International Archives of Medical and Health Research

Original Article

Print ISSN: 2705-1420; Online ISSN: 2705-1439
DOI: https://doi.org/10.33515/iamhr/2021.010/02

Microbial studies in acute suppurative otitis media in children attending a tertiary health facility in North-western Nigeria

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ABSTRACT

Background: Acute suppurative otitis media (ASOM) is one of the most common otorhinolaryngological childhood infections globally, associated with prescription of antimicrobial agents even against a background of increasing bacterial resistance to antibiotics. **Aim**: This study is aimed at evaluating the microbial isolates of ASOM in children, attending Usmanu Danfodiyo University Teaching Hospital, Sokoto, North-western Nigeria. **Materials and Methods:** A cross-sectional study design was used to investigate 58 patients who met the inclusion criteria. Methods of data collection were interviewer administered questionnaire, clinical examination, and laboratory investigation. Quantitative variables were summarized using mean and standard deviations, while qualitative variables were summarized using frequencies and percentages. **Results**: The proportion of sterile cultures was 3.3%, while the remaining showed different species of aerobes (96.7%), anaerobes (1.6%) and fungi (4.9%). Ratio of gram-positive to gram-negative aerobic bacteria was 3.5: 1.The gram-positive aerobes isolated were Streptococcus pneumonia (37.7%), Streptococcus pyogenes (14.8%) and Staphylococcus aureus (23.0%); while Moraxella catarrhalis (11.5%) was the main gram-negative aerobe. Bacteroides fragilis (1.6%) was the only anaerobe, while Aspergillus niger (3.3%) was among the fungi isolated. Amoxicillin/clavulanic acid showed 100.0% sensitivity; followed directly by erythromycin (91.5%). **Conclusion**: This study showed that ASOM is more likely a mono-aerobic infection than polymicrobial, with high sensitivity to amoxicillin/clavulanic acid. Its treatment should include among others, early commencement of antibiotics with good gram-positive and gram-negative aerobic coverage.

Keywords: Acute suppurative otitis media, microbes, antimicrobials, sensitivity

INTRODUCTION

Acute suppurative otitis media (ASOM) is one of the most common otorhinolaryngological childhood infections throughout the world, and is associated with incessant prescription of antimicrobial agents even against a background of increasing bacterial resistance to antibiotics.[1-5] A recent worldwide systematic review estimated that there are 709 million new cases of acute otitis media annually, with greater than half in children under 5 years of age.[6] The incidence rates range from about 3.64 for Central Europe to as high as 43.36 for Sub-Saharan Africa.[6] Many local studies have also highlighted its high prevalence when compared to other otorhinolaryngological diseases like labyrinthitis, allergic rhinitis, epiglottitis, laryngitis, or even pharyngotonsillitis.[3,7,8]

This high prevalence of ASOM in developing countries of the world is probably because of poverty, ignorance, dearth of specialists and limited access to medical care.[9,10] Thus, when poorly managed and allowed to complicate, the disease can pose serious health-economic burden on the patient. ASOM is defined clinicopathologically as inflammation of the middle ear cleft of rapid onset and infective origin, associated with suppuration from the middle ear through a transient perforated tympanic membrane.[5] The condition usually starts as an acute otitis media with signs of inflammation, fullness and erythema, as well as symptoms associated with inflammation such as otalgia, irritability and fever. But this diagnosis is often missed in children especially in malaria endemic regions because

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Received: 21-05-2021 Revised: 08-07-2021 Accepted: 12-07-2021 Published: 26-07-2021

the initial onset of fever is treated as plasmodiasis, and only recognized when the ear begins to suppurate.[11]

Pathophysiologically, the initial acute otitis media without suppuration can be referred to as either stage I (tubal occlusion) or stage II (pre-suppuration) of the disease, while ASOM proper is stage III (suppuration). After suppurating, the disease may either abate (stage IV) or progress into complications (stage V). Interestingly, early diagnosis of acute otitis media, including the quality, adequacy and timely institution of treatment in terms of proper antimicrobials is key to preventing progression through these stages. A combination of microbiological, environmental, and early childhood anatomical variations like the uniqueness of their Eustachian tube, well-endowed lymphoid follicles (adenoids) in their nasopharynx, and immaturity of their immune system, predispose children to developing the infection.[12]

Since the most common cause of ASOM is bacterial infection of the middle ear, emphasis has been on culture of middle ear effusion and not necessarily ear swabs from the external auditory canal (EAC) as they do not represent the actual aetiologic microbes in suppurative otitis media.[13,14] Majority of studies are biased towards identifying causative organisms in chronic suppurative otitis media(CSOM) than ASOM, probably because of the lack of consensus regarding the transition time from acute to chronic form of suppurative otitis media. However, the leading causes of bacterial ASOM in the order of prevalence are Streptococcus pneumoniae, non-typeable Haemophilus influenzae, Moraxella catarrhalis, and group A Streptococcus.[4,5,15] Less frequently reported are Streptococcus pyogenes and Staphylococcus aureus.[5,16] A study conducted on ASOM in Sokoto state, Nigeria isolated Staphylococcus aureus (46.2%), Escherichia coli (23.1%), Proteus and Pseudomonas species (12.8% each) and Klebsiella species (5.1%).[2] While in south-western Nigeria, Streptococcus pneumoniae (38.1%), Moraxella catarrhalis (19.0%) and Staphylococcus aureus (16.7%) were cultured as predominant bacteria in ASOM.[17] Another study on 272 patients with ASOM in Akwa Ibom state, Nigeria isolated Aspergillus niger as the predominant fungus, followed by Candida albicans (24.4%), Cryptococcus neoformans (20.5%), Candida species (13.5%) and Aspergillus flavus (9.0%).[18]

Many antimicrobial agents including penicillins, cephalosporins, vancomycin and azithromycin have been used for the treatment of ASOM. However, bacterial resistance to these antimicrobials has become an increasing source of concern globally, making treatment controversial and continuously changing.[5,19] Amoxicillin has been the first line antibiotic for treating ASOM, even with a high prevalence of drug-resistant Streptococcus pneumoniae, because resistance to beta-lactam antibiotics, such as amoxicillin, develops as a stepwise process.[5] Aminoglycosides especially gentamycin and the quinolones have remained sensitive and cost-effective over the years in the treatment of ASOM especially in poor resource countries.[2,20,21] Demonstrable variable percentages of sensitivities of middle ear fungal isolates from ASOM to fluconazole, voriconazole, ketoconazole and nystatin have been identified.[18]

Despite the global advancements in antimicrobial therapy and the many interesting transformative developments in laboratory and clinical management of infectious diseases, ASOM still suffers a dearth of knowledge in management especially in the suburbs and most primary and secondary level health care institutions. With poor or inadequate management, the disease can become persistent, recurrent, resistant or even progress to become CSOM with all its untoward complications. This study, therefore aimed to determine the microbiological isolates of ASOM in children, with their antimicrobial sensitivity pattern in UDUTH, North-western Nigeria. Findings from this study will direct physicians on the proper management of the condition.

MATERIALS AND METHODS

Study Area, Design, and Population

Sokoto state is located to the extreme Northwestern corner of Nigeria, within the Sudan savanna belt. Usmanu Danfodiyo University Teaching Hospital, the study center is situated in Wamakko LGA, within the Sokoto metropolis. It is a tertiary institution with 850 bed capacity, serving as referral centers to several hospitals within the North-western region. This was a cross-sectional hospital-based study conducted among children aged less than 18 years that attended the Ear, Nose and Throat (ENT), paediatric, and general outpatient clinics of UDUTH between December 2017 and June 2018. The inclusion criteria were new paediatric patients with a clinical diagnosis of ASOM and an active otorrhoea. Diagnosis of ASOM was based on the presence of a tympanic membrane perforation with otorrhoea of < 2 weeks, originating from the middle ear.[13,22] Patients with non-active ASOM, those who had received antimicrobial medication either ototopic or systemic 1 week before presentation, HIV/AIDS, malnourished children and patients whose caregivers declined participating in the study were excluded. A total of 58 patients who met the inclusion criteria between December 2017 and June 2018 were recruited for the study.

Data Collection and Analysis

The methods of data collection employed include questionnaire survey by interview, clinical examination, and laboratory investigation. The procedure for collection of the middle ear discharge was innocuous and carried out by an Otorhinolaryngologist. Conchae were cleaned and sterilized with gauze soaked in 70% alcohol to remove contaminants. The EAC was also cleaned and sterilized using gauze-wig soaked and squeezed in 70% alcohol, and preliminary otoscopy done. Otomicroscopy was carried out to locate perforation on the tympanic membrane, and aid aspiration of the middle ear exudate using sterile disposable plastic Pasteur pipettes. Anaerobic samples were expressed immediately into tubes containing thioglycolate broth (transport medium) under an anaerobic chamber, while samples for aerobic and fungal culture were expressed onto a well labeled sterile swab stick (in Amies transport media) enclosed in airtight plastic tubing. Bilaterally discharging ears had their samples collected separately. All samples were sent within 2 hours to the Microbiology Department of UDUTH, Sokoto for microbiologic culture and sensitivity analysis.

For bacterial isolation, the middle ear discharges were inoculated on well-labeled dried Chocolate, MacConkey and 5% Sheep Blood agar plates at 37^0c for 18-24 hours aerobically and anaerobically, except for Chocolate agar that was incubated in a candle jar. Visual examination was done for bacterial growths after 18-24 hours, and plates with no growth were discarded, and labeled sterile for bacteria. But where there were growths, bacteria was identified by standard techniques based on morphological, cultural, and biochemical characteristics.[23-24] Antimicrobial sensitivities were carried out using the Kirby Bauer disk diffusion method.[25]

For fungal isolation, the swab sticks were streaked directly on the well labeled Sabouraud's Dextrose Agar (SDA) plates and incubated at room temperature aerobically for 3-7 days. The growths were identified based on their morphological and cultural characteristics, and microscopic examination done using lactophenol blue staining technique.[26]Antifungal sensitivities were carried out using standard protocols.[25] The Statistical Package for the Social Sciences (SPSS) version 23 software (IBM Corp, Armonk, NY, USA) was used for the data processing. Quantitative variables were summarized using mean and standard deviations, while qualitative variables were summarized using frequencies and percentages.

Ethical Consideration

Institutional ethical approval was sought and obtained. Assents were gotten from the parents and guardians to enroll their children/wards into the study.

RESULTS

Socio-demographic profile of study subjects

A total of 58 patients were studied, of which 61 middle ear discharges were collected from either the right, left or both ears. Their ages ranged from 5 months to 15 years, with a mean age of 4.5 years. Majority of the patients were males (60.4%), with a male to female ratio of 1.5:1. Close to half 27 (46.6%) of the patients, were yet to be enrolled into school (Table 1).

Table 1: Socio-demographic profile of study subjects

Variables	Frequency (%) n = 58
Age group (years)	
< 1	5 (8.6)
1-5	37 (63.8)
6-10	13 (22.4)
11-15	3 (5.2)
Sex	
Male	35 (60.4)
Female	23 (39.6)
Tribe	
Hausa	28 (48.3)
Fulani	16 (27.6)
Yoruba	9 (15.5)
Igbo	3 (5.2)
*Others	2 (3.4)
Religion	
Islam	53 (91.4)
Christianity	5 (8.6)
Educational level	
Yet to be enrolled	27 (46.6)
Day-care	4 (6.9)
Nursery	9 (15.5)
Primary	13 (22.4)
Secondary	5 (8.6)

*Others (Tiv, Ibibio, etc.)

Laterality of ASOM in study subjects

Acute suppurative otitis media (ASOM) was diagnosed in the right ear in a larger proportion of study subjects (46.4%), and both ears were affected in a few of them (15.5%) [Figure 1].

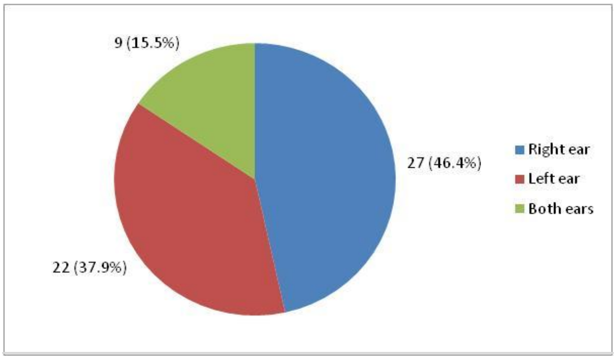

Figure 1: Laterality of ASOM in study subjects

Microbes isolated from aspirates

The microbes isolated in this study are shown in Table 2. Out of the 61 aspirates collected, 2 (3.3%) were sterile culturing neither bacteria nor fungi. The remaining 59 (96.7%) cultured different species of bacteria and fungi. The ratio of aerobes: anaerobes: fungi was 60.4: 1: 3.1, while the ratio of gram-positive: gram-negative aerobic bacteria was 3.5: 1. Streptococcus species (52.5%) was the most isolated gram-positive aerobe, followed by Staphylococcus aureus (23.0%), while Moraxella catarrhalis (11.5%) was the most isolated gram-negative aerobe. Only 1 (1.6%) species of anaerobe Bacteroides fragilis was isolated, while Aspergillus niger (3.3%) and Candida albicans (1.6%) were the fungal isolates. One patient (1.7%) displayed polymicrobial infection which comprised Staphylococcus aureus, Bacteroides fragilis, and Candida albicans.

Antibiotic sensitivity pattern of the isolated bacteria

The antibiotic sensitivity pattern of the isolated bacteria is shown in Table 3. Overall, amoxicillin/clavulanic acid (100.0%) showed the best sensitivity, followed by erythromycin (91.3%) and ceftriaxone (89.8%). The Bacteroides fragilis isolated was sensitive to many antibiotics including metronidazole and clindamycin.

Antifungal sensitivity pattern of the isolated fungi

All fungal isolates showed excellent susceptibility to all the antifungals tested (Table 4).

Table 2: Microbes isolated from aspirates

Variables	Frequency (%)	Percentage of total aspirates
A. Aerobes		
Gram-positive		
Streptococcus pneumonia	23 (37.7)	
Streptococcus pyogenes	9 (14.8)	75.4
Staphylococcus aureua	14 (23.0)	
Gram-negative		
Moraxella catarrhalis	7 (11.5)	
Escherichia coli	2 (3.3)	
Enterobacter species	1 (1.6)	
Citrobacter species	1 (1.6)	21.3
Proteus mirabilis	1 (1.6)	
Pseudomonas aeruginosa	1 (1.6)	
Total isolates	59 (96.7)	
B. Anaerobes		
Bacteroides fragilis	1 (1.6)	1.6
Total isolates	1 (1.6)	
C. Fungi		
Aspergillus niger	2 (3.3)	4.9
Candida albicans	1 (1.6)	
Total isolates	3 (4.9)	
D. Sterile aspirates	2 (3.3)	3.3
Total aspirates	**61 (100.0)**	

DISCUSSION

This study revealed a higher prevalence of ASOM among children aged 1 – 5 years (63.8%), which was almost three-times the value for those aged 6 – 10 years (22.4%). These findings were similar to those reported in France and Bangladesh, reiterating ASOM as a childhood disease.[28-29] The reasons for this high prevalence in this age group has been linked to immaturity of their immune system and the uniqueness of their Eustachian tube which is relatively shorter, wider, and straightened. Hence, infected materials from the nose, adenoids and sinuses readily pass along the Eustachian tube to the tympanic cavity; particularly during coughing, sneezing, vomiting, crying, and supine breastfeed or bottle feeding.[5,30]

Table 3: In vitro antibiotic sensitivity pattern of the isolated bacteria

Isolated aerobes (n)	Antibiotics, n (%)								
	Gent	Chl	Am/Clav	Ery	Cot	Oflx	Ceft	Met	Amx
Streptococcus pneumonia (23)	8 (34.8)	15 (65.2)	23 (100.0)	21 (82.6)	15 (65.2)	19 (82.6)	21 (82.6)	3 (13.0)	4 (17.4)
Streptococcus pyogenes (9)	3 (33.3)	7 (77.7)	9 (100.0)	8 (88.8)	7 (77.7)	6 (66.6)	8 (88.8)	1 (11.1)	1 (11.1)
Staphylococcus aureus (14)	11 (78.6)	13 (92.9)	14 (100.0)	14 (100.0)	10 (71.4)	12 (85.7)	13 (92.9)	5 (35.7)	3 (21.4)
Moraxella catarrhalis (7)	7 (100.0)	7 (100.0)	7 (100.0)	5 (71.4)	5 (71.4)	5 (71.4)	7 (100.0)	3 (42.9)	1 (14.3)
Escherichia coli (2)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)	-	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)
Enterobacter species (1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	-	1 (100.0)	1 (100.0)
Citrobacter species (1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	-	1 (100.0)	-
Proteus mirabilis (1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)	-
Pseudomonas aeruginosa (1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	1 (100.0)	-
Bacteroides fragilis (1)	-	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	-	1 (100.0)	1 (100.0)	-
Total (59)	**35 (59.3)**	**49 (83.1)**	**59 (100.0)**	**54 (91.5)**	**38 (64.4)**	**23 (37.7)**	**53 (89.8)**	**19 (32.2)**	**12 (20.3)**

Gent- Gentamycin (10μg); Chl- Chloramphenicol (10μg); Am/clav- Amoxicillin/clavulanic acid(30μg); Ery- Erythromycin (5μg); Cot- Cotrimoxazole (25μg); Oflx- Ofloxacin (30μg); Ceft- Ceftriaxone (30μg); Met- Metronidazole (5μg); Amx- Amoxicillin (25μg)

Table 4: In vitro antifungal sensitivity pattern of the isolated fungi

Fungal isolate (n)	Antifungals, n (%)					
	Clot	Nys	Flu	Gsf	Ket	ter
Aspergillus niger (2)	2 (100.0)	1 (50.0)	2 (100.0)	2 (100.0)	2 (100.0)	2 (100.0)
Candida albicans (1)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)	1 (100.0)
Total (3)	**3 (100.0)**	**2 (66.7)**	**3 (100.0)**	**3 (100.0)**	**3 (100.0)**	**3 (100.0)**

Nys- Nystatin (100U); Flu- Fluconazole (25μg); Gsf- Griseofulvin (2μg); Ket- Ketoconazole (10μg); Ter- Terbinafine (10μg)

The decline in the incidence of ASOM after this age is probably because the Eustachian tube matures by age of 7 years.[5] However, a study conducted in a semi urban community of Osun State, Southwestern part of Nigeria found the prevalence lowest in those <1 year, which is different from findings in this study, where their prevalence was third (8.6%) on the list.[10] The reason for this discrepancy might be that our study which is hospital-based, does not usually depict the true prevalence of a disease in a community.

A male to female ratio of 1.5: 1 was recorded from this study. This is in agreement with findings reported in Benin, Ibadan, and South Africa.[31-33] No rationale for this apparent disparity in sex prevalence has been identified. However, it may be socio-culturally related in this study, as the female child unlike their male counterparts have special dressings (hijab) that cover their ears and thus reduces the stigma that is attributed to discharging ear. On the contrary, since the male child does not wear this covering, the parents might tend to seek more urgent medical attention to reduce this stigma. Others have attributed it to higher activity of the male children compared with the females, which exposes them to aural trauma and infectious conditions.[10] A similar study in Yemen, noted female predominance, although adults were part of their study population; while studies conducted in Benin and Kano noted an almost equal sex distribution.[19-21]

This study revealed a slightly increased unilateral right ASOM over the left in a ratio of 1.2:1 and a unilateral over bilateral disease (5.4:1), which is similar to findings in Yemen.[19] Left ear predominance, and even equal distribution of the disease between both ears have also been reported in Nigeria and South Africa.[17,33-35] This preponderance of the right ear over the left might just be an incidental finding. However, there is a possible association between bilateral infection and severity of disease.[17] Thus, it is only reasonable to consider bilateral ear involvement as a more severe disease requiring more attentive management protocol.

This study revealed a high prevalence of aerobic bacteria (96.7%) than fungi (4.9%) and anaerobes (1.6%). And the ratio of monomicrobial to polymicrobial infection was 13.9:1. These findings strongly suggest that ASOM is more likely a mono-aerobic infection than polymicrobial. A similar study in Abakaliki, a town in south-eastern Nigeria, cultured more mono-microbials (81.5%) than poly-microbials (6.2%).[35] Also in Lagos, south-western Nigeria, more aerobes (85.7%) were cultured than anaerobes (14.3%) from ASOM.[17] Anaerobes are usually associated with cholesteatoma and granulations especially in CSOM; thus the reason for its relatively low prevalence.

This study revealed a higher prevalence of Gram-positive aerobes when compared with the Gram-negative aerobes in a ratio of 3.5:1. This again strongly suggests that ASOM is more likely to be Gram-positive aerobic infection than Gram-negative. Predominant aerobic bacterial isolates from this study were Streptococcus pneumonia (37.7%), Staphylococcus aureus (23.0%), Streptococcus pyogenes (14.8%) and Moraxella catarrhalis (11.5%) and is similar to findings in Zaria, Abakaliki and Yemen.[8,19,35] An earlier study in Sokoto had isolated Staphylococcus aureus as the most common bacteria causing ASOM,but failed to isolate Streptococcus pneumonia, Streptococcus pyogenes, and Moraxella catarrhalis, which are aerobes documented worldwide to cause ASOM.[2,5] The reason for this difference might be due to the methodology employed in their study, in which ear swabs were taken from the EAC without any transport or preservative media (Amies media) employed. However, a study in Lagos, southwestern Nigeria that obtained middle ear exudates prospectively via aspiration using sterile disposable plastic pipettes and cultured them within 2 hours of collection, isolated Streptococcus pneumonia, Streptococcus pyogenes, and Moraxella catarrhalis for ASOM.[17]

The prevalence of fungi infection in this study was 4.9%. A study in Uyo, south-south Nigeria reported 45.6% of fungal isolates from patients with ASOM, even though their definition of ASOM wasn't clearly outlined.[18] However, studies in Benin and Abakaliki among children attending a tertiary health facilities, had fungal prevalence of 6.8% and 21.3% respectively[31,35] All these findings further reiterates the role of fungus in middle ear infections. Some have postulated that the prolonged use of topical broad spectrum antibiotics may lead to suppression of bacterial flora and subsequent emergence of opportunistic fungal flora in different areas of the body including the middle ear.[5] This occurs following entry of fungal spores from the external environment into the moist and alkaline medium of middle ear discharge, which finally leads to the development of mycotic otitis media causing intractable otorrhoea.[18]

Accelerated patterns of bacterial resistance have been reiterated, and invariably mandates an evidence-based approach to managing ASOM.[5] This study reported a 100.0% sensitivity with amoxicillin/clavulanic acid, followed directly by erythromycin (91.5%) and ceftriaxone (89.8%), similar to findings in Benin.[31] Contrarily, a study in Kano noted better sensitivities of gentamycin and chloramphenicol.[21] Amoxicillin /clavulanic acid enjoys good patronage in this study area especially among the ENT surgeons, being the most prescribed empirical antibiotic in ASOM. It can therefore be deduced from findings in this study, that amoxicillin/clavulanic acid and macrolides should be used as first-line drugs in children with ASOM. All these further reiterate that variations in the degree of susceptibility of bacteria to antibiotics occur, and they stress the need for local studies in this respect to guide the rational use of the existing antibiotics. The result from this study further suggests that should additional ototopic antibiotic therapy be considered in children with ASOM for better clinical outcome, ofloxacin which has none of the ototoxic risks of chloramphenicol can be used.

The possible side effects of quinolones on pre-pubertal children are eliminated when used as ototopics.

Only 4.9% of the aspirates in this study cultured fungi, of which 100.0% *in vitro* susceptibility to all the antifungals assessed was noted. The fungi isolated in this study might be contaminants, and further reiterates ASOM as a monoclonal aerobic infection. This contrasted with studies in Uyo, south-south Nigeria possibly because of the different sample collection techniques employed bybothstudies.[18] The cautious use of ototopical antifungals has been re-emphasized because of their ototoxic potentials.[5]

CONCLUSION

This study showed that, the pattern and types of microbial isolates identified to be implicated in ASOM in this study, is not different from those documented in other literatures, even though there are slight differences in their frequency. The disease is more likely a mono-aerobic infection than polymicrobial. Its treatment should include among others, early commencement of antibiotics with good gram-positive and gram-negative aerobic coverage, to eradicate the disease. The *in vitro* antibiotic sensitivity identified amoxicillin/clavulanic acid, followed by erythromycin as most adequate.

Acknowledgments

The authors appreciate the staff of the Microbiology Department, UDUTH, Sokoto, Nigeria.

Source of support

Nil.

Conflict of interest

None declared.

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How to cite this article: Inoh MI, Iseh KR, Mohammed Y, Aliyu DJ, Yikawe SS, Inoh EE. Microbial studies in acute suppurative otitis media in children attending a tertiary health facility in North-western Nigeria. Int Arch Med Health Res 2021; 2(1): 9-16.