International Journal of Advanced Community Medicine

E-ISSN: 2616-3594
P-ISSN: 2616-3586
www.comedjournal.com
IJACM 2020; 3(2): 59-62
Received: 14-02-2020
Accepted: 24-03-2020

Dr. Gulsiv Nair
Assistant Professor, Department of Microbiology, Al Azhar Medical College and Superspecialty Hospital, Thodupuzha, Kerala, India

Dr. M Lakshminarayana
Statistician cum Assistant Professor, Department of Community Medicine, Hassan Institute of Medical Sciences, Hassan, Karnataka, India

Dr. Lavanya Nagaraj
Professor and Head, Department of Pharmacology, Sree Narayana Institute of Medical Science, Chalakka, Ernakulam, India

Dr. Naveen Kumar M
Professor and Head, Department of Pharmacology, Al Azhar Medical College and Superspecialty Hospital, Thodupuzha, Kerala, India

Dr. Thilak SA
Professor, Department of Community Medicine, Al Azhar Medical College and Superspecialty Hospital, Thodupuzha, Kerala, India

Corresponding Author:
Dr. Naveen Kumar M
Professor and Head, Department of Pharmacology, Al Azhar Medical College and Superspecialty Hospital, Thodupuzha, Kerala, India

Antibiotic resistance in causative agents of ear discharge: A deafening problem

Dr. Gulsiv Nair, Dr. M Lakshminarayana, Dr. Lavanya Nagaraj, Dr. Naveen Kumar M and Dr. Thilak SA

DOI: https://doi.org/10.33545/comed.2020.v3.i2a.214

Abstract
Discharge from the ear is common, the management of which is complicated by rising antimicrobial resistance. Ear discharge samples received at the microbiology laboratory in Al Azhar Medical College from June 2018 to May 2019 were processed, and organisms identified and susceptibility tested.
The predominant organism was *Pseudomonas aeruginosa* (24/53, 45.28%). The susceptibility of these isolates to fluoroquinolones (91.67%) and aminoglycosides (95.83%) was good.
Eleven isolates were Gram positive, with 8 *Staphylococcus aureus* and 3 coagulase negative Staphylococcus. Five isolates were MRSA (62.5%). Susceptibility to ampicillin (27.27%), amoxiclav (36.36%), 3rd generation cephalosporins (54.55%), azithromycin (54.55%), and fluoroquinolones (45.45%) was disappointing. Cotrimoxazole susceptibility was 72.73%.
Seven isolates were Enterobacterales. Susceptibility to ampicillin, amoxiclav, cefuroxime and macrolides (each 14.29%) was alarming. Ceftriaxone and cotrimoxazole showed susceptibility of 57.14%. Fluoroquinolone susceptibility (71.43%) was also poor.
Antimicrobial therapy based on microbiological evidence is essential for the management in the face of high antibiotic resistance.

Keywords: Ear discharge, pseudomonas, antibiotic resistance, fluoroquinolones

Introduction
Discharge from the ear is a very common problem in the out patient setting in the medical practice [1]. It can be caused by diseases such as acute and chronic otitis externa, malignant otitis externa, acute and chronic otitis media, with or without cholesteatoma.
Otitis media is a very common diseases in young children worldwide [2]. Apart from the morbidity due to the illness itself, the long term sequelae, increased antibiotic consumption from a young age, loss of school hours and work hours are also extremely worrisome [3].
In addition, middle ear infections were found to be a very frequent cause of deferral of numerous childhood vaccinations [4], leading to an increased burden of those diseases as well. In the developing world, middle ear infections are an important cause of preventable hearing loss [5].
The most common organisms isolated include *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella* species, Proteus, *E.coli* etc. [6, 7, 8]. Organisms like Streptococcus pneumoniae, *Haemophilus influenzae* etc. were also identified as very common aetiological agents for acute disease in a systematic review, but the authors had also included patients without ear discharge as a main symptom [9].

Materials and Methods
The study was conducted on samples of ear discharge from patients coming to Al Azhar Medical College and Superspeciality Hospital, Thodupuzha, Kerala, which is a tertiary care centre, from June, 2018 to May, 2019. The present study was cleared by the Dissertation Review Committee without any ethical, financial or scientific concerns being raised. The samples were cultured on blood, MacConkey and chocolate agar and incubated at 35°C - 37°C for 18 hours. Growth on the culture plates were carefully examined for colony morphology, and identification was done with standard microbiological techniques like Gram staining, catalase and oxidase tests, standard biochemical reactions. *Staphylococcus aureus* (ATCC® 25923), *E. coli* (ATCC® 25922) and *Pseudomonas aeruginosa* (ATCC® 27853) (ATCC, Virginia, U.S) were used as controls.

Antibiotic susceptibility testing by Kirby-Bauer disc diffusion method was done according to CLSI recommendations on Mueller Hinton Agar.
Antibiotic discs [HiMedia, Mumbai, India] of the following strengths were used – Ampicillin (10 µg), Amoxycillin-clavulanate (20/10 µg), Cefuroxime (30 µg), Cefixime (5 µg), Ceftriaxone (30 µg), Ceftazidime (30 µg), Co-trimoxazole (1.25/23.75 µg), Azithromycin (15 µg), Ciprofloxacin (5 µg), Levofloxacin (5 µg), Gentamicin (10 µg), Amikacin (30 µg), Piperacillin-Tazobactam (100/10 µg). Pseudomonas isolates were tested with Ceftazidime (30 µg), Ciprofloxacin (5 µg), Levofloxacin (5 µg), Gentamicin (10 µg), Amikacin (30 µg), Piperacillin-Tazobactam (100/10 µg) due to inherent resistance to many commonly used antibiotics.

Results and Discussion

A total of 53 samples consisting of swabs from ear discharge were processed from June 2018 till May 2019.
Of these, samples from male patients accounted for 41.5% (22 of 53), while those from female patients accounted for 58.5% (31 of 53) (Figure 1).

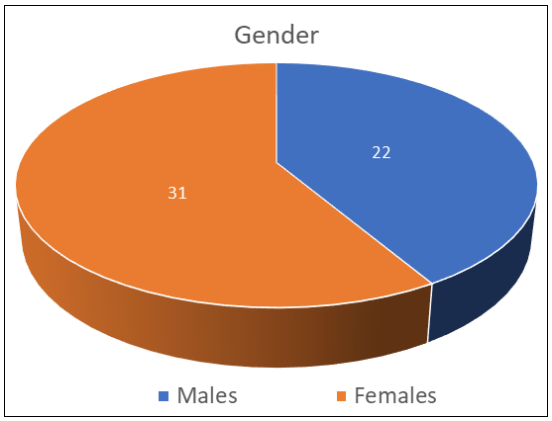


Fig 1: Gender distribution of Patients (Females- 31; Males- 22)

Age Wise Distribution

Table 1: Age wise distribution

Age	0-20	21-40	41-60	61-80	>80
Nos	12	17	15	08	01

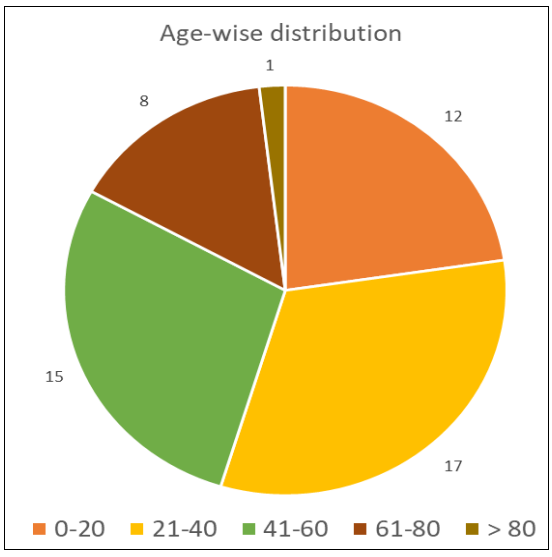


Fig 2: Age wise distribution

A large fraction of the samples were from of the samples were from young and middle age patients (Figure 2). This is mostly consistent with the findings in other parts of India and the world, even though the distribution is not as strongly skewed towards small children in our study.

Distribution of Organisms

Seven of the samples yielded no growth. Of the 46 samples which produced growth, five were found to have fungal colonies (10.87%). Of which two had growth of only Candida species, one grew only Aspergillus species, while the remaining two grew both Candida and Aspergillus. Of the rest 41 having bacterial growth, one sample was reported as having two organisms, namely *Pseudomonas aeruginosa* and *Klebsiella oxytoca*. The predominant organism was found to be *Pseudomonas aeruginosa* (24/53, 45.28%), followed by Staphylococcus aureus (8/53, 15.09%).

Table 2: Distribution of isolates

Organism	No. of isolates
No growth	07
Pseudomonas aeruginosa	24
Staphylococcus aureus	08
Coagulase negative Staphylococcus	03
Klebsiella pneumoniae	02
Klebsiella oxytoca	02
Enterobacter species	02
Proteus mirabilis	01
Candida species	04
Aspergillus species	03

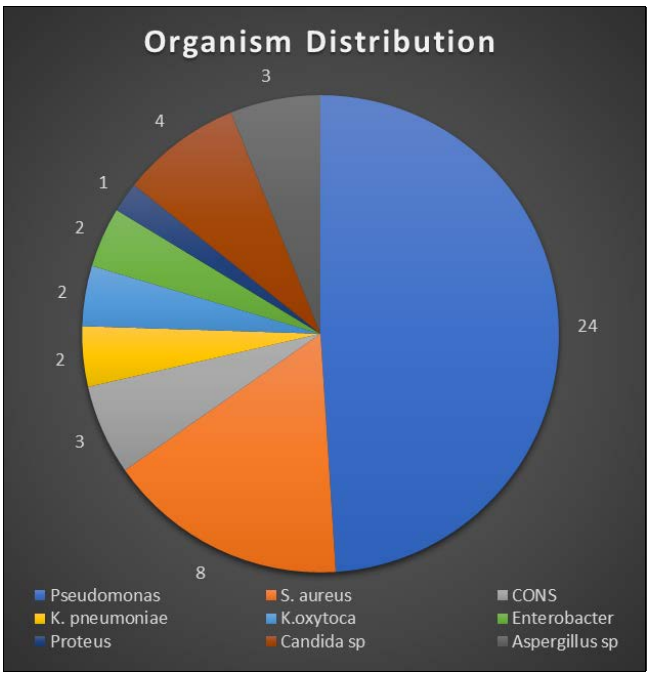


Fig 3: Distribution of isolates

Antibiotic Susceptibility Pattern

Pseudomonas, being the organism predominantly isolated and also being inherently resistant to many of the commonly used antibiotics, including ampicillin, amoxicillin, cefixime, cefotaxime, ceftriaxone, macrolides, co-trimoxazole etc., has been considered separately.

Susceptibility of Pseudomonas Isolates

Table 3: Pseudomonas Susceptibility

Antibiotic	Susceptibility
Ciprofloxacin	22/24 (91.67%)
Levofloxacin	22/24 (91.67%)
Ceftazidime	17/24 (70.83%)
Gentamicin	23/24 (95.83%)
Amikacin	23/24 (95.83%)
Piperacillin-Tazobactam	24/24 (100%)

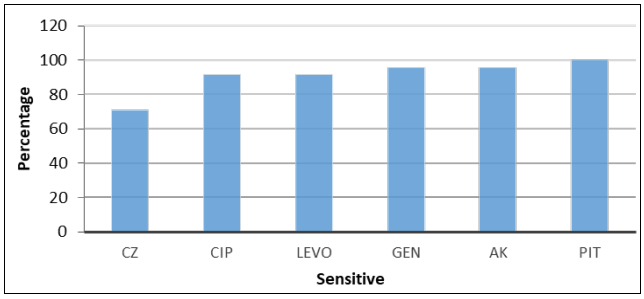


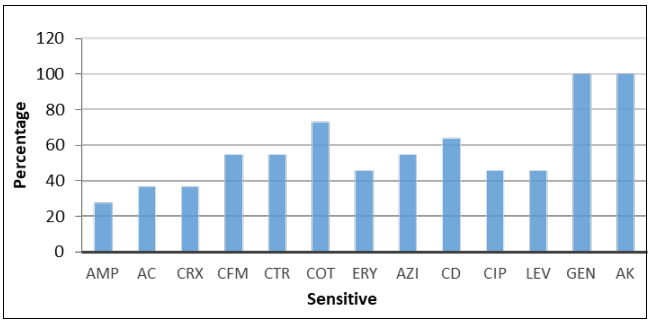
Fig 4: Pseudomonas Susceptibility

*AMP- Ampicillin, AC-Amoxicillin-Clavulanic acid, CRX-Cefuroxime, CTR-Ceftriaxone, CZ- Ceftazidime, COT- Co-trimoxazole, AZI-Azithromycin, CIP- Ciprofloxacin, LEVO- Levofloxacin, GEN- Gentamicin, AK- Amikacin, PIT- Piperacillin- Tazobactam. In our study, Pseudomonas was found to be quite susceptible to fluoroquinolones and aminoglycosides with over 90% susceptibility. This is quite similar to the findings by Appiah-Korang [6], Gorems *et al.* [13]. All isolates were susceptible to Piperacillin tazobactam.

Susceptibility of Gram Positive Organisms

Table 4: Gram positive organism susceptibility

Antibiotic	Susceptibility
Ampicillin	3/11 (27.27%)
Amoxicillin- Clavulanate	4/11 (36.36%)
Cefuroxime	4/11 (36.36%)
Cefixime	6/11 (54.55%)
Ceftriaxone	6/11 (54.55%)
Co-trimoxazole	8/11 (72.73%)
Erythromycin	5/11 (45.45%)
Azithromycin	6/11 (54.55%)
Clindamycin	7/11 (63.64%)
Ciprofloxacin	5/11 (45.45%)
Levofloxacin	5/11 (45.45%)
Ceftazidime	17/24 (70.83%)
Gentamicin	11/11 (100%)
Amikacin	11/11 (100%)



*AMP-Ampicillin, AC-Amoxicillin-Clavulanic acid, CRX-Cefuroxime, CTR-Ceftriaxone, CZ-Ceftazidime, COT- Co-trimoxazole, AZI-Azithromycin, CIP-Ciprofloxacin, LEVO-Levofloxacin, GEN-Gentamicin, AK- Amikacin

Fig 5: Gram positive organism susceptibility

Eleven of the isolates were Gram positive cocci (20.75%). All were identified as Staphylococcus, of which, *Staphylococcus aureus* accounted for 8 isolates, while 3 were coagulase negative Staphylococcus. Five of the 8 *Staphylococcus aureus* isolates were methicillin resistant (62.5%). Sensitivity to penicillins and cephalosporins ranged from 27 to 55%, as was the case with macrolides. Almost three quarter of the isolates were sensitive to Co-trimoxazole. Sensitivity to fluoroquinolones was just under 50%. Only the aminoglycosides showed 100% susceptibility. This is much lesser than what was reported by Agarwal *et al.* [7], Kumar *et al.* [8], Vishwanath *et al.* [14] etc.

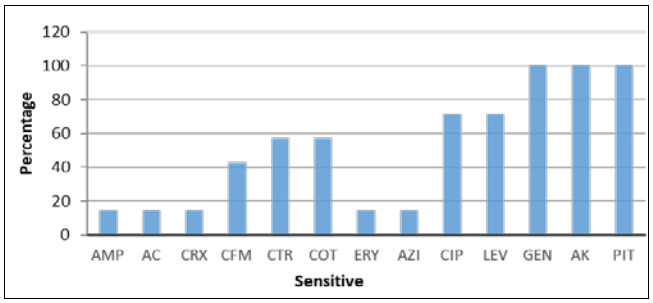
All of this is worrying as most of the commonly prescribed antibiotics in clinical practice was found to have poor susceptibility.

Susceptibility of Gram Negative Organisms

Seven of the isolates were Gram negative bacilli, excluding Pseudomonas, which has been considered separately.

Table 5: Gram negative organism susceptibility

Antibiotic	Susceptibility
Ampicillin	1/7 (14.29%)
Amoxicillin- Clavulanate	1/7 (14.29%)
Cefuroxime	1/7 (14.29%)
Cefixime	3/7 (42.86%)
Ceftriaxone	4/7 (57.14%)
Co-trimoxazole	4/7 (57.14%)
Erythromycin	1/7 (14.29%)
Azithromycin	1/7 (14.29%)
Ciprofloxacin	5/7 (71.43%)
Levofloxacin	5/7 (71.43%)
Gentamicin	7/7 (100%)
Amikacin	7/7 (100%)
Piperacillin-Tazobactam	7/7 (100%)



*AMP-Ampicillin, AC-Amoxicillin-Clavulanic acid, CRX-Cefuroxime, CTR-Ceftriaxone, CZ-Ceftazidime, COT- Co-trimoxazole, AZI-Azithromycin, CIP- Ciprofloxacin, LEVO-Levofloxacin, GEN-Gentamicin, AK-Amikacin, PIT- Piperacillin-Tazobactam

Fig 6: Gram negative organism susceptibility

The penicillins and cephalosporins had very dismal susceptibility rates, from just under 15% to just under 60% for third generation cephalosporins. Co-trimoxazole susceptibility was 57.14%. Macrolide susceptibility was 14.29%. Among the oral drugs, only the fluoroquinolones showed a relatively respectable susceptibility of 71.43%.

All isolates were susceptible to aminoglycosides and piperacillin-tazobactam.

This was similar to Gorems *et al.* [13], and except for aminoglycosides and piperacillin-tazobactam, lesser than what was found by Vishwanath *et al.* [14] and Haneefa *et al.* [15].

Conclusion

Patients presenting with discharge from the ear is very common in the outpatient setting, and if not adequately and properly managed, can lead to long term morbidity and disability. The problem is exacerbated by occurrence of antimicrobial resistance in the causative organisms. The high resistance seen with most of the commonly prescribed oral antibiotics is extremely alarming, with most of the isolates being, more often than not, resistant. Only adequate management based on microbiological evidence can help to treat the patient and minimize treatment failures, and subsequent increase in morbidity and costs.

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