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Original Research Paper

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AN INSIGHT INTO THE BACTERIAL ETIOLOGY AND ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF BACTERIA CAUSING EAR INFECTIONS IN A TERTIARY CARE HOSPITAL IN NORTH INDIA.

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ABSTRACT

Background: Due to the inappropriate use of antibiotics along with poor compliance of the patients, resistance patterns have developed to commonly prescribed antibiotics for ear infections, especially in children. Otitis media, a common ear infection is one of the key contributors to antibiotic resistance. It is estimated that up to 40% of all preventable hearing impairments are caused by ear infections, leading to frequent antibiotic usage, especially in developing countries. Considering the upsurge in drug resistance, a study was conducted to provide an update on current bacteriological profile and antimicrobial susceptibility pattern as it would be useful for clinicians to start with the appropriate antibiotics at the earliest and to reduce the burden of emerging drug resistance especially during the ongoing Covid-19 pandemic. **Material method:** A retrospective study over a period of three years, starting from January 2018 to December 2020 in a tertiary care hospital where all ear discharge/ pus samples were processed. A total of 1050 ear discharge samples were cultured according to the standard microbiological procedures. Isolates were identified by conventional methods and antibiotic susceptibility profiles were determined by standard disk diffusion method. All this data was then evaluated retrospectively. Data was analyzed by SPSS version 22 and the P value of less than 0.05 was considered as statistically significant for the same. **Results:** Staphylococcus aureus and Pseudomonas aeruginosa were the most common microbes to be isolated. Gram positive cocci had high sensitivity to doxycycline and linezolid while Gram negative bacilli were sensitive to amikacin, imipenem, and piperacillin and tazobactam among the wide spectrum of antibiotics which were tested. These results indicate a rise in drug resistance in both Gram positive and Gram-negative microorganisms to many commonly prescribed antimicrobial agents by means of multiple drug resistance mechanisms. **Conclusion:** Patterns of sensitivity and resistance, help in proper selection of empiric therapy and prevention of emergence of resistant strains. Both culture and susceptibility tests have paramount importance for better management of ear infections, especially the drug-resistant ones.

KEYWORDS : Bacterial etiology, antimicrobial susceptibility patterns, ear infections, North India.

BACKGROUND:

The human ear can be divided into External, Middle and Internal ear or labyrinth. External ear consists of auricle or pinna, external acoustic canal and tympanic membrane. Middle ear together with Eustachian tube, aditus, antrum and mastoid air cells is called middle ear cleft while the internal ear consists of bony and membranous labyrinth.[1] So the ear infections include infections of any of the above said parts of ear. The most common ear infection is otitis media which is also the most common cause of earaches and discharges from ear. Otitis media (OM), inflammation of the middle ear following infection is a frequent cause of infant distress, often associated with children, and can also affect adults.[2] There are several types of OM, including acute otitis media (AOM), recurrent acute otitis media (RAOM), otitis media with effusion (OME) and chronic otitis media (COM) but acute and chronic suppurative otitis media are the two most common forms.[3] Acute suppurative otitis media (ASOM) is an acute inflammation of middle ear cleft by pyogenic organisms while chronic suppurative otitis media (CSOM), is a perforated tympanic membrane with a persistent ear discharge from the middle ear for more than 2-6 weeks despite treatment though otolaryngologists tend to adopt longer duration of 3 months.[4]

Ear infections often accompanies common cold, flu and upper respiratory tract infections as the middle ear is connected to the upper respiratory tract via the Eustachian tube. Microorganisms present in the nose or sinus cavities enter the middle ear through the Eustachian tube and start growing there. Also when Eustachian tube is clogged or blocked, middle ear becomes damp and warm, thus becoming a perfect breeding ground for microbes. Allergies, post nasal drainage, sinus infections, common cold viruses and adenoid problems can all interfere with the Eustachian tube's ability to let air pass into the middle ear thus leading to infections.[6]

It is often difficult to diagnose OM due to a lack of correlation between clinical features and responsible pathogens and their drug susceptibility patterns. The routine unavailability of

an othoscope in health facilities, particularly in developing countries, limits the ability of health workers to make better diagnoses and classifications of OM since it is necessary to differentiate the different spectrum of clinical findings necessary to define the case.[6] In addition, empiric antibiotic therapy may not always be effective since drug susceptibility patterns change over time and may contribute to the development of antimicrobial resistance.[7]

The most common bacteria involved in such infections are *Haemophilus influenzae, Streptococcus pneumoniae, Streptococcus pyogenes, Staphylococcus aureus, Moraxella catarrhalis,* and *Pseudomonas aeruginosa* from contaminated water.[8] Majority of otogenic complications like intracranial abscess, meningitis and facial nerve palsy, are result of attico-antral type of Otitis Media, especially if left untreated bacteriological profile of which seems to be shifting towards Gram negative pattern with *P. aeruginosa* being the most common, along with other organisms like *Bacillus, Proteus and Escherichia coli* as shown by the other studies conducted over the years.[9]

Along with the shifting bacteriological profile of ear infections, an emergence of multidrug resistant microorganisms has also been noticed worldwide. Among the Gram-negative bacteria, the common multi drug resistant pathogens are *Klebsiella* spp., *E. coli*, and *P. aeruginosa*, and they show resistance to major anti-Gram negative agents (beta-lactams, fluoroquinolones and aminoglycosides).[10]Serious infections caused by Gram-positive bacteria are also being increasingly difficult to treat because of microbes, like methicillin-resistant *S. aureus* (MRSA), and penicillin-resistant *S. pneumoniae*.[11]

Detection of multidrug resistant isolates limits the therapeutic options for treating such common but painful and debilitating infections. This accounts for a major health and economic problems, especially in the developing countries where resources for diagnosis and treatments are limited.[12] Therefore, objective of this study was to determine the changing bacteriological profile of otitis media infections and their antibiotic resistance pattern which will be helpful in assisting physicians in empirical therapy and setting therapeutic protocols.

MATERIAL AND METHODS

This is a retrospective study over a period of three years starting from January 2018 to December 2020 conducted at a tertiary care hospital in Chandigarh. All the ear discharge pus from ear samples that were received from the patients over this period were processed using standard microbiological methods, where a Gram stain and culture of each sample was done. Further, isolation and identification of organisms were performed in our clinical microbiology laboratory by detecting their morphological and biochemical characteristics. Antibiotic sensitivity was put up using Kirby Bauer disc diffusion method according to the organism isolated and the zones were read according to the CLSI guidelines. All the data generated thus was evaluated later.

RESULTS:

A total of 1050 samples were received over a period of 36 months. Majority of participants were males (n=661, 63%) in comparison to females (n=388, 37%). Growth was present in 607 (57.8%) out of which 365 samples were from males and 188 were from female patients and 54 were from children while 443(42.2%) were sterile/or were reported as normal flora.

Among the 607 samples which showed growth, 330(54.3%) samples showed growth of Gram positive organisms, 262(43.2%) showed growth of Gram negative organisms, 5 (0.8%) isolates grew fungus while 10 (1.6%) had growth of more than 3 organisms.

Gram positive organisms (n=330) isolated were *Staphylococcus aureus* 259(78.5%), Other *Staphylococcus* species 45(13.6%) and *Enterococcus* species 26 (7.89%).

Gram Negative organisms (262) isolated were *Pseudomonas* 163(62.2%), *Klebsiella* species 30(11.4%), *Escherichia coli* 24(9.1%), *Proteus* species 20(7.6%), *Acinetobacter* species 12(4.6%), *Citrobacter* species 6(2.3%), *Morganella* species 3(1.1%), *Providencia* species 2(0.8%) and *Enterobacter* species 2 (0.8%).

Amongst the total isolates *Staphylococcus aureus* was the most common isolate to be isolated 42.7% to be followed by *Pseudomonas* 26.9%, Other *Staphylococcus* species 7.4%, *Klebsiella* species 4.9%, *Enterococcus* species 4.3%, *Escherichia coli* 4.0%, and the miscellaneous including *Proteus* species, *Acinetobacter* species, *Citrobacter* species, *Morganella* species, *Providencia* species, *Enterobacter* species and fungi etc. 9.8%. Among the 259 isolates of *Staphylococcus aureus,* Cefoxitin was susceptible in 53.2% (138) [indicating 53.2% isolates being methicillin susceptible Staphylococcus aureus] while 46.8% (121) were resistant to cefoxitin. Penicillin susceptibility was seen in only 7.7% (20) while 92.3% (239) of the isolates were resistant to it. Erythromycin was susceptible for 36.7% (95) isolates, 3.8% (10) were moderately susceptible while 59.5% (154) were resistant. Clindamycin was susceptible for 69.5% (180) isolates and resistant in 30.5% (79). Doxycycline was susceptible for 86.9% (225), moderately sensitive for 3.8% (10) and 9.3% (24) isolates were resistant. Ciprofloxacin was susceptible for 27.0% (70), moderately susceptible for 20.8% (54) and resistant for 52.2% (135). Gentamicin was susceptible for 62.2% (161), moderately susceptible for 5.8% (15) and resistant for 32.0%(83). Cotrimoxazole was susceptible for 58.7% (152), moderately susceptible for 17.4% (45) and resistant for 23.9% (62). Linezolid was susceptible for 99.6% (258) isolates and resistant for 0.4%(1) isolate. Fig.1 Among the 45 isolates of Other *Staphylococcus* species Cefoxitin was susceptible for 71.1% (32) susceptible [indicating isolates being methicillin susceptible] while 28.9% (13) isolates were resistant to cefoxitin. Penicillin susceptibility was seen in only 22.2% (10) while 77.8% (35) of the isolates were resistant to it. Erythromycin was susceptible for 44.4% (20) isolates, 2.2% (1) were moderately susceptible while 53.4% (24) were resistant. Clindamycin was susceptible for 75.5% (34) and resistant for 24.5% (11). Doxycycline was susceptible for 88.9% (40), moderately sensitive for 2.2% (1) and 8.9% (4) isolates were resistant to it. Ciprofloxacin was susceptible for 57.8% (26), moderately susceptible for 13.3% (6) and resistant for 28.9% (13) of the isolates. Gentamicin was susceptible for 68.9% (31) and resistant for 31.1% (14) isolates. Cotrimoxazole was susceptible for 44.4% (20), moderately susceptible for 4.4% (2) and resistant for 51.1% (23) of the isolates. Linezolid was susceptible for 100% (45) isolates.

For *Enterococcus* species High level gentamicin was susceptible in 80.8% (21) and resistant in 19.2% (5) of the isolates. Ciprofloxacin was susceptible in 57.7% (15) moderately susceptible in 7.7% (2) and resistant in 34.6% (9). Erythromycin was susceptible 53.8% (14), moderately susceptible in 7.7% (2) and resistant in 38.5% (10). Tetracycline was susceptible in 65.4% (17) and resistant in 34.6% (9) isolates. *Enterococcus* was 100% susceptible for vancomycin and linezolid.

For *Pseudomonas* species antibiotic sensitivity was put up for Amikacin, ciprofloxacin, ceftazidime, piperacillin-tazobactam, imipenem and aztreonam. And in amikacin 65.7% (107) isolates were susceptible, 1.2% (2) was moderately susceptible while 33.1% (54) isolates were resistant. For ciprofloxacin 52.2% (85) isolates were susceptible, 3.0% (5) were moderately susceptible while 44.8%

(73) were resistant. For ceftazidime 51.5% (84) isolates were susceptible, 5% (8) were moderately susceptible while 43.5% (71) isolates were resistant. For piperacillin-tazobactam 72.4% (118) were susceptible, 6.1% (10) were moderately susceptible while 21.5% (35) isolates were resistant. For imipenem 62.5% (102) isolates were susceptible, 9.2% (15) isolates were moderately susceptible while 28.3% (46) isolates were resistant and for aztreonam 75% (88) isolates were susceptible, 21.5% (35) isolates were moderately susceptible and 24.5% (40) isolates were resistant.

For rest of the gram negative organisms (99) antibiotic sensitivity was put up for amikacin for which 73.7% (73) isolates were susceptible, 5.0% (5) moderately susceptible and 21.3% (21) were resistant. Ciprofloxacin for which 42.5% (42) isolates were susceptible, 6.0% (6) moderately susceptible and 51.5% (51) isolates were resistant. Ceftazidime for which 32.3% (32) isolates were susceptible and 67.7% (67) isolates were resistant. Cefotaxime for which 43.4% (43) isolates were susceptible and 56.6% (56) isolates were resistant. Cefepime for which 53.5% (53) isolates were susceptible, 10.1% (10) isolates were moderately susceptible and 36.4% (36) isolates were resistant, piperacillin-tazobactam for which 71.7% (71) isolates were susceptible, 3.0% (3) were moderately susceptible while 25.3% (25) were resistant and for Imipenem 67.7% (67) were susceptible, 4.0% (4)were moderately susceptible and 28.3% (28) were resistant. For Acinetobacter species in addition to the above drugs other drugs tested were ampicillin-sulbactam, tobramycin and tetracycline. Ampicillin-sulbactam was susceptible for 33.3% (4), moderately susceptible to 25% (3) and resistant to 41.7% (5) isolates, tobramycin was susceptible for 50.0% (6) isolates, 16.7% (2) moderately susceptible while 33.3% (4) were resistant and tetracycline was susceptible for 41.7% (5) and resistant for 58.3% (7) isolates of *Acinetobacter.*

DISCUSSION

CSOM and its complications are the most common conditions seen by otologists, pediatricians, and general practitioners. There is a great risk of irreversible complications associated with this disease. The earlier the bacteriological diagnosis of all cases, the more accurate and effective the treatment will be.[13]

We observed growth in 57.8% of the ear specimens with *Staphylococcus aureus* (42.6%) being the most commonly isolated pathogen followed by *Pseudomonas* 26.8%. Most of the studies have reported *Pseudomonas* as the most common agent responsible for ear infections, followed by *Staphylococcus aureus*.[14] Few have reported incidence of *Pseudomonas* to be relatively low.[15] In our study *Staphylococcus aureus* is the most common agent isolated from the ear specimens which is comparable with other studies[16]Due to the high prevalence of resistant strains in the external auditory canal and upper respiratory tract, Staphylococcus aureus has become more common in the middle ear.[17],[18] According to Prakash et al., Staphylococcus aureus was the predominant isolate (41.25%).[19] In the present stud,46.8% of *Staphyloccus aureus* were MRSA (Methicillin Resistant *Staphylococcus aureus)* while the rest were MSSA [Methicillin sensitive *Staphylococcus aureus*]. Most of the studies have reported high level of oxacillin resistance19 though in few studies oxacillin sensitive strains were seen in abundance, in our study also MSSA were on the higher side. It was found to be most sensitive to Linezolid 99.6%, followed by Doxycycline 86.9% while susceptibility to clindamycin, gentamicin and cotrimoxazole was approximately 65%. According to Worku and Bekele all their isolates (98.6%) were found to be resistant to either one and more drugs and multidrug resistant against two to more drugs was 97.1% as well.[20].

In this study gram negative bacteria antibiogram reveals they were sensitive to amikacin (73.7%), piperacillin-tazobactam (72%) and imipenem (67.7%), except for *P. aeruginosa* that was most susceptible to piperacillin-tazobactam (72.4%) followed by amikacin (65.7) and imipenem (62.5%).

CONCLUSION

This retrospective study revealed, *Staphylococcus aureus* as the most common causative agent of ear infections followed by *Pseudomonas* and their patterns of sensitivity and resistance, will help in the proper selection of empiric therapy and prevention of the emergence of resistant strains during the Covid-19 era. The study also proves that culture and susceptibility testes have paramount importance for the better management of otitis media and drug-resistant infections. For this reason, trends in antibiotics must be followed up periodically and continuously to prevent the emergence of resistant strains.

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