

The prevalence and antimicrobial resistance of *Pseudomonas* species in patients with chronic suppurative otitis media

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ABSTRACT

Background: Chronic suppurative otitis media (CSOM) is the result of an initial episode of acute otitis media and is characterized by a persistent discharge from the middle ear through a tympanic perforation for at least 2 weeks duration. It is an important cause of preventable hearing loss, particularly in the developing world.

Objective: To get an overview on the bacterial ear infection profile in general and to assess the antibiotic resistance of Pseudomonas infection (PS) particularly since it is usually the commonest infection to cause otitis media and the most difficult to treat due to the problem of multi drug resistance..

Methods: A cross sectional study was done which included 405 patients of CSOM patients, 196 (48%) case were males, 209 (52%) case were females. Swabs for aural discharge were taken from those patients. Discharge is cultured by inoculating it into blood, Mac Conkey agar, chocolate agars and Sabouraud agar (for fungi). If the isolate shows to be Pseudomonas isolate growth then another culture of the isolate is performed on Muller Hinton Agar. Then the antibiotic susceptibility and resistance of Pseudomonas isolate is assessed by (Kirby-Bauer Method)

Results: 196 (48%) case were males, 209 (52%) case were females with a male to female ratio 1:1. One hundred fifteen (73%) cases were infected with Pseudomonas species (PS).

The sensitivity of the *Pseudomonas* isolates to the following antibiotics was Amikacin 91.7%, Imipenem 89.7%, Ceftazidime 81.8%, Ciprofloxacin 73.7%, Garamycin 72.9%, Tobramycin 67.7%, Ticarcillin 66.7%, Cefoperazone 42.9%

Conclusion: *Pseudomonas* species is the commonest microorganism in cases of CSOM. Microbiological identifications and antibiotic resistance determination of pathogens isolated from the middle ear in patients with CSOM not responding to empirical antibiotic treatment gives possibility of the choice of an effective antibiotic and its proper dosage. Cefoperazone, a relatively new antibiotic that is used in Iraq to combat pseudomonas infections has proven to be poorly effective compared with other previously used antibiotics.

Keywords: Chronic suppurative otitis media, acute otitis media, *Pseudomonas*, cefoperazone, Kirby-Bauer Method, Muller Hinton Agar.

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Chronic suppurative otitis media (CSOM) is defined as a chronic inflammation of the middle ear and mastoid cavity, which presents with recurrent ear discharges or otorrhoea through a tympanic perforation¹.

The disease is the residue of an acute suppurative infection usually acquired in infancy or early childhood². The disease commonly starts with painless perforation of the ear drum and purulent discharge. The perforation is usually central and often large. It remains for several years. During this time, there are episodes of painless discharge of foul-smelling pus associated with a blocked ear canal and poor hearing. Between these episodes, the perforation remains, but the ear is usually dry and hearing can be normal or at least adequate³.

Generally, patients with tympanic perforations which continue to discharge mucoid material for periods of from 6 weeks to 3 months, despite medical treatment, are recognized as CSOM cases. The WHO definition requires only 2 weeks of otorrhoea¹, but otolaryngologists tend to adopt a longer duration, e.g. more than 3 months of active disease⁴.

Inadequate antibiotic treatment, CSOM were previous tympanostomy tube insertion; having had more than 3 upper respiratory tract infections and/or acute OM in the past 6 months; having parents with a low education level and having older siblings⁵, nasal disease⁶, poor access to

medical care⁷, bottle-feeding⁸, passive exposure to smoking⁹, attendance in congested centers such as day-care facilities¹⁰, and a family history of otitis media^{11,12}. The predisposition of certain races, such as the South-western American Indians¹³, Australian Aborigines¹⁴, Greenlanders, and Alaskan Eskimos¹⁵, to CSOM is also well documented. These risk factors probably favor the development of CSOM by weakening the immunological defenses, increasing the inoculum, and encouraging early infection¹⁶.

Poor housing, hygiene and nutrition are associated with higher prevalence rates, and improvement in these aspects was found to halve the prevalence of CSOM in Maori children between 1978 and 1987¹⁷. Proximity to a health care facility significantly reduced the otitis media attack rate among Arizona Indian children living in reservations¹⁸.

In CSOM the bacteria may be aerobic (e.g. *Pseudomonas aeruginosa*, *Escherichia coli*, *S. aureus*, *Streptococcus pyogenes*, *Proteus mirabilis*, *Klebsiella* species) or anaerobic (e.g. *Bacteroides*, *Peptostreptococcus*, *Propionibacterium*)^{19,20}. The bacteria are infrequently found in the skin of the external canal, but may proliferate in the presence of trauma, inflammation, lacerations or high humidity²¹. These bacteria may then gain entry to the middle ear through a chronic perforation²². The most common organisms are *Pseudomonas* spp. which rapidly

develop resistance to antibiotics²³ among these bacteria, *P. aeruginosa* has been particularly blamed for the deep-seated and progressive destruction of middle ear and mastoid structures through its toxins and enzymes²⁴.

Otitis media presents an early acute phase, with essentially reversible mucosal and bony pathological changes, which continues to a late chronic phase with well established, intractable mucoperiosteal disease. The recurrent episodes of otorrhea and mucosal changes are characterized by osteoneogenesis, bony erosions, and osteitis that include the temporal bone and ossicles²⁵. The mucous membrane may be thickened by edema and submucous fibrosis and infiltration with chronic inflammatory cells. Mucosal edema may proceed to the formation of polyps. Persistent suppuration may precede formation of granulation tissue and bone resorption. In more advanced cases, osteitis of ossicles, mastoid bone and labyrinth²⁶.

Extracranial complications occur most commonly, and include mastoiditis, cholesteatoma, permanent hearing loss, paralysis of facial nerve. Intracranial complications are less common, and include meningitis, brain abscess, and hydrocephalus and lateral sinus thrombosis²⁷. In Australia, approximately 60% of extracranial and intracranial complications of otitis media occur in children²⁸.

Methods. A cross sectional study was done which included 405 patients of CSOM patients (patients with aural discharge for 2 weeks or more). The patients came to the ENT consultant clinic in Al-Khadimiya Teaching Hospital in the period 2008-2011. Swabs for aural discharge were taken from those patients from which a smear is stained with gram stain and examined by light microscope. Also the discharge is cultured by inoculating it into blood, MacConkey and chocolate agars then were incubated for 24 hr to show the responsible micro-organisms. Another inoculation into Sabouraud agar (for fungi) and incubated for 48 hr. If the growth shows a pseudomonal growth this is verified using Gram stain and colonial morphology, motility and oxidase test.

Colonies which displayed a positive oxidase reaction were subcultured, on Muller Hinton Agar for the purpose of assessing the antibiotic susceptibility and resistance using the Disk Diffusion Susceptibility Testing (Kirby-Bauer Method). After incubation at 35°C for 16-18 hrs, zone size was measured²⁹ and interpreted according to the clinical and laboratory standards institute (CLSI).

The antibiotic susceptibility and resistance is assessed by (Kirby-Bauer Method) by using commercially obtained disks for the following antibiotics: The following antibiotic disks were produced by BIOANALYSE company: imipenem (IM 10µg/disk), piperacillin (PIP 100µg/disk), cefipime (CP 30µg/disk), cefotaxime (CE 30µg/disk), ceftriaxone (CTX 30µg/disk), carbinicillin (CAB 100µg/disk), ticarcillin (TIC 75µg). The following antibiotic disks were produced by Al-Raze Center for Research and Medical Therapeutic Production: tobramycin (TB 10µg), ciprofloxacin (CIP 5µg), amikacin (AK 30µg), garamycin (GR 10µg). The following antibiotic disks were produced by BD Company: aztreonam (ATM 30µg), ceftazidime (CZ 30µg), cefoperazone (CEP 75µg) containing disks were prepared in the

laboratory. Appropriate concentration of cefoperazone (1 gm Cefobid [trade name for cefoperazone] vial source manufactured by Pfizer) was diluted in appropriate volume of sterile distilled water and incubated with disks which were made of filter paper. The disks were allowed to dry for 2 hr at room temperature and were stored under desiccation at -40°C.

Demographic data were demonstrated using percentages for male to female ratio. Prevalence of the pathogenic micro-organisms which were discovered and sensitivities of the tested antibiotic disks were shown by percentages.

Results. Over a period of 3 years (between March 2008 till March 2011), a total of 405 cases of chronic otitis media were collected in the years 2008-2011 (Figure 1). 196 (48%) cases were males. 209 (52%) cases were females with a male to female ratio 1:1.1.

Regarding the pathogenic micro-organisms as found by the culture method (Figure 2): 150 (37%) cases were infected with *Pseudomonas* species (PS), 58 (14.3%) cases were infected with *Staphylococcus aureus* (SA), 34 (8.3%) cases were infected with *Proteus* species (PR), 27 (6.6%) cases were infected with *Staphylococcus epidermidis* (SE), 15 (3.7%) cases were infected with *Escherichia coli* (EC), 14 (3.4%) cases were infected by *Enterobacter* (E), 4 (0.9%) cases were infected by *Klebsiella* (K), 3 (0.7%) cases were infected by *Streptococcus pneumoniae* (SP), 4 (0.9%) cases were infected by fungi (F), 40 (9.8%) cases there was mixed infection (M), 53 (13%) cases there was no growth (NG).

Regarding the sensitivity of *Pseudomonas* species isolates to the following antibiotics it is shown below (Figure 3): Amikacin (AK) 91.7%, Imipenem (IM) 89.7%, Ceftazidime (CZ) 81.8%, Ciprofloxacin (CIP) 73.7%, Garamycin (GR) 72.9%, Tobramycin (TB) 67.7%, Ticarcillin (TIC) 66.7%, Cefoperazone (CEP) 42.9%, Piperacillin (PIP) 20.7%, Ceftriaxone (CTX) 3.4%, Carbinicillin (CAB) 0.0%, Cefotaxime (CE) 0.0%, Aztreonam (ATM) 0.0%, Cefipime (CP) 0.0%

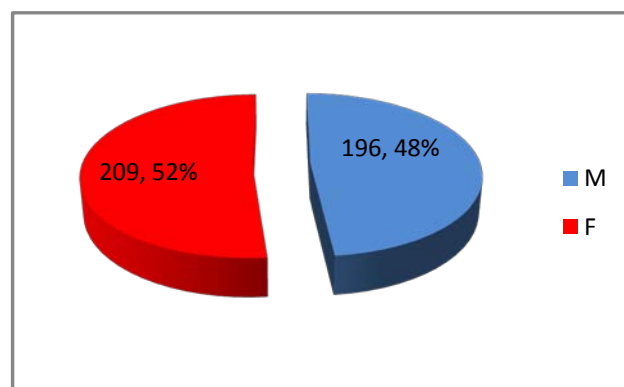


Figure 1: Male to female ratio of CSOM case.

Discussion. The male to female ratio in this study is 1:1.1. Compared to another study which has showed that the ratio is 1:1.7³⁰. Generally no gender bias is obvious in previous studies and it can occur in any age group³¹. The results show clearly that *Pseudomonas* species infections are the

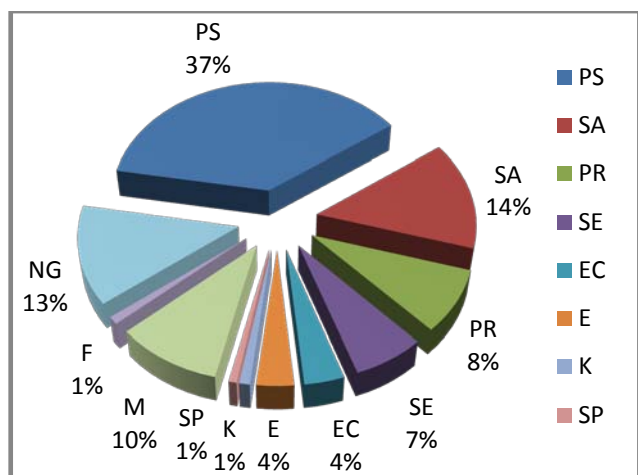


Figure 2: percentage of pathogenic microorganisms.

commonest constituting 37% of all cases, In addition to that *Pseudomonas* species infections are the most virulent regarding the rapidity of progress and the severe complication that may happen due to the deteriorating global problem of multi drug resistance . Todar described *Pseudomonas* as being notorious for its resistance to antibiotics and for this, it is dangerous and dreaded pathogen.³² The species *Pseudomonas* comprises of more than 140 species, only a few of these are pathogenic to men like *P. aeruginosa*, *P. oryzihabitans*, and *P. plecoglossicida*.³³ but *Pseudomonas aeruginosa* is by far the most frequent cause and the most important pathogen in the species³⁴. The others are essentially saprophytic and occur widely in nature³⁵.

Other bacteria found by culture are: (14.3%) 58 cases *Staph. aureus*, 34 (8.3%) cases *Proteus* species, 27 (6.6%) cases *Staph. Epidermidis*, 15 (3.7%) cases. Although *Staph. Epidermidis* is well known as normal flora of the external ear ,it can sometimes become pathogenic causing otitis media especially when the defense mechanisms are weak³⁶. *E. coli* ,14 (3.4%) cases *Enterobacter*,4 (0.9%) cases *Klebsiella*,3 (0.7%) cases *Strep. pneumoniae* ,4 (0.9%) cases fungi ,40 (9.8%) case mixed infection ,53(13%) case no growth, While in a study done in Basrah 2005, results were as follows: *Staphylococcus aureus* 25%, *Pseudomonas*18.8% *Streptococcus pneumoniae* 18.8%,*Proteus* sp. 8.3%,*Klebsiella* sp. 6.3%, *E. coli* 4.2%, No growth 18.8%³⁷.

In Nigeria a study showed that *Pseudomonas*30 (44%), *Staphylococcus* 18 (27%), *Proteus* 12 (18%), *Klebsiella* species 8 (12%), and (0.02%) 2 were incidental fungal isolates (*Candida* species). 8 (12%) were contaminants while 10(15%) did not have any growth at all³⁸.

Amikacin in this study is the most effective antibiotic in terms of sensitivity 91.7% .this finding coincides with that of a study in singapore³⁹90.4%, and Spain 91%⁴⁰. Cefoperazone a third generation cephalosporin has been introduced in Iraq relatively recently (in the last few years) to combat the problem of emerging drug resistance.

Antibiotic sensitivity regarding cefoperazone was 42.9%. In a study done in India, the sensitivity was

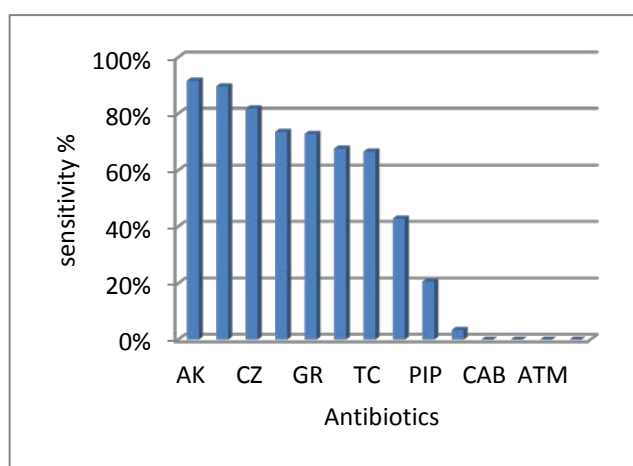


Figure 2: Pseudomonas isolates sensitivity to antibiotics.

55.87%⁴¹. In another study done in Lithuania the sensitivity was 31.7%²⁴. In a study done in Bulgaria, the sensitivity for cefoperazone was 15 %³⁴.

In conclusion, *Pseudomonas* infection in chronic otitis media is a major health problem due to its high prevalence and resistance to many drugs. Even some relatively newly developed and used drugs like cefoperazone are not very effective in combating the rapidly emerging problem of multidrug resistance. New researches should be done to explore in depth the mechanisms of drug resistance leading to concerted efforts on the way of developing new antibiotic drug therapies.

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