Original Article

Ear infections in Karachi: The frequency and antibiotic resistance of bacterial isolates

Farhan Essa Abdullah[1], Pooja Kumari Khatri[2], Najla Abdulnabi Alzadjali[3], Anum Deedar Ali[4], Geeta Bhagia[5]

ABSTRACT

Objective: This 12-month retrospective study was undertaken to determine the frequency of ear infections in children and adults, and the sensitivity of bacterial isolates to antibiotics available for their treatment

Methodology: Ear swabs of 197 subjects with ear infections were processed in a local lab with branches in key areas of Karachi City from January 2009 to December 2009. The isolates from ear discharge were identified on conventional basis and their sensitivity to 24 antibiotics was determined by the Kirby-Bauer Agar Disc Diffusion Method.

Results: Among the patients, 100 were females and 97 males; infections were more common in children between 1 to 10 years. *Staphylococcus aureus* and *Pseudomonas aeruginosa* were mostly isolated among 10 bacterial species; *Klebsiella pneumoniae* was more often grown from female infected ears. The most effective antibiotics determined for possible empirical prescription included Pipericillin+Tazobactam, Cefoperazone+Sulbactam, Imipenam, and Fosfomycin. While Ciprofloxacin (57.7%) and Amoxyclav (36.2%) exerted transitional activity, a majority of the isolates were indifferent to Cotrimoxazole, Cefixime, Lincomycin, Doxycycline and Polymyxin B.

Conclusion: The increasing resistance of causative organisms in our environment to multiple antibiotics encourages the C/S of specimens prior to drug prescription in order to reduce the chances of treatment failure and amplified antibiotic resistance. When unavoidable, however, a selection of drugs is offered for empirical preference.

KEY WORDS: Otitis media, suppurative otitis, bacteriology, antimicrobial therapy.

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1. Dr. Farhan Essa Abdullah, MBBS, MPhil, PhD (Microbiology), Assistant Professor of Microbiology and Immunology, Dow Medical College & Dr Essa's Laboratory & Diagnostic Center
2. Pooja Kumari Khatri,
3. Najla Abdulnabi Alzadjali,
4. Anum Deedar Ali,
5. Geeta Bhagia,

2-5: Undergraduate Student of MBBS, Dow University of Health Sciences, Karachi, Pakistan.

Correspondence:

Dr. Farhan Essa Abdullah,
Dr. Essa's Laboratory, B-122 Block- H, Shahrah-e-Jehangir,
North Nazimabad, Karachi, Pakistan.
E-mail: farhanessa@gmail.com

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INTRODUCTION

Suppurative disease of the middle ear is a constant challenge for otologists to treat. Most developing countries apparently lack accurate data about its incidence[1] although infective complications ranging from chronic mastoiditis and ossicular damage to cerebral abscess may lead to disability.

Microbial infection can indeed involve different parts of the ear, but irritation of the squamous epithelium or skin appendages of the external auditory canal occurs less frequently because of lateral migration of keratin and debris, low pH, and wax formation which contains a variety of antimicrobial substances.[2]

Otitis media, however, is a common infection of the middle ear cleft, mostly reported in infants 6-36 months, more often in boys, which is usually preceded by self-limiting viral otitis involving the upper respiratory tract. Bacterial superinfection may nevertheless follow, often due to pneumococci, streptococci and *Hemophilus influenzae.* The drum may be red, opaque and bulging.[3]

Chronic suppurative otitis media (CSOM) affects the tympanic membrane and contiguous ear structures. Bacteria classically enter the middle ear through the Eustachian tube and the resultant infection swells the middle ear lining which in turn causes blockage in the tube. This leads to the formation of fluid buildup and as it increases, can cause temporary hearing loss and severe pain. Unchecked, the fluid buildup can reach levels pressuring the ear drum and damaging it, necessitating antibiotics, decongestants, analgesics and myringotomy.[4]

Clinically CSOM presents with ear discharge and conductive deafness. The presence of otalgia, foul smelling discharge, and blood stained pus are indicators of mounting complications which can present as furunculosis due to *Staphylococcus aureus*, and bullous myringitis affecting the tympanic membrane caused by *Mycoplasma pneumoniae.*

Numerous studies on the microbial flora involved in ear infections elsewhere[1,2,4,5] and in Pakistan[3,6-11] have been well documented. Authors in general agree that for treatment "Watchful waiting" may be acceptable for a few cases, but possibly all patients with CSOM should receive antimicrobial therapy to minimize mastoid pathologies. Selection of a potentially effective drug, however, in the absence of discharge culture analysis, depends on the regional prevalent microflora.[8]

In our environment, gram-negative rods such as *Pseudomonas* and *E.coli* are increasingly isolated from ear discharge; studies also show that these organisms are gaining resistance to multiple antibiotics[9] possibly because of their frequent prescription. Hence our study was encouraged to determine the effective antibiotics on isolates grown from infected ears of local patients, and also to ascertain the drugs which are mostly ineffective or partially effective whose use should be restricted or their prescribed dose adjusted.

METHODOLOGY

Sterile calcium alginate cotton swabs were used to collect ear discharges of 197 patients who presented in the branches of Dr Essa's Lab in key areas of Karachi City from January 2009 to December 2009. The nature of each specimen was noted, whether wet, dry, odorous, purulent or blood-stained, and history of duration of ear ache, any prior antibiotherapy, fever, tinnitus or vertigo, was recorded wherever possible.

The specimens were promptly swabbed on Blood agar (Oxoid), Chocolate agar, KLED medium and EMB agar (Merck) plates. One inoculated Chocolate blood agar culture with BVX factors (BBL) was kept in a candle jar in case *Hemophilus influenzae* was implicated, and additionally a swabbed Sabouraud Dextrose (Difco) plate was maintained at room temperature for seven days. Gram-stained slide preparations were routinely made to observe association of bacteria with leucocytes. Resultant microbial growth after 24 hours incubation at 37^0C were identified on the basis of customary characteristics and their sensitivity to 24 antibiotics were determined using Sensitivity agar (Oxoid) and the classical Kirby-Bauer Agar Disk Diffusion Method.[12] The antibiotic discs included Cephalosporins (n=7), Penicillins (n=4), 5-Fluoroquinolones (n=4), Aminoglycosides (n=2) and one each of a Carbapenem, Tetracycline, Phenicol, and Lincosamide.

RESULTS

The most common bacterial isolates identified in the culture of 197 ear swabs of patients with exudative Otitis media in the year 2009 in Karachi was *Staph. aureus* (38.26%) of which approximately 54% were Methicillin-resistant, followed by *Pseudomonas aeruginosa* (36.73%), *Klebsiella pneumoniae* (9.69%), *Proteus mirabilis* (7.14%), *E.coli* (4.08%) and *Enterobacter* (2.55%); the least common were the gram-positive *Diphtheroids, Enterococci and*

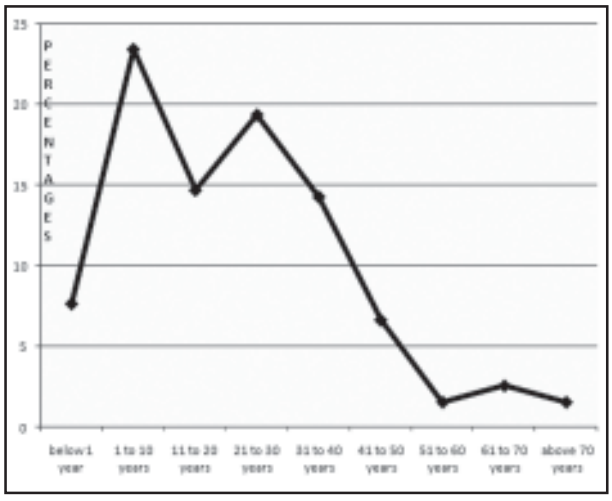

Fig-1: Graphical representation of association of ear infection with age.

Pneumococci (Table-I). Two males had Otomycosis; *Aspergillus* was grown from both subjects, but the data was excluded in this report. Staphylococci was present in 39 male and 36 female ears, pseudomonas in 38 male and 34 female patients, suggesting a minor male preponderance. However, Klebsiella was recovered from 13 female patient ear swabs (68.42%) and only six infected ears of males (31.58%). *Diphtheroids* were in two female patient specimens only, while enterococci and pneumococci were present in one male patient each. These results suggest that staphylococci and pseudomonas were more often isolated from male ear discharges, while *Klebsiella*, *Proteus*, *Enterobacter* and *Diphtheroids* occurred more often in female ear pus. Overall, females (50.77%) were only slightly more often encountered as patients than males (49.23%) with ear discharge.

Figure-I presents the association of age with Otitis media. While the prevalence of infection was highest in children aged 1 to 10 years (23.46%), the incidence peaked in age group 21 to 30 and then reduced with age to 1.53% in those above 70 years. Indeed, the majority of cases were noted between 1 to 40 years (totaling a comparative 71.82%).

According to the results obtained from *in vitro* agar diffusion analysis (Table-II), the antibiotics which were most effective covering a majority of the ear pus isolates included Pipericillin+Tazobactam (97.4%), Cefoperazone+Sulbactam (96.6%), and Imipenam (95.7%), all three available in only injectable form. Fosfomycin (79.6%) followed, a drug provided in capsule, syrup and also injectable variety. Those that were least effective were Gentamicin (34.02%), Chloramphenicol (30%), Amoxicillin (22.2%), Cotrimoxazole (15.1%), and Cefixime (15%). Indeed, the isolates were significantly resistant to Lincomycin (85.7%), Doxycycline (92%), and Polymyxin B (98.3%).

DISCUSSION

In our study, staphylococci, pneumococci and diphtheroids grown from infected ear pus may well have originated from the throat: staph in particular, which is an ubiquitous bacterium has been seen most often in ear pus.[1-11] Less commonly, microbes may intrude into the middle ear in tainted water or inserted on hair pins, car keys and the like beyond the cerumen and its associated antimicrobial factors in the outer ear.[5]

Discharge is in the majority of cases due to chronic Otitis media and must always receive prompt attention in order to prevent the spread of infection to the mastoid antrum and subsequent progressive deafness; etiological agents usually include, as also noted in our scrutiny, pseudomonas (36.73%) and *Proteus* (7.14%), but often the major pathogens reported in chronic Otitis are enteric bacilli which we have seen, such as *E.coli* (4.08%) and *Enterobacter* (2.55%). These results are not considered unusual since fingers can carry fecal flora in spite of thorough rinsing with soap and water.[5]

In CSOM, pus may accumulate and finally burst through the ear drum; in order to avoid a ragged tear, a minor surgical incision is made in the ear drum, a requirement resorted to much less frequently since the advent of effective chemotherapy. However, the era of antibiotics has not only initiated the continuing introduction of a variety of antimicrobial agents, but has done so at a price: the propagation of an increasing number of resistant organisms at the expense of sensitive strains[13-15] as has been seen for instance in the resistance of pseudomonas and *E.coli* to ciprofloxacin, and the cocci to many drugs in our study.

Indeed, a serious outbreak of infectious diseases caused by resistant organisms to multiple antibiotics has occurred in many developing countries. Studies show that out of 10 million annual antibiotic

Table-I: Gender association and isolates from 197 specimens.

Organism	*Male Patients*	*Female Patients*	*Total*	*%*
Staph. aureus	39	36	75	38.26
Ps. aeruginosa	38	34	72	36.73
Kleb.pneumoniae	6	13	19	9.69
Pr. mirabilis	6	8	14	7.14
E.coli	4	4	8	4.08
Enter. aerogenes	2	3	5	2.55
Diphtheroids	0	2	2	1.02
Enterococci	1	0	1	
Pneumococci	1	0	1	
Total:	97 (49.23%)	100 (50.77%)	197	

Table-II: Percentage sensitivity of isolates to antibiotic used

Antibiotics	*Sensitivity %*	*Resistance %*
Tazabactam+ Pipericillin (Tazocin)	97.4	2.6
Cefoperazone+ Sulbactam (Sulzone)	96.6	3.4
Imipenam	95.7	4.3
Fosfomycin	79.6	20.4
Ceftazidime	76.7	23.3
Cefotaxime (Claforan)	76.6	23.4
Ceftriaxone (Rocephin)	70.6	29.4
Sparfloxacin	70.37	29.6
Ofloxacin	65.8	34.2
Enoxacin	60.5	39.5
Ciprofloxacin	57.7	42.3
Cefuroxime	48.1	51.9
Cephradine (Velosef)	41.2	58.8
Penicillin	38.0	62.0
Amoxyclac (Augmentin)	36.2	63.8
Tobramycin (Nebcin)	34.4	65.6
Gentamicin	34.02	65.9
Chloramphenicol	30.0	70.0
Amoxycillin	22.2	77.8
Cortrimoxazole (Septran)	15.1	84.9
Cefixime (Cefspan)	15.0	85.0
Lincomycin	14.3	85.7
Doxycycline	8.0	92.0
Polymyxin B (Lidosporin)	1.7	98.3

prescriptions for ear infections, apparently 8.5 to 9.5 million did not help.[15] Roughly 80% of infections will clear up without antibiotics[16] but children tend to be prone to get chronic infected ears if not treated appropriately. According to Oguntibeju[17] 75% of children experience Otitis media 3 or 4 times during the first 3 years of their life. Likewise, we noted that ear infections were most common amongst age group 1 to 10 years; possibly this occurs because a child's Eustachian tube is shorter and at more of a horizontal angle than that of adults.

Ear infections are fairly frequent in both the sexes according to several studies. In 2000[9], the prevalence of ear infections was 43.2% in females and 56.8% in males; another study conducted in 2008[12] reported males (54%) and females (46%) with Otitis media, while in 2009[11], the disease proportion was 47.22% in females and 52.77% in males, very similar to results in our learning where the gender association was 50.5% females and 49.5% males among 197 patients.

Antibiotic treatment of purulent discharge associated with chronic CSOM allows the ear to dry out gradually, thus facilitating surgery, or, if surgery is contraindicated, significantly reduces the risk of adjacent structures being damaged. Drugs selected must be able to penetrate the mucus membrane of the middle-ear and inside the mastoid process, and also have activity against the most common pathogens. *Pseudomonas aeruginosa*, *Staph. aureus* and *Proteus mirabilis* have been reported to make up 70-90% of the isolates implicated in chronic Otitis;[1,5,6] Anwarus–Salam et al. also reported that pseudomonas and staphylococci together accounted for approximately 70% of culture findings in Karachi,[8] while we have likewise recorded a preponderance (75%) of staphylococci together with pseudomonas, in our subjects. The relevant drugs which affected approximately 97% of our isolates were two injectables – Pipericillin and the 3rd generation Cephalosporin Cefoperazone - both endowed with enhanced activity because of the addition of the beta-lactamase inhibitors Tazobactam and Sulbactam, respectively. Interestingly, in a study conducted in 2008 by Mirza et al. almost 100% of their isolates were reported sensitive to Pipericillin+Tazobactam.[10]

Next in degree of affectivity was Imipenam, an injectable Carbapenem, which covered 95.7% of the isolates. But inhibiting 79.6% of the bacteria recovered from our patients' ears was Fosfomycin, marketed in convenient capsule, suspension and injectable forms, and known to have a wide spectrum of action on gram-negative pathogens and obstinate enterococci. However, Fosfomycin is possibly less popular in use because it has to be administered 6 hourly.

The three injectable 3rd generation Cephalosporins, Ceftazidime (76.7%), Cefotaxime (76.6%) and Ceftriaxone (70.6%) were somewhat less effective, but differing in degree to a study conducted in 2009[11] which reported maximum resistance of their isolates to Cefotaxime and Ceftriaxone. We also noted that Cefixime (15%), also a 3rd generation Cephalosporin, did poorly because it hardly discourages gram-positive pathogens.

Next in degree of inhibition were the four Fluoroquinolones Sparfloxacin (70.3%), Ofloxacin (65.8%), Enoxacin (60.5%) and Ciprofloxacin (57.7%).

Possibly Ciprofloxacin exerted the weakest action of the four because it tends to be over-prescribed by local physicians.

In 2003, the most effective drug was said to be Gentamicin[17], but in our experience, isolates have acquired resistance to Gentamicin and even to Tobramycin, both Aminoglycosides available in convenient topical form, because of frequent and long term use. And possibly the same reasoning may explain the poor action of the less costly drugs Amoxycillin (22.2%), Cotrimoxazole (15.1%), Lincomycin (14.3%), Doxycycline (8%) and Polymyxin B (1.7%), each representing a different class of antimicrobial agents. These drugs had to attempt countering not only *Pseudomonas aeruginosa*, but also Methicillin-resistant *Staph. aureus* (MRSA) which accounted for approximately 54% of our staphylococci isolates. Indeed, the dramatic increase in the prevalence of community-acquired MRSA infections during the last 10 years offers another challenge to the clinician, especially in the treatment of pediatric patients in whom therapeutic choices are limited.[18] In addition, the phenomenon of transfer of resistance and the widespread repeated use of multiple antibiotics when just one would be sufficient, have together evoked changes in the nature of infections; gram-negative bacteria have in particular overtaken gram-positive species in the frequency of appearance in pathological processes. Hence knowledge of the species of organism most often implicated in an infection, which used to be sufficient to determine adequate treatment, is now no longer enough, a development demanding the sensitivity testing of each isolated strain to several antibiotics. This has been routinely done in the current exercise, aiding the clinician to consider cost effective analysis of treatment options.[19]

CONCLUSION

An audit of ear infections in 197 patients in Karachi is presented. *Staphylococcus aureus* and *Pseudomonas aeruginosa* were the major isolates among 9 bacterial species. The degree of activity of 24 antimicrobial agents on the isolates is listed: the inventory presents option for empirical therapy, and also underlines the need for regular culture/sensitivity processing of ear discharge for confident drug selection.

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Author's Contribution:

FEE: Concept, design, editing, manuscript writing and approval of manuscript.
PKK: Data collection, interpretation and manuscript writing.
NAA, ADA, GB: Data collection and statistical analyses.