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ANTIBIOTIC RESISTANCE/SUSCEPTIBILITY PROFILE OF BACTERIA ASSOCIATED WITH EAR INFECTIONS AMONG INDIVIDUALS IN WUKARI LGA

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Abstract Ear infection (otitis media) is a common clinical problem throughout the world and a major cause of preventable hearing loss in the developing world. Antibiotic resistance is increasingly a health threat to human and as such need immediate action to combat its spread. The aim of this study is to determine the antibiotic resistance and susceptibility profiles of isolated bacteria from suspected individual with ear infection in Wukari LGA. A total of forty nine (49) ear discharge specimens were collected using sterilized swab sticks from each patent suspected to be suffering from ear infection. It was carried out by means of random-sampling among individual in Wukari. Results show a strong association ($p<0.05$) between age and sex at risk of acquiring otitis media. The finding predominant bacterial isolates were; Bacillus subtilis (20.29%). Followed by Paenibacillus alvei with (24.64%) and *Staphylococcus aureus* with (20.29%). Most of the isolated pathogenic bacteria showed the highest antibiotic resistance to Ampiclox, Rocephin, Amoxicillin and Ciprofloxacin. On the other hand, almost all the isolated pathogenic bacterial species were significantly, Gentamycin, Pefloxacin, Streptomycin and Erythromycin were seen to be highly effective against the two leading bacteria associated with ear infection. Septrin and Erythromycin were seen to be highly effective against all the three leading pathogenic microorganisms identified in this study. Septrin, Streptomycin, Pefloxacin, Gentamycin and Erythromycin can therefore be used for treatment of ear infection in the study area. Since almost all the isolates bacteria showed a considerable level of resistance to more than one antibiotic that are commonly used in primary health care centre, this indicated that the isolates were multi-drug-resistant (MDR), for a successful patient management and prevention of the emergence of multi-drug-resistant bacteria, treating bacterial ear infections in the study should be done base on culture and antibiotic sensitivity test result.

Key words: Bacteria, Antibiotic, Resistance, Susceptibility, Ear infection, Otitis media and Wukari.

Introduction

Antimicrobial resistance (AMR) occurs when bacteria, viruses, fungi and parasites change overtime and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death (WHO, 2021). As a result, the medicines become ineffective and infections persist in the body, increasing the risk of spread to others (WHO, 2021). Antimicrobials including antibiotics, antivirals, antifungals and antiparasititics are medicines used to prevent and treat infections in humans, animals and plants. Microorganisms that develop antimicrobial resistance are sometimes referred to as "superburgs" (WHO, 2021). According to World Health Organization (2020), antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria change in response to the use of these medicines. Bacteria, not humans or animals, become antibiotic-resistant. These bacteria may infect humans and animals, and the infections they cause are harder to treat than those caused by non-resistant bacteria. Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality.

Ear infection (Otitis media) is a major health problem throughout the world and occurs with a high incidence and prevalence (Afolabi *et al*., 2012) cause of preventable hearing loss (WHO, 2015) in both developed and developing countries (Afolabi *et al*., 2012). Its chronic form is a serious problem in all age groups with less chance of recovery (Ullauri *et al.*, 2009; WHO, 2015), although is higher in males than females (Seid *et al.*, 2013). In certain cases, this condition can lead to serious life-threatening complications, such as hearing impairment, brain abscesses, or meningitis, mostly in childhood and late in life (Fauci *et al*., 2008; WHO, 2015). The microorganisms may gain entry to the middle ear through a chronic perforation. Children tend to have higher predisposition to ear infection than adults because anatomy of the eustachian tube in children permits easier access of organism through the nasopharynx (Seid *et al.*, 2013). The causative agents of ear infection might be bacterial, viral, or fungal. However, the major causative agents of ear infection are bacterial isolates such as *Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Streptococcus pyogenes, Proteus mirabilis, Klebsiella spp*., or mixed bacterial infection (Afolabi, *et al*., 2012).

The prevalence of otitis media varies from place to place. In the developed world like United States of America (USA) and Europe, it is declining because of awareness; but in developing countries, it is on the rise (Adoga *et al.*, 2010). In developing countries untreated otitis media leads to purulent otitis often with perforation and further complications including recurrent acute otitis media, persistence of middle ear effusion which requires the insertion of drainage tube and often leads to hearing impairment, mastoiditis, meningitis, chronic otitis media, brain abscess and sepsis (Seid *et al.*, 2013). This study aims to determine the prevalence of some bacteria associated with ear infection and its antibiotic resistance and susceptibility profiles of individuals in Wukari Local Government Area.

Materials and Methods

Description of Study Area

Wukari is a Local Government Area in Taraba State, Nigeria. Its headquarters is in the town of Wukari on the A4 highway. The Donga River flows through the area and the Benue River forms a boundary with Nasarawa State to the northwest (Agwaranze *at al*., 2024). It has an area of 4,308 km^2 and a population of 241,546 at the

2006 census (Brown *et al*., 2023). The postal code of the area is 670 (NIPOST, 2009).

Sample Sites

The study was carried out in Wukari. The samples were collected randomly from East Primary School, Government Day Secondary School and Federal University Wukari, all in Wukari Local Government Area of Taraba State and brought to Laboratory for analysis.

Collection of Sample

A total of Fourty Nine (49) ear discharge/pus specimens were collected aseptically using sterilized swab sticks from each patient/ individual suspected to be suffering from ear infection (otitis media) and those experiencing middle ear pain, iches and hearing difficulty/ hearing loss. The samples were transported to the Microbiology Laboratory Federal University Wukari for analysis within 5 - 7 hours after collection.

Laboratory Diagnostic Methods

Few drops of normal saline were added aseptically to each sample in the swab sticks and streaked on labelled Nutrient agar and MacConkey agar plates then incubated at 37°C for 24hrs. After 24hrs, culture plates were observed for significant growth. Mixed cultures were then sub-cultured on Nutrient agar plates using sterilized 0.001 mL inoculation loop and incubated for 24hrs to obtain pure cultures. From the pure cultures, microbiological and biochemical tests were carried out. Gram staining was done to differentiate between Gram positive and Gram negative bacteria. The biochemical tests done to identify the organisms include catalase test, coagulase test, oxidase test and indole test (Cheesbrough, 2006).

Antimicrobial Susceptibility Testing

Susceptibility testing was done on Mueller–Hinton agar using disk diffusion technique according to Kirby–Bauer Method (Bauer *et al.,* 1966). The test was performed by applying a bacterial inoculum of approximately 1–2×10^8CFU/mL to the surface of a large (150 mm diameter) Mueller-Hinton agar plate. 10 commercially-prepared, fixed concentration, paper antibiotic disks were placed on the inoculated agar. Plates were incubated for 24 hours at 35°C prior to determination of results. The zones of growth inhibition around each of the antibiotic disks were measured to the nearest millimeter. The diameter of the zone is related to the susceptibility of the isolate and to the diffusion rate of the drug through the agar medium. The zone diameters of each drug were interpreted using the criteria published by the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (CLSI, 2021).

Statistical Analysis

Data was entered and analyzed using (SPSS) statistical package (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Discrete variables were expressed as percentages. Chi square test was used to compare the proportion of bacterial isolates with patients' age and sex and P value of <0.05 was considered statistical significant.

Results and Discussion

Ear infection is a more frequent treatable health care problem worldwide, yet if left untreated, it can cause a serious complication such as a speech development disorder, hearing loss, distress in patients and their family quality of life, and economic burden on the health care system (World Health Organization, 2015). The burden and prevalence of ear infection are more intense in developing countries due to the poor living standard and hygienic conditions along with lack of proper nutrition (Afolabi *et al*, 2012; Muluye *et al*, 2013; Yiengprugsawan and Hoga, 2013). Thus, highlighting the etiologies of ear infection and their antibiotic susceptibility pattern will help to lessen the severe complication of the infection and guide the empirical antibiotic prescribed by the physicians, especially for developing countries (Muluye *et al*, 2013; Llor and Bjerrum, 2014). On top of these issues, increased antimicrobial resistance is one of the greatest global public health challenges, which has been accelerated by prescription of antibiotics more frequent than appropriate worldwide. Infection with antibiotic-resistant bacteria may cause severe illness, increased mortality rates, and an increased risk of complications and admission to hospital and longer stay (Llor and Bjerrum, 2014; Livermore, 2012; Kollef, 2008).

The result presented in Table 1 shows that females were at more risk of acquiring middle ear infection than males, with females at 56.5% and males at 43.5%. The proportion of ear infection was significantly higher in females compared to males (P = 0.433994). This result agrees with the finding of Hassan and Adeyemi (2007) females were more affected by ear infection than males. Contrarily, in reports from Ethiopia (Muluye *et al.,* 2013) and Nigeria (Egbe *et al.,* 2010), the proportion of ear infection was significantly higher in males compared to females. On the other hand, other studies (Abera and Kibret 2011; Seid *et al.,* 2013; Wasihun and Zemene, 2015), reported that there is no significant difference on the incidence of ear infections between males and females. In a ten-year retrospective analysis in Ethiopia, it revealed that gender has no influence on the risk of acquiring middle ear infection. Likewise, most investigators have reported no clear gender-based difference exists in the risk of acquiring middle ear infection (Yiengprugsawan and Hoga, 2013).

However, it was found that age has a strong association with the risk of acquiring middle ear infection (otitis media). In this study, the highest proportion of otitis media was found among patients from 11 to 20 years of age which agrees with reports from Ethiopia (Muluye *et al.,* 2013; Seid *et al.,* 2013) and other countries (Ahmad 2013; Iseh and Adegbite, 2004). Higher frequency of ear infection among young age groups might be due to the short, broad and straight nature of the Eustachian tube, frequent exposure to upper respiratory tract infections, lack of hygiene, lower immune status, and malnutrition (Ahmad 2013; Muluye *et al.,* 2013; Seid *et al.,* 2013; Wasihun and Zemene, 2015). For example, children are highly vulnerable to frequent ear infection due to pathogenic bacteria colonization in the middle ear or upper respiratory tract (Muluye *et al.,* 2013; Mittal *et al.,* 2014; Lasisi, 2008).

The frequency of positive ear discharge cultures was higher in the age group 11-20 years (60.8%) followed by the age group 0-10 (26.1%) (Table 1). The chi-square test showed age and frequency of bacterial positive ear discharge within the short study period were strongly associated (*p <.05).*

Table 1: Distribution of Ear Infection in Relation to Age and Sex of Individuals

Variables	Frequency of Otitis Media (%)		Total N (%)	*P value*
Sex				
Male	20(43.5)		22(44.9)	0.433994
Female	26(56.5)		27(55.1)	
Age group in years	Male	Female		
0-10	5(10.9)	7(15.2)	14(28.6)	
11-20	14(30.4)	14(30.4)	29(59.2)	
21-30	1(2.2)	4(8.7)	5	
31-40	0	1(2.2)	1	

Figure 1: A Graphic Representation of the Distribution of Ear Infections in Relation to Age and Sex of Individuals

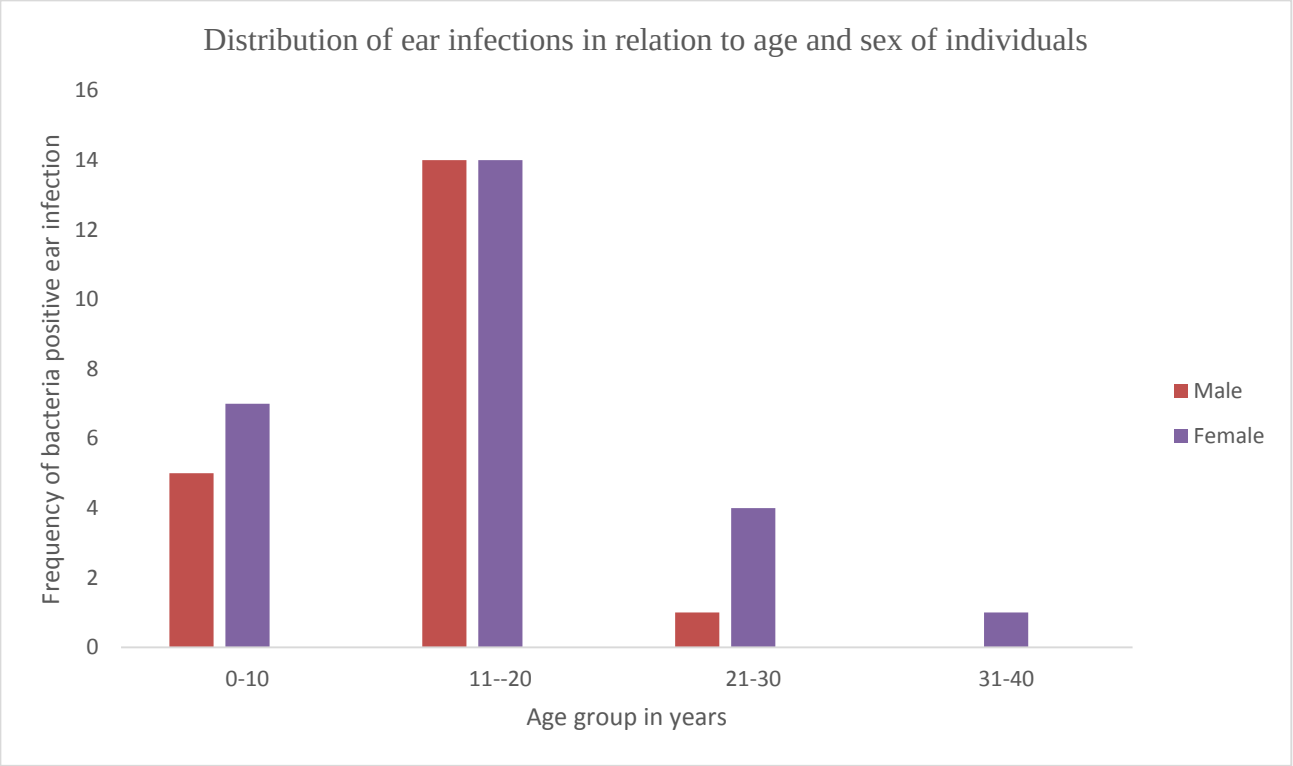

Table 2: Microbiological and Biochemical Test Results of Isolated Bacteria

Gram staining	Catalase test	Oxidase test	Coagulase test	Indole test	Bacteria
Positive cocci in cluster	+	-	+	-	*Listeria monocytogenes*
Positive bacilli in chain	+	+	+	+	*Paenibacillus alvei*
Positive cocci	+	-	+	-	*Brevibacterium linens*
Positive cocci in cluster	+	-	+	-	*Staphylococcus aureus*
Positive cocci in cluster	+	+	-	+	*Staphylococcus sciuri* (CoNS)
Positive cocci in chain	+	+	+	-	*Bacillus subtilis*
Positive bacilli in chain	+	-	+	-	*Corynebacterium mucifaciens*

The research finding shows that out of the 46 bacteria positive samples, 7 different pathogenic bacteria species were identified. Among these bacterial species, the predominant bacterial isolate was *Bacillus subtilis* (27.54%), the second predominant was *Paenibacillus alvei* (24.64%) followed by *Staphylococcus aureus* (20.29%) (Table 3).

In this study, the most predominant pathogenic bacterium associated with middle ear infection was *Bacillus subtilis* (27.54%), the second was *Paenibacillus alvei* (24.64%) followed by *Staphylococcus aureus* (20.29%) which is in contrast to studies from parts of Ethiopia who reported *Proteus* spp. were the foremost bacteria associated with middle ear infection followed by the later ones (Ferede *et al.*, 2001; Muleta *et al.*, 2004; Abera and Biadegledne, 2009; Tesfaye *et al.*, 2009; Abera and Kibret, 2011; Seid *et al.*, 2013; Muluye *et al.*, 3013) except for *Staphyloccus aureus.* And several other published data pieces from Africa and elsewhere in the world reported *Pseudomonas* spp., mainly *P. aeruginosa*, is the primary pathogenic bacteria associated with middle ear infection (Afolabi *et al.*, 2012; Mansoor *et al.*, 2009; Osazuwa *et al.*, 2011; Tanon-Anoh *et al.*, 2006; Illing and Olaleye, 2011; Bovo *et al.*, 2012; Weckwerth *et al.*, 2009; Alsaimary *et al.*, 2010). One possible explanation for this difference might be due to climate and geographical variations between Ethiopia and those countries and as well the country of this present study; Nigeria. It is worthy of notice that this study and many other previously reported data indicated *S. aureus* second in common bacterial isolates that often associated with middle ear infection (Abera and Biadeglegne, 2009; Seid *et al.*, 2013; Osazuwa *et al.*, 2011; Illing and Olaleye, 2011; Alsaimary *et al.*, 2010), though it is the third in this study.

Table 3: Frequency of Microbial Isolates of Ear Infection

Bacterial species	Frequency	Percentage (%)
Listeria monocytogenes	10	14.49
Paenibacillus alvei	17	24.64
Brevibacterium linens	3	4.35
Staphylococcus aureus	14	20.29
Staphylococcus sciuri	5	7.24
Bacillus subtilis	19	27.54
Corynebacterium mucifaciens	1	1.45
Total	69	100

Antibiotic susceptibility profiles are shown in Table 4. Ampiclox, Rocephin, Amoxicillin, and Ciprofloxacin showed the highest antibiotic resistance rates to almost all bacterial pathogens isolated from middle ear discharge. All the isolated organisms were highly resistant to amoxicillin (57.9% - 100%) except *Listeria monocytogenes* which was sensitive to it by 60.0%. Almost all the isolated pathogens showed a high susceptibility to Zinnacef, ranging from 57.9-100% with moderate resistance. Ampiclox, Rocepphin, and Amoxicillin were highly resistant to *Bacillus subtilis.* The bacterium was susceptible only to Streptomycin and Erythromycin. The second most isolated bacterium, *Paenibacillus alvei* showed high resitance to Ampiclox, Rocepphin and Erythromycin and high sensitivity to Ciprofloxacin, Pefloxacin, Septrin, Gentamycin and Streptomycin. Almost all the isolated pathogenic bacterial species were significantly susceptible to Septrin, Streptomycin, Pefloxacin, Gentamycin and Erythromycin. Particularly, Gentamycin, Pefloxacin, Streptomycin and Erythromycin were seen to be highly effective against the two leading bacteria associated with ear infection. Septrin and Erythromycin were seen to highly effective against all the three leading pathogenic microorganisms identified in this study.

Ear infection is among the most common illnesses that leads to over prescription of antibiotic use, one of the reasons for the emergence of antibiotic resistant pathogenic bacteria (Yiengprugsawan and Hoga, 2013; Llor and Bjerrum, 2014). In view of this evidence, this study revealed that most of the isolated pathogenic bacteria have become resistant to all the easily available antibiotics. In this study, generally, Ampiclox, Rocephin, Amoxicillin, and Ciprofloxacin showed the highest antibiotic resistance rates to almost all bacterial pathogens isolated from middle ear discharge; similar high percentage of resistance was also reported from Ethiopia and elsewhere in the world (Afolabi *et al.*, 2012; Abera and Kibret, 2011; Seid *et al.*, 2013; Zou *et al.*, 2012; Udobi *et al.*, 2013). All the isolated organisms showed high resistance to Amoxicillin (57.9% - 100%) except *Listeria monocytogenes* which was sensitive to it by 60.0%. Almost all the isolated pathogens showed a high susceptibility to Zinnacef, ranging from 57.9-100% with moderate resistance. Ampiclox, Rocepphin, and Amoxicillin were the most clinically used antibiotics that showed a higher resistance rate to *Bacillus subtilis.* The bacterium showed susceptibility only to streptomycin and erythromycin. The second most isolated bacterium, *Paenibacillus alvei* showed high resitance to Ampiclox, Rocepphin and Erythromycin, and high sensitivity to Ciprofloxacin, Pefloxacin, Septrin, Gentamycin and Streptomycin; in the same manner, high percentage of resistance was also reported from Ethiopia and elsewhere in the world (Afolabi *et al.*, 2012; Abera and Kibret, 2011; Seid *et al.*, 2013; Zou *et al.*, 2012; Udobi *et al.*, 2013). Importantly, this study revealed almost all the isolated pathogenic bacterial species were significantly susceptible to Septrin, Streptomycin, Pefloxacin, Gentamycin and Erythromycin. Particularly, Gentamycin, Pefloxacin, Streptomycin and Erythromycin were seen to be highly effective against the two leading bacteria associated with ear infection. Septrin and erythromycin were seen to have high efficacy against all the three leading pathogenic

microorganisms identified in this study. This is contrary to the results of research of several authors who showed high efficacy of Ciprofloxacin against *Staphylococcus aureus* (Afolabi *et al.*, 2012; Abera and Biadeglegne, 2009; Abera and Kibret, 2011; Aslam *et al.*, 2004; Kwiecinska-Pirog *et al.*, 2013; Mosges *et al.*, 2011; Renukananda *et al.*, 2014) which in this research was shown to be more susceptible to Septrin and Erythromycin and only moderately sensitive to Ciprofloxacin.

The presence of high levels of resistance to Amoxicillin, Ampiclox, and Rocepphin, in the three leading pathogenic bacteria associated with middle ear infection in this study might be due to lack of current awareness on antimicrobial resistance among physicians and nurses, unavailability of local antibiogram data, misuse of antibiotics, and self-prescription by patients and negligence on patient part.

Table 4: Antibiotic Susceptibility Profile of Pathogenic Bacteria Isolated from Ear Infection Base on Species
Key: S= Sensitive; R= Resistant

Antibiotics	Bacterial species													
	L. monocytogenes		*P. alvei*		*B. linens*		*S. aureus*		*S. sciuri*		*B. subtilis*		*C. mucifaciens*	
	S%	R%	*S%*	*R%*	*S%*	*R%*	*S%*	*R%*	*S%*	*R%*	*S%*	*R%*	*S%*	*R%*
Amoxacillin (30µg)	60.0	40.0	32.3	64.7	0.00	100.00	28.6	71.4	20.0	80.0	42.1	57.9	0.00	100.0
Zinnacef (20µg)	70.0	30.0	64.7	32.3	66.7	33.3	21.4	78.6	40.0	60.0	57.9	42.1	100.00	0.00
Ampiclox (30µg)	40.0	60.0	23.5	76.5	33.3	66.7	14.3	85.7	0.00	100.0	21.1	78.9	100.00	0.00
Gentamycin (10µg)	90.0	10.0	76.5	23.5	100.0	0.00	7.1	92.9	0.00	100.0	84.2	15.8	100.00	0.00
Pefloxacin (10µg)	80.0	20.0	76.5	23.5	33.3	66.7	35.7	64.3	60.0	40.0	63.2	36.8	0.00	100.0
Rocepphin (25µg)	0.00	100.0	11.8	88.2	0.00	100.0	57.1	42.9	60.0	40.0	31.6	68.4	0.00	100.0
Ciprofloxacin (10µg)	10.0	90.0	70.6	29.4	66.7	33.3	50.0	50.0	40.0	60.0	47.4	52.6	0.00	100.0
Streptomycin (30µg)	60.0	40 0	88.2	11.8	100.0	0.00	35.7	64.3	60.0	40.0	89.5	10.5	0.00	100.0
Septrin (30µg)	0.00	100.0	76.5	23.5	80.0	20.0	100.00	0.00	100.0	0.00	57.9	42.1	100.0	0.00
Erythromycin (10µg)	10.0	90.0	5.9	94.1	0.00	100.00	100.00	0.00	80.0	20.0	89.5	10.5	0.00	100.0

Conclusion

In conclusion, ear infection is a common clinical problem throughout the world and the major cause of preventable hearing loss in the developing world. This study revealed that age and the risk of acquiring middle ear infection are strongly associated and *Bacillus subtilis, Paenibacterium alvei,* and *Staphylococcus aureus*. Almost all the isolated bacteria showed a considerable level of resistance to more than one antibiotic that are commonly used in primary health care centers, meaning that about 80% of ear discharge isolates were multi-drug-resistant (MDR). In general, the result of this study revealed that antibiotic-resistant bacteria are increasing in Wukari Local Government Area and becoming a major public health problem in the management patients with middle ear infection.

Recommendations

It strongly recommended that nationwide antimicrobial surveillance to make it alternative antibiotics along with strict adherence to antibiotic policy to reduce the spread of drug resistant microbes in the country. Periodic and continuous follow-up of antibiotic usage is necessary. For successful patient management and prevention of the emergence of Multi-drug-resistant bacteria, treating bacterial ear infections based on culture and antibiotic sensitivity test results in the study area is advisable.

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