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Original Research Paper

Bacteriological Profile and Antibiotic Susceptibility Pattern in Surgically Treated Complicated Cases of Mastoiditis: A Retrospective Cohort

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ABSTRACT

Background: Mastoiditis is a serious complication of the AOM. The treatment of mastoiditis is mainly conservative and the surgical interventions are reserved only for the life-threatening complications. However, the empirical treatment regimen is failing to treat mastoiditis in recent times and a rise in recurrent and resistant cases has been observed. Antibiotic resistance against the causative bacterial strains is the suspected cause of ineffective medical treatment. **Objective:** The purpose of this study is to improve the medical treatment of mastoiditis by identifying the causative organisms and their antibiotic susceptibility pattern in children with acute/chronic mastoiditis and associated complications who had a history of failed conservative treatment and underwent inevitable surgical procedures. **Study Design:** A Retrospective Cohort Study of the preoperatively collected samples of pus culture and sensitivity reports of 56 children with complicated mastoiditis, surgically treated at Children Hospital and Institute of Child Health, Lahore, from May 2021 – June 2022. **Results:** The most frequent pathogens were *Proteus spp. (Mirabilis)* (n=16, 29%), *Pseudomonas Aeruginosa* (n=12, 21%), and Staphylococcus Aureus (n=11, 19.6%). The intravenous antibiotics found to be the most sensitive against mastoiditis bacteria (in descending order) were Tanzobactam-Piperacillin (n=49, 88%), Sulbactam-Cefoperazone (n=48, 86%), Vancomycin (n=45, 80%), and Clarithromycin (n=43, 77%). Whereas the empirical oral antibiotic treatment were ineffective for more than 50% of the cases, based on the drug susceptibility results. **Conclusion:** The emergence of resistance in bacterial strains responsible for mastoiditis was found to be the main cause of failed conservative treatment and development of recurrent, persistent, and/or complicated mastoiditis.

Keywords: acute mastoiditis, culture and sensitivity, pathogens, antibiotics, complications

INTRODUCTION

Acute Otitis Media (AOM) is the most common localized infection in pediatric age group and mastoiditis is its most common complication [1]. Mastoiditis is defined as an inflammation of the mastoid cells of the temporal bone. According to the experts, it usually presents as an infection secondary to the middle ear infection [2]. The early management of middle ear infections greatly reduces the chances of mastoiditis. Although ear infections and mastoiditis can occur at any age; however, it is more common in pediatric age group with the mean age of 2 years [3]. There are multiple

factors in early years of life which can contribute to the recurrent upper respiratory tract infections, otitis media, adenoiditis, and mastoiditis, such as shorter and relatively horizontal Eustachian tube, malnutrition, poor hygiene, trauma to the ear, etc. [4] As the epithelium lined septations or the mastoid air cells are continuous along the middle ear cavity, there is a free communication between these two spaces, aditus and antrum, therefore the infection can easily pre-exist at both sites [5]. The radiological findings can show the presence of fluid in the mastoid due to ipsilateral AOM, but clinicians do not label it as mastoiditis. The correct term for all the otitis media infections is 'otomastoiditis' [6]. Mastoiditis is mainly a clinical diagnosis and is a very serious medical condition. Its diagnosis depends on certain signs and symptoms which indicate pus in the mastoid cavity, such as periauricular swelling, high grade fever, hearing loss, severe headache, etc., mostly in the background of AOM [7]. On hematological investigations the inflammatory markers are raised (C-Reactive Proteins, Erythrocyte Sedimentation Rate ESR) along with high WBC count, and high absolute neutrophil count. Multiple reports suggest that with appropriate intravenous antibiotics in adequate amount and myringotomy, acute mastoiditis can be successfully treated and mastoidectomy is rarely indicated. However, with the failure of medical treatment, surgery is inevitable [8,9].

Prior to the era of antibiotics, almost 50% of the cases of Acute Otitis Media (AOM) tended to rapidly progress into Acute Mastoiditis with its severe intracranial and extracranial complications, which were mainly treated via surgery i.e., Cortical Mastoidectomy [10]. With the advent of antibiotics, the rate of progression in the severity of the disease has declined considerably. Globally, the incidence of progression of AOM to mastoiditis is less than 1% and surgical interventions are reserved for the treatment of complicated cases of mastoiditis only [11]. Over the time, the treatment strategy of mastoiditis has been revised multiple times in the developed countries, adhering to the conservative treatment, close follow-up, and supportive treatment [12]. The early use of antibiotics is controversial due to accelerating antibiotic resistance because of their misuse and overuse. The results of these regimens are documented as controversial in many reports and reviews [13-15].

The most common otopathogen responsible for mastoiditis in young children is *Streptococcus Pneumoniae.* The accelerating burden of recurrent ear infections, associated hearing loss, and mastoiditis along with its serious consequences compelled the pharmaceuticals to formulate an infection control vaccine [16]. In 2008, Pneumococcal Conjugate Vaccines 7-Valent (PCV-7) was intially introduced in an attempt to control the infections caused by *Strep. Pneumoniae*. Later, a new variant PCV-13 was also introduced. The vaccine was gradually implemented into the vaccination regimen of many countries during the past years. The pneumococcal vaccine is given in three doses from birth to infancy at the age of 2, 4 and 12 months. A tremendous decline in the cases of AOM and acute mastoiditis is witnessed while comparing pre and post PCV era [17, 18]. In recent years, a surge in the cases of mastoiditis is observed. The empirical treatment against the mastoid air cells infection has failed to completely cure the disease. Moreover, the antibiotics are observed only to halt the disease for a certain period of time but fail to completely eradicate the disease, resulting in its recurrence [19]. According to the literature, the main pathological organisms responsible for mastoiditis are *Strep. Pneumoniae, Staphylococcus Aureus,* and *Hemophilus Influenzae*. *Pseudomonas Aueroginosa* is usually common either in the cases of sample contamination, or in mastoiditis with intracranial and extracranial complications [20].

MATERIALS AND METHODS

This study is based on the retrospective review of 56 pediatric cases of complicated mastoiditis with the history of failed conservative treatment. These 56 children developed intracranial and extracranial complications over the time and were admitted in Pediatric ENT (Ear, Nose, and Throat) Department with a number of serious complications which needed immediate surgical treatment. By using aseptic measures, samples of pus from the mastoid cavity were collected and were sent for culture and sensitivity examination. Those reports revealed the bacteriological strain that was causing the infection as well as its antibiotic susceptibility profile. The results were then compared with the treatment history of that specific patient in order to establish a relationship between the antibiotics that the causative bacteria the patient was resistant to, and the antibiotics taken by the patient prior

to the surgery. The purpose was to understand why the medical treatment failed in those children and if the bacterial resistance was the cause of it. Culture and sensitivity evaluation of all the pus samples was done by expert pathologists. The identity and the personal information of all the patients is kept confidential. The main strength of this study is that we are reporting the culture and sensitivity samples taken directly from the mastoid cavity, not from the external auditory canal or nasopharynx. This per-operative sample collection with aseptic technique excludes the chances of sample contaminations and false results.

INCLUSION CRITERIA

- Parents who gave written and verbal consent for the complete medical as well as surgical treatment during the hospital stay.
- Patients who were given oral as well as intravenous antibiotics before but failed to respond.
- Patients who were not immunocompromised or had no co-morbidities that could cause failure of the conservative treatment or the progression of the disease in any possible way.
- Patients who were always compliant to the medical treatment and avoided self-medication throughout the course of the disease.
- Patients who had complete medical record of different antibiotics which they took before developing the serious complications.
- Patients who were fully vaccinated according to the EPI (Extanded Programme on Immunization).

EXCLUSION CRITERIA

- Patients with unclear medical history, incomplete medical record, and non-cooperative attendants.
- Parents who refused surgical treatment and specific investigations, including culture and sensitivity analysis of pus samples.
- Patients with co-morbidities, such as Leukemia, Immunodeficiency syndromes, Tuberculosis, Tumors, etc.
- Parents who could not maintain the proper follow-ups.
- Patients with the mastoid pus cultures showing no growth were not included in this study.
- Partially vaccinated or unvaccinated children were excluded from this study.

RESULTS

Considering the aforementioned inclusion and exclusion criteria, 56 patients were included in this retrospective cohort study. The past medical and surgical records of the patients were reviewed. Out of these 56 patients, 37 were male and 19 were females accounting for male to female ratio of 1.9:1. Most of the patients were admitted through OPD (n=48). No specific pattern between the disease and the increase/decrease in the age was observed; however, the incidence peaked around 2-5 years of the age (n= 23, mean= 2.5 years, SD= 1.4). On history, 32 patients were having mastoiditis of acute onset while 24 patients were having chronic mastoiditis which either did not resolve over the time or developed recurrence due to partial or incomplete medical treatment. All the patients included in the study had complete medical record of the antibiotics they took during the course of the disease.

Mode of Admission	**Frequency (n)**	**Percentage (%)**
OPD	48	86%
Emergency	8	14%
Gender	**Frequency (n)**	**Percentage (%)**
Male	37	66%
Female	19	34%
Age Group	**Frequency (n)**	**Percentage (%)**
1 month- 2 years	11	20%
2-5 years	23	41%
5-10 years	4	7%
10-14 years	18	32%
Pathology	**Frequency (n)**	**Percentage (%)**
Acute Mastoiditis	32	57%

Chronic Mastoiditis	24	43%
Site of Infection	**Frequency (n)**	**Percentage (%)**
Left	26	46%
Right	21	38%
Bilateral	9	16%

Table 1: Demographic and Clinical information of selected patients at the time of presentation (n= 56)

On the basis of culture and sensitivity reports of the per-operative mastoid pus samples, 9 different types of pathogens were isolated. For the ease of analysis, the pathogens were categorized into Gram Positive and Gram Negative Bacteria. The most common pathological organisms for mastoiditis (in descending order) were *Proteus spp*. (*Proteus Mirabilis*), *Pseudomonas spp*. (*Pseudomonas Aeruginosa*), and *Staph. Aureus*.

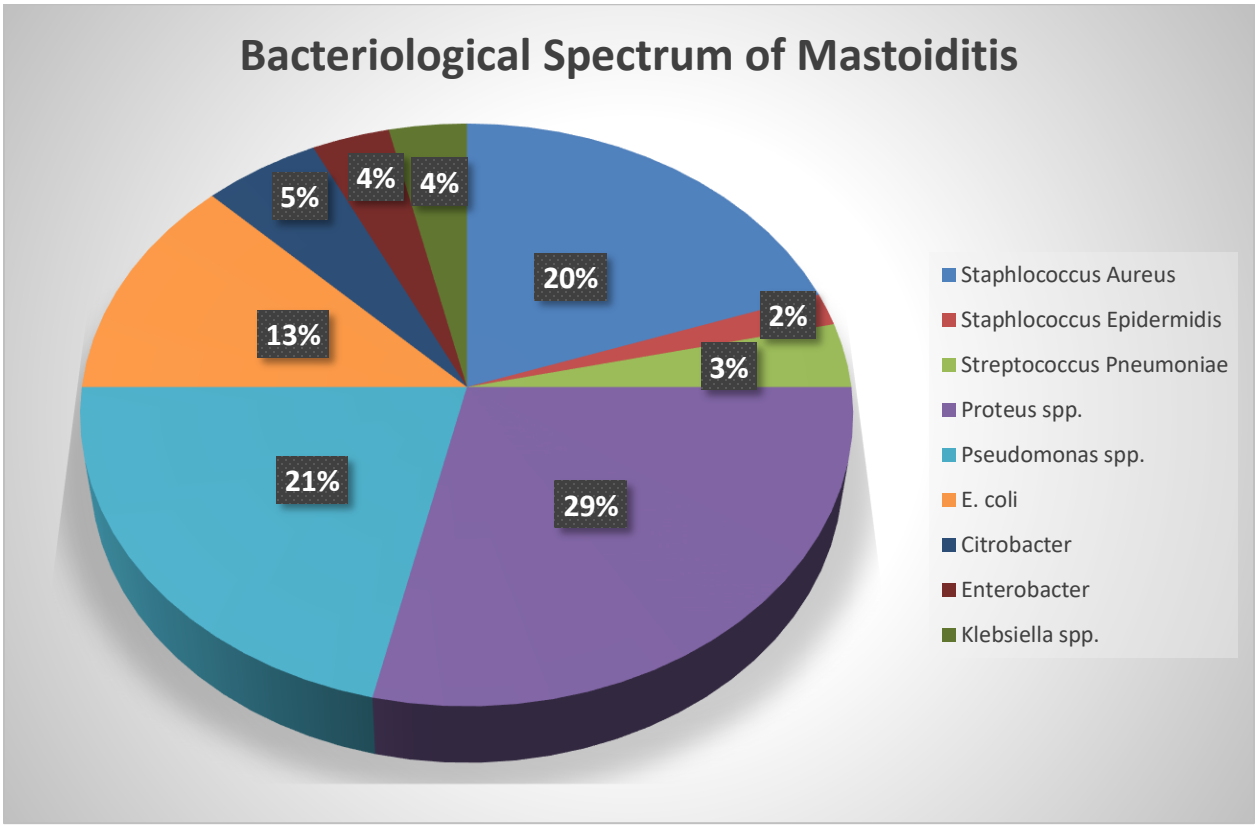

Figure 1. Pie chart showing the bacteriological spectrum of mastoiditis in 56 selected children

The antibiotic susceptibility test revealed that in more than 50 percent of the cases, pathogens were resistant to the routinely prescribed oral antibiotics; therefore, administration of second- or third-line intravenous antibiotics was indicated. The antibiotics which were found to be the most sensitive against mastoiditis bacteria (in descending order) were Tanzobactam-Piperacillin (n=49, 88%), Sulbactam-Cefoperazone (n=48, 86%), Vancomycin (n=45, 80%), and Clarithromycin (n=43, 77%).

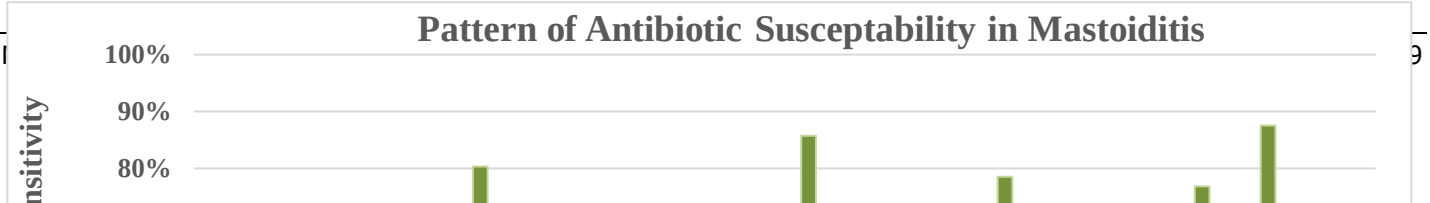

Figure2: Summary of Antibiotic susceptibility pattern observed in Culture reports of mastoid pus samples of 56 patients

Gram Positive bacteria included, *Stap. Aureus* (n=11, 19.6%), *Staph. Epidermidis* (n=1, 1.78%), and *Strep. Pneumoniae* (n=2, 3.57%).

Antibiotics	Gram Positive Bacterial Isolates					
	S. Aureus (n=11)		S. Epidermidis (n=1)		S. Pneumoniae (n= 2)	
	Frq.	%Age	Frq.	%Age	Frq.	%Age
Amoxicillin	5	9%	0	0%	1	2%
Ampicillin	6	11%	0	0%	1	2%
Co-amoxiclave	5	9%	1	2%	0	0%
Teicoplanin	4	7%	0	0%	0	0%
Vancomycin	9	16%	1	2%	2	4%
Cefixime	7	13%	1	2%	1	2%
Cefotaxime	8	14%	1	2%	1	2%

Ceftazidime	7	13%	1	2%	1	2%
Ceftriaxone	7	13%	1	2%	1	2%
Sulbactam-Cefoperazone	11	20%	1	2%	2	4%
Ciprofloxacin	9	16%	1	2%	1	2%
Nitrofurantoin	4	7%	0	0%	0	0%
Meropenam	8	14%	1	2%	2	4%
Amikacin	6	11%	0	0%	0	0%
Gentamycin	6	11%	0	0%	1	2%
Clarithromycin	7	13%	0	0%	1	2%
Tazobactam-Piperacillin	10	18%	1	2%	2	4%
Linezolid	8	14%	0	0%	1	2%

Table 2. Antibiotics susceptibility of Gram Positive causative agents of mastoiditis

Gram Negative Bacteria included *Proteus spp.* (n=16, 29%), *Pseudomonas spp.* (n=12, 21%), *E. coli* (n=7, 13%), *Citrobacter* (n=3, 5%), *Enterobacter* (n=2, 4%), and *Klebsiella* spp. (n=2, 4%).

Antibiotics	**Gram Negative Bacterial Isolates**											
	Proteus spp. (n=16)		**Klebsiella spp. (n=2)**		**Pseudomonas spp. (n=12)**		**Enterobacter (n=2)**		**Citrobacter (n=3)**		**E. Coli (n=7)**	
	Frq.	**%Age**	**Frq.**	**%Age**	**Frq.**	**%Age**	**Frq.**	**%Age**	**Frq.**	**%Age**	**Frq.**	**%Age**
Amoxicillin	9	16%	1	2%	8	14%	1	2%	1	2%	3	5%
Ampicillin	8	14%	1	2%	7	13%	2	4%	1	2%	4	7%
Co-amoxiclave	9	16%	1	2%	9	16%	1	2%	1	2%	4	7%
Teicoplanin	4	7%	0	0%	5	9%	1	2%	0	0%	5	9%
Vancomycin	15	27%	2	4%	11	20%	2	4%	2	4%	7	13%
Cefixime	12	21%	1	2%	8	14%	1	2%	2	4%	5	9%
Cefotaxime	11	20%	2	4%	9	16%	1	2%	1	2%	5	9%
Ceftazidime	12	21%	1	2%	9	16%	1	2%	1	2%	5	9%
Ceftriaxone	12	21%	1	2%	9	16%	1	2%	1	2%	4	7%
Sulbactam-Cefoperazone	16	29%	2	4%	12	21%	2	4%	2	4%	7	13%
Ciprofloxacin	13	23%	2	4%	9	16%	1	2%	1	2%	4	7%

Nitrofurantoin	6	11%	1	2%	5	9%	0	0%	1	2%	3	5%
Meropenam	12	21%	2	4%	10	18%	2	4%	2	4%	6	11%
Amikacin	8	14%	1	2%	7	13%	1	2%	1	2%	4	7%
Gentamycin	7	13%	1	2%	6	11%	1	2%	1	2%	4	7%
Clarithromycin	9	16%	1	2%	9	16%	1	2%	1	2%	5	9%
Tazobactam-Piperacillin	15	27%	2	4%	12	21%	2	4%	2	4%	7	13%
Linezolid	11	20%	0	0%	6	11%	1	2%	1	2%	3	5%

Table 3. Association of antibiotic sensitivity with the pathological Gram Negative Bacteria in case of mastoiditis

DISCUSSION

In this study, we have assessed the complicated cases of mastoiditis who were given antibiotics before surgery but somehow, those antibiotics were proved ineffective as conservative treatment for mastoiditis. Later, the mastoiditis and its complications were treated via surgery and per-operatively the pus samples were collected from the mastoid abscess to investigate the culture and sensitivity of the pathological organisms. Our aim was to compare the bacteriological profile of mastoiditis and its antibiotic susceptibility with the antibiotics that were given to the patients as medical treatment for complicated cases of mastoiditis. And the results collected in this study were astonishing. According to the past medical record, most of the subjects were given the antibiotics which were later found to be highly ineffective against the resistant pathological strains of pus cultures. In the early course of mastoiditis and AOM, the disease is easily manageable and requires little to no treatment. In most of the cases, the disease resolves spontaneously[1, 2]. For a spontaneously resolving disease, it is difficult to suggest the appropriate antibiotic by determining its efficacy. Furthermore, it requires a large sample size to assess the efficacy of new drug regimen versus conventional drug therapy. There are multiple studies with controversial results on this topic [4, 5]. However, our present study does not discuss the generic treatment plan for mastoiditis and AOM. It only discusses the pathological profile of the rare and severe cases of mastoiditis who presented with intracranial and/or extracranial spread. Majority of the studies suggest that once the involvement of mastoiditis is confirmed on clinical examination, intravenous medication should be started in adequate and appropriate doses to avoid the possible complications [6-8]. This strategy is followed globally, especially in the developing countries because of high prevalence, morbidity, and mortality rate of mastoiditis. Others suggest watchful waiting for 48-72 hours before starting the antibiotic therapy to see if the antibiotics are truly required or not. But it should be done with regular monitoring by hospitalizing the patient for 3 days, if feasible. So, the final decision of starting an antibiotic regimen mainly depends on the clinician's assessment, availability of resources, patient's feasibility, and severity of the disease [8]. Although in most of the cases, mastoiditis is an extended infection of middle ear, but the bacteriological spectrum of both these infections differ greatly from each other. The most frequent etiological agents for mastoiditis found in our research were Proteus Mirabilis, Pseudomonas Aueroginosa and Staphylococcus Auerus. Viral and fungal infections of mastoiditis were not included in this study. Viral etiology was only present in fraction of the cases and antibiotics are not quite effective against viral and fungal etiology so these cases were omitted while selecting the affected patients [9]. Because of the exponentially increasing antibiotic resistance, selection of appropriate antibiotic has become very difficult. Extended Spectrum Beta Lactamases (ESBL) producing strains of Klebsiella, E.coli, Staph. Aureus, Pseudomonas, and Proteus spp. were isolated in the culture and sensitivity tests, resulting in the persistent, recurrent mastoiditis eventually needing surgical mastoidectomy for the complete eradication of the infection [9, 10]. Cephalosporin and Penicillin are

usually the most commonly prescribed antibiotics to treat AOM and mastoiditis in out-door as well as admitted patients. The analysis of the past medical record of patients showed that most of the patients were given Amoxicillin, Ampicillin, Cefixim, and Ceftraixone via oral or intravenous route before they got hospitalized. Amoxicillin might not be the most effective medication against ESBL producing strains or other penicillin resistant strains, but it remains the drug of choice for the uncomplicated cases of AOM and Mastoiditis due to its low cost, higher safety and acceptability by the patient, lesser side effects, and excellent track record. Likewise, Cephalosporin (e.g., Ceftriaxone) is still preferred by many physicians because of its longer half-life, needing single dose per day, and hence ensuring better compliance from the patient [14, 15]. The high potency antibiotics or the combinations of different newer antibiotics should be reserved only for the complicated mastoiditis and its associated, serious complications. Despite the proven advent and efficacy of conventional antibiotic regimen, mastoiditis fails to resolve at times. Failure of symptomatic resolve within the initial 72 hours of appropriate medication calls for surgery and is labeled as failure of conservative management [20]. Switching from single to multidrug regimen is suggested by many, but the most appreciated treatment option is early tympanocentesis along with ear swab sample collection for culture and sensitivity and initiating the appropriate antibiotics by following the results of culture and sensitivity report. Antibiotics in combination are only reserved to very serious conditions where the mastoiditis is associated with the extended infections to the brain. Rarely, multidrug therapy is given along with the neurosurgical interventions i.e., mastoidectomy to avoid serious complications. In such scenarios, Corticosteroids and Anticoagulants are also indicated [21]. *Proteus* species including *Proteus Vulgaris*, *Proteus Mirabilis*, and *Bacillus Proteus*, related incidences of mastoiditis are gradually and continuously increasing in number. It is one of the most infectious etiologies of the ear and often related to the failed medical treatment. Despite the antibiotic compliance, the infection usually continues to flourish and frequently results in intracranial complications. The antibiotic treatment suggested for the effective control of *Proteus* mastoid infection is single drug regimen, a 7-14 days course of Ceftriaxone, Gentamycin, or oral fluoroquinolone, etc. In our study, Proteus was the most frequent pathological agent of mastoiditis among all. And hence all the cases included in the study were of complicated mastoiditis, the association of Proteus with the severe disease is justified [21, 22]. The second most prevalent strain causing mastoiditis was *Pseudomonas spp*. The Pseudomonas mastoiditis is known for its resistance against antibiotics and recurrence. It is usually an opportunistic infection of mastoid but once it gets access to the mastoid air cavity, the eradication becomes almost impossible. Therefore, it is associated with high mortality rate. Once the intracranial extensions occur, the mortality rate increases to 72 percent. The recommended treatment is combination drug therapy, along with topical antibiotics, and planned surgical intervention such as mastoidectomy, depending upon the clinical assessment [22]. *Staphylococcus Aureus* is the third most common etiological agent of mastoiditis in our study. It is usually associated with the acute mastoiditis. The acute infection of mastoid bone is often aggressive, and its intracranial complications are common. If the patient of acute mastoiditis is to be given antibiotic prior the culture and sensitivity report, then the anti-staphylococcal drug must be added to the regimen [23]. Pneumococcal vaccination is a part of EPI program and is given to the infant at the age of 2, 4 and 12 months of age. The documented status of PCV Vaccination of all the children was retrieved proving that all of them were vaccinated against *Strep. Pneumoniae*. For *Streptococcus Pneumoniae*, the drug of choice is cephalosporin, and the ideal route of administration is intravenous within hospital settings to ensure proper dosage for appropriate duration. In our study, only 2 cases were positive for *Streptococcus Pneumoniae* infection of mastoid part of temporal bone, despite of being vaccinated with PCV as per regular schedule [24-25].

CONCLUSION

Like any other infection, the etiological agents of mastoiditis are continuously evolving in terms of their drug susceptibility. For the attending physicians, it is important to be aware of the bacteriological profile, drug sensitivity and resistance pattern for the effective and early management of mastoidtis. Due to limited resources, it is difficult to perform culture and sensitivity

of ear swab of every patient suspected with mastoiditis. But once the patient fails to respond to the antibiotic regimen, culture and sensitivity test is a must in order to accurately identify the causative organism and the best suited antibiotic.

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