well documented as opportunistic pathogen.

In our study, *S.aureus* and *P.aeruginosa* accounts for 76.99% of total bacterial etiology of tubo-tympanic CSOM. Considering the combination of monomicrobial and polymicrobial growth, there was no significant difference between frequency of *S.aureus* and *P.aeruginosa* with their occurrence increased to a total of 89(39.38%) and 85(37.61%) cases respectively ($P> 0.01$). The isolation of Enterobacteriaceae group of bacilli (*Proteus spp*, *Klebsiella*, *E.coli* and Citrobacter) suggested fecal contamination of local water bodies which could probably be the source of transmission as the people in rural areas of Chhattisgarh use small stagnated pond water for various daily chores like bathing, washing clothes and utensils etc.

Rare single etiological agent of CSOM found in this study included *Providentia rettgeri*, *Acinetobacter baumannii*, CDC Group II nonfermenter Gram Negative Bacilli and *Enterococcus spp* (Fig. 3&4). Notable finding also included fungal isolates (n=08, 3.5%, *Candida parasilopsis* 02, *Aspergillus niger* 04 and *A.flavus* 02). Our observation of fungal etiology was also compounded by earlier studies of Shrestha *et al.*, Mirza *et al.*, and Vishwanath *et al.*, who also found 9.5, 11, 9.6% fungal isolate as the etiological reason of tubo-tympanic CSOM.[4,11,25] This could probably be due to the humid tropical geography of the region and the local belief among the community of instillation of oil in ear canal as the traditional medicine. However, due to lack of laboratory facility, we were not able to process fungi for sensitivity testing of antifungal agents.

Our study showed the variable degree of drug resistance exhibited by various bacterial etiological agents. We have noticed that microbial drug resistance has slowly but progressively marked its effect as previously used drug of choice Penicillin, Ciprofloxacin and Cotrimoxazole have shown significant decrease in sensitivity as compared to other antimicrobials. This is more pertinent with the significant observation of our study that Ciprofloxacin, which was once reported as the choice of drug for CSOM in 2013 by Moorthy *et al.*, was found to be resistant in many isolates of *S.aureus* MSSA and MRSA.[18] *P.aeruginosa* too has shown decreased

sensitivity to Ciprofloxacin in comparison to other antimicrobials. Gentamicin which is also frequently used for empirical treatment of CSOM had also shown decreased sensitivity against *P.aerugninosa* in comparison to Amikacin, Tobramycin and combination of Piperacillin and Tazobatam. The significant drug resistance exhibited by *S.pyogenes* to Clindamycin, *P.aeruginosa* to ceftazidime and Enterobacteriaceae group of bacilli to Cefotaxime, Amoxyclav and Cotrimoxazole posed a serious threat of emergence of multidrug resistance strains and subsequent complication in management of such infection. It's a alarming sign for health policy makers to strictly take all necessary measure to prevent empirical treatment before the situation gets worsened. Injudicious use of antimicrobial due to human negligence and frequent empirical treatment are primarily responsible for development of antibiotic resistance. As soon as symptom subside, many patients stop taking antibiotic before completion of therapy and allow partially resistant microbes to flourish and transform into more lethal drug-resistant form. Such practice should be stopped by proper counseling of patients and educating general public about the consequences of antimicrobial drug resistance. Topical antibiotic ear drop suffice for the treatment of uncomplicated safe CSOM along with adjuvant consisting of anti-histaminics and decongestants in majority of cases. Oral antibiotics should be indicated only if systemic complaints are present along with ear complaints.

Poorey *et al.*, Ghosh *et al.*, and Sharma *et al.*, showed Amikacin as the most effective drug.[12,14,23] However our observation differs as antimicrobial sensitivity pattern showed variation between different aerobic microbial organisms. MSSA exhibited the maximum sensitivity to Oxacillin sensitive group of antibiotics and Clindamycin whereas MRSA and CONS were found to be most sensitive to only Clindamycin among primary line of antimicrobials. Linezolid and Gentamicin were recorded as the highly sensitive antibiotic among secondary line of antimicrobials for MSSA, MRSA and CONS. For Gram negative organism, frequently used Amikacin showed a poor response of 50% sensitivity against *K.pneumoniae* thus stressing the need of judicious use of antimicrobial. The Tobramycin and Piperacillin - Tazobactam showed excellent sensitivity to *P.aeruginosa* and thus could be a choice of drug against *P.aeruginosa* in monomicrobial CSOM. All variation in anti-biogram between various causative organisms strongly recommends evidence based treatment of all CSOM cases.

All the patients treated on the basis of drug sensitivity testing responded favorably. Most of the patients showed drying of ear discharge by 1 week of treatment. The culture negative patients were treated by regular dry mopping of ear, or/and Ciprofloxacin, Gentamicin alone or in combination with topical antifungal Clotrimazole ear drops. All the patients were successfully treated leading to the probable interpretation that either these samples had contained only mucoid discharge from goblet cells in middle ear or probably some other bacterial and fungal etiological agents were present which could not be isolated, although seems as the rarest possibility.

The etiology of TT CSOM is primarily documented with aerobic microorganism as evidenced in our and various earlier mentioned studies.[8,9,11-25] Therefore any probability of culture negative cases due to anaerobic etiology appeared minimal and consequently did not have any significant negative impact on the present study.

Table 5: Positivity of different microbial causative agent in various studies

Organism	Shrestha et al.	Moorthy et al.	Poorey et al.	Ghosh et al.	Prakash M. et al.	Vishwanath et al.	Prakash R. et al.	Present study
S.aureus	74(32.2)	7(11.3)	20(19.6)	37(28.4)	33(41.2)	20(17.4)	93(48.6)	89(39.3)
MRSA	NR	NR	NR	NR	NR	NR	NR	9(3.9)
CONS	NR	5(8.0)	NR	5(3.8)	9(11.2)	10(8.7)	4(2.1)	28(12.3)
S.pyogenes	NR	1(1.6)	4(3.9)	4(3.0)	NR	NR	NR	7(3.0)
S.pneumoniae	14(6.1)	NR	NR	3(2.3)	NR	2(1.7)	2(1.0)	NR
P.aeruginosa	62(26.9)	33(54.0)	36(35.2)	50(40.7)	30(37.5)	37(32.2)	38(19.8)	85(37.6)
Klebsiella sp	24(10.4)	5(8.0)	26(25.4)	10(7.6)	6(7.5)	8(6.9)	18(9.4)	14(6.1)
Proteus mirabilis	16(6.9)	5(8.0)	10(9.8)	7(5.3)	4(5.0)	3(2.6)		15(6.6)
Proteus vulgaris	NR	4(6.4)	NR	NR	NR	1(0.9)	4(2.1)	1(0.004)
E.coli	16(6.9)	2(3.2)	6(5.8)	8(6.1)	4(5.0)	2(1.7)	14(7.3)	11(4.8)
Citrobacter spp	NR	NR	NR	2(1.5)	NR	NR		8(3.5)
Acinetobacter baumannii	NR	NR	NR	NR		2(1.7)	6(3.1)	1(0.004)
Enterobacter aerogenes	NR	NR		NR	NR	1(0.9)	NR	6(2.6)
Diphteroid	NR	NR	NR			NR	10(5.2)	NR
Morganella morganii	NR	NR		NR	NR	NR	2(1.0)	NR
Aspergillus spp	16(6.9)	NR	NR			8(7.0)	NR	6(2.6)
Candida spp	8(3.4)	NR		NR	NR	3(2.6)	NR	2(.008)

Conclusion

Season, locality and ethnicity are the prime reason of variation in microbial etiology of TT CSOM in particular locality and population. Considerable decrease in sensitivity of various frequently used antibiotics has alarmingly points out the utmost need of strictly implementing the requirement for any health center to establish and conduct routine clinico-microbiological monitoring of microbial flora of CSOM with anti-biogram based treatment for better surgical outcome and avoidance of antibiotic resistance.

Financial source: Study was the part of requirement of laboratory investigation of CSOM cases.

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