AMERICAN JOURNAL OF BIOLOGY AND NATURAL SCIENCES

https://biojournals.us/index.php/AJBNS

ISSN: 2997-7185

Article

Antimicrobial Resistance Patterns in Bacterial Otitis Media: A Systematic Review of Global Trends and Clinical Implications

Israa Mamdooh Subhi[1], Saba Nazeih Abdulghaffar*[2], Husam Ibrahim Kadhim[3]

1. Department of Nursing Techniques, Medical Technical Institute-Baghdad, Middle Technical University, Baghdad, Iraq

2,3. Department of Medical Laboratory Techniques, Medical Technical Institute-Al Mansour, Middle Technical University, Baghdad, Iraq

*Correspondence: sabanazeih@mtu.edu.iq

Citation: Subhi, I.M., Abdulghaffar, S.N. and Kadhim, H.I. Antimicrobial Resistance Patterns in Bacterial Otitis Media: A Systematic Review of Global Trends and Clinical Implications. American Journal of Biology and Natural Sciences 2026, 3(8), 1-13.

Received: 15th Jun 2026
Revised: 05th Jul 2026
Accepted: 20th Jul 2026
Published: 05th Aug 2026

Abstract: This systematic review and meta-analysis provide an overview of bacterial causative agents for otitis media and antimicrobial resistance patterns against major otitis media pathogens. Out of a total of 180 records that were identified initially (both from database and manual searches), duplicates removal left 122 individual records. After screening titles and abstracts, 24 articles were reviewed in full text, and ultimately, 18 studies were included in the meta-analysis. Frequent reporting of gram-negative pathogens as major causative organisms were seen in the present study and highlighted multiple reports on particular Pseudomonas aeruginosa, *Escherichia coli, Klebsiella pneumoniae* 5 and Proteus spp. Pathogens were generally highly susceptible to most aminoglycosides (amikacin and gentamicin), fluoroquinolones (ciprofloxacin and levofloxacin) carbapenems and colistin. Regarding Gram-positive bacteria Staphylococcus aureus, notably methicillin-resistant strains (MRSA), was similarly associated with resistance, indicative of its endemic β-lactam and multi-class antibiotic resistance. The pooled meta-analysis resulted in a statistically significant overall antibiotic resistance rate of bacterial isolates related to otitis media (pooled prevalence= 0.61 [95% CI: 0.54–0.68], $P < 0.001$). Such analysis concluded that around 61% of bacterial pathogens found across the studies investigated showed resistance to typically-used antimicrobial agents. There was substantial between-study heterogeneity ($I^2 = 72.4\%$) in the analysis of subpopulations, likely due to geographic locations, distribution of bacterial species, antibiotic prescribing practices and laboratory methods among studies included. This meta-analysis shows the considerable burden of antibiotic resistance in bacterial pathogens causing otitis media. Staphylococcus aureus and Pseudomonas aeruginosa were identified as the most common resistant organisms, whereas aminoglycosides and fluoroquinolones retained higher efficacy in general.

Keywords: Meta-Analysis, Otitis Media, Antibiotics, Bacterial Resistance

Introduction

Otitis media (OM) is one of the most common infectious diseases globally to be diagnosed among children, responsible for considerable morbidity and healthcare costs across different clinical environments [1][2]. Otitis media is defined as the inflammation of the middle ear cavity and contains a clinical spectrum that ranges from acute otitis media (AOM) to chronic suppurative otitis media (CSOM), which makes it challenging for antimicrobial management relating to persistent bacterial colonization and biofilm formation [3][4][5]. Although OM is a relatively common childhood condition, it continues to be a considerable public health burden globally with around 709 million cases each year and the highest burden in children under five years of age, particularly in low- and middle-income countries where access to specialist otolaryngologic care remains limited.

The microbiological etiology bacterial OM has changed over the last few decades, due to implementation of pneumococcal conjugate vaccines (PCVs) and the evolving AMR patterns of predominant pathogens [6]. The classical triad of OM pathogens consists of Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis which together account for 80–90% of culture positive AOM in children [7][8]. With universal PCV implementation, the epidemiological landscape has changed greatly, with declining vaccine-serotype S. pneumoniae and rising numbers of non-vaccine serotypes and non-typeable H. influenzae (NTHi), which is now the most frequently isolated pathogen in many regions [9][10]. Because NTHi and M. catarrhalis have a greater propensity to produce beta-lactamase and multi-drug resistance than pneumococcal equivalents [11], the held microbiological transitions have critical relevance for empirical antimicrobial selection [12].

Antimicrobial resistance in OM pathogens is an urgent and worsening risk to global public health, amplifying the inherent difficulties of treating infections located anatomical confined zones that often limit antimicrobial penetration [13][14]. In response, AMR was highlighted by the World Health Organization as one of the top ten global public health threats facing humanity [15] and respiratory pathogens (including those associated with OM) are responsible for a high proportion of the burden of resistant infections [16][17]. For OM specifically, the resistance of first-line agents such as amoxicillin, trimethoprim-sulfamethoxazole and macrolides resulted from a clear mix of selective pressure due to widespread antibiotic prescriptions spreading around the geographic area and horizontal transmission between respiratory commensals [18]. AMR in OM has important clinical implications, beyond treatment failure to include increased duration of symptoms, higher rates of complications (including mastoiditis and intracranial extension), and rising costs associated with second-line or parenteral therapies [19].

Antimicrobial resistance mechanisms in OM pathogens are poly-expressional and progressively complicated. The production of beta-lactamase, is mainly mediated by the TEM-1 and ROB-1 enzymes in H. influenzae or BRO-1/BRO-2 in M. catarrhalis which cause resistance to ampicillin and amoxicillin when unprotected by beta-lactamase inhibitors [11][20]. Pneumococcal resistance is mediated by mutations in penicillin-binding proteins (PBPs) and mosaic PBP genes that alter target-site affinity for beta-lactam antibiotics, while macrolide-resistant strains primarily express the erm(B)-mediated methylation of the ribosomal target or mef(A)-mediated efflux pumps [21]. Less well studied, fluoroquinolone resistance has also recently developed among S. pneumoniae isolates, with some strains harboring mutations in DNA gyrase and topoisomerase IV genes however, the prevalence remains low in OM-specific populations relative to that reported for invasive disease isolates [22].

That geographic variation in resistance patterns further complicates clinical decision making and guideline development. Data from surveillance in the United States and Western Europe show that pneumococcal penicillin resistance rates have remained relatively stable after the introduction of PCV13 but regions with suboptimal vaccination use or inconsistent antibiotic stewardship have substantially increased levels of resistance [23]. The lack of routine microbiological diagnostics and the reliance on empirical therapy — often based solely on clinical presentation [24]. These differences highlight the need for region-specific resistance data to shape evidence-based treatment algorithms instead of global recommendations based on surveillance from high-income countries.

Clinical AMR implications in OM are not restricted to individual patient management but also entail even larger public health aspects, taking into account the selection pressure of multiple

antibiotic courses in otitis-prone children who receive frequent antibiotic treatments during early life [25][26]. Every antibiotic exposure raises the likelihood of colonization with resistant strains inside an individual, where these can then circulate into household and community reservoirs through contact spread [27]. This interplay between the host, the pathogen and the antimicrobial exposure requires changes of strategy towards good prescribing, diagnostic stewardship and novel therapeutic strategies like antimicrobials as peptides, bacteriophage therapy or NTHi/M. catarrhalis specific vaccines.

While the importance of AMR in OM is well recognized, there are still few comprehensive syntheses of global resistance trends: systematic reviews attempting to quantify these have often been restricted by individual pathogens, geographic regions or time periods [28][9][10][8]. Despite antimicrobial resistance [29] having been the subject of exhaustive research for otitis media, there is considerable variation in resistance patterns by clinical disease subtype. Acute otitis media is predominantly associated with respiratory pathogens (e.g. Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis), whereas chronic suppurative otitis media is more commonly characterized by polymicrobial communities in which Gram-negative organisms such as Pseudomonas aeruginosa are prevalent. Thus, study of antimicrobial resistance in otitis media should take into account epidemiological and microbiological property-specific features of such diseases. This is the first combined systematic review, and provides an overview of antimicrobial resistance patterns against key OM pathogens, over time, by geography and in relation to clinical outcomes relevant to this area.

Methods

Protocol

This systematic review was conducted and reported according to the PRISMA 2020 statement [30].

Search Strategy

A comprehensive, systematic search of four major electronic databases (PubMed/MEDLINE, Scopus, Web of Science and Embase) from the inception of the databases up to December 2024 was conducted. This systematic review aimed to summarize the trends in antimicrobial resistance in bacteria involved in otitis media among children. The single and/or combination keywords included, "otitis media," "acute otitis media," "chronic suppurative otitis media," CSOM, AOM, "antimicrobial resistance," antibiotic resistance, drug resistance, bacterial, Streptococcus pneumoniae, *Haemophilus influenzae*, *Moraxella catarrhalis*, beta-lactamase, penicillin resistance, macrolide resistance and multidrug resistant. Supplementary Material 1 provides the full search strings for each of the databases. No restrictions based on the language was applied but translated non-English articles as necessary. Furthermore, we hand-searched the reference list of all included studies and other related reviews to find any potentially relevant publications that were not identified by searching in this electronic format.

Eligibility Criteria

Eligible studies were identified using the following inclusion criteria: (1) original data on antimicrobial susceptibility testing of aerobic bacterial pathogens isolated from patients with clinically or microbiologically-defined otitis media (acute, chronic, or recurrent); (2) standardized laboratory methods for resistance detection including disk diffusion, broth microdilution or automated susceptibility testing systems [e.g., VITEK, Phoenix]; (3) quantitative measures of resistance rates (numerator and denominator/percentage) for at least one class of antibiotic; and (4) an adequately defined study population with specified geographic location and time frame. Studies involving non-standardized susceptibility testing methods, reviews, editorials, case reports, conference abstracts and letters to the editor were also excluded. We excluded studies reporting only outcomes on otitis externa, mastoiditis or non-specific postoperative infections not potentially attributed to otitis media.

Study Selection

Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) was used to manage the screening process. Excluded studies were noted and reported in the PRISMA flow diagram.

Data Extraction

Data were extracted from included studies using a standardized, pilot-tested form. Data extraction variables included: first author, year of publication, study design (observational or experimental), country and geographical region, study period, demographics of patients in the studied cohort (age range and number of samples tested), type of otitis media found (AOM, CSOM or recurrent OM), bacterial species identified in the study, antimicrobial agents tested on isolates collected from the clinical sample(s), definition and breakpoints for resistance used to define resistant organisms in each work (CLSI [Clinical Laboratory Standards Institute], EUCAST [European Committee on Antimicrobial Susceptibility Testing] or other defined susceptibility method), total number of isolates tested against a particular antimicrobial agent per taxa / class / family, total number and percentage (%) data for isolates that were multidrug resistant as well as fully-resistant against common antibiotics after exposure to this drug/antibiotic drugs where specific mechanisms resistance was reported such as amongst others beta-lactamase production PBP mutations efflux pumps etc.. When reports published were inadequate or ambiguous, we were able to contact authors of primary studies by e-mail in order to clarify details or obtain additional data.

Quality Assessment

For methodologic quality assessment, we evaluated the included observational studies (cross-sectional, cohort and surveillance studies) using the Newcastle–Ottawa Scale (NOS), adapted for prevalence studies [31]. The NOS assesses studies in terms of selection, including sample representativeness and justification for sample size and response rate; comparability, predominantly through control for confounding; and outcome, including resistance assessed in a standardized manner, appropriate statistical analysis performed, and reporting quality.

Data Synthesis and Statistical Analysis

We synthesized data from included studies narratively and, where appropriate, quantitatively via meta-analysis. In anticipation of heterogeneity among study populations, geographic regions, time periods, and laboratory methods, we applied a random-effects model (DerSimonian-Laird method). The I^2 statistic estimates the percentage of variability in effect estimates that is attributable to true heterogeneity between studies and not sampling error, and assesses statistical heterogeneity among included studies. Heterogeneity was defined as low (I^2 = 0–25%), moderate (I^2 = 26–50%), substantial (I^2 = 51–75%) and considerable (I^2 >75%) according to [32]. This heterogeneity was subsequently explored with respect to potential clinical, methodological and geographical sources of variation (i.e. patient populations, established otitis media subtype and distribution of bacterial pathogens as well as antibiotic prescribing practices, geographical setting or study design and microbiological detection method).

To test for heterogeneity, we applied Cochran's Q test. Heterogeneity sources were pre-specified subgroup analyses for geographic region (high-, low- and middle-income countries), time period prior to PCV7, concurrent with the use of PCV7 or PCV10, post-PCV13, type of otitis media (AOM vs. CSOM) and bacterial species. When a meta-analysis included at least 10 studies, publication bias was visually assessed by funnel plots and statistically using Egger's regression test [33][34]. Statistical analysis All statistical analyses were performed using R software version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) with the meta and meta for packages and Stata version 17.0 (StataCorp LLC, College Station, TX, USA).

Results

This flow chart is based on the PRISMA-guided identification and selection of studies. Out of a total of 180 records that were identified initially (both from database and manual searches), duplicates removal left 122 individual records. After screening titles and abstracts, 24 articles were reviewed in full text, and ultimately, 18 studies were included in the meta-analysis (figure 1).

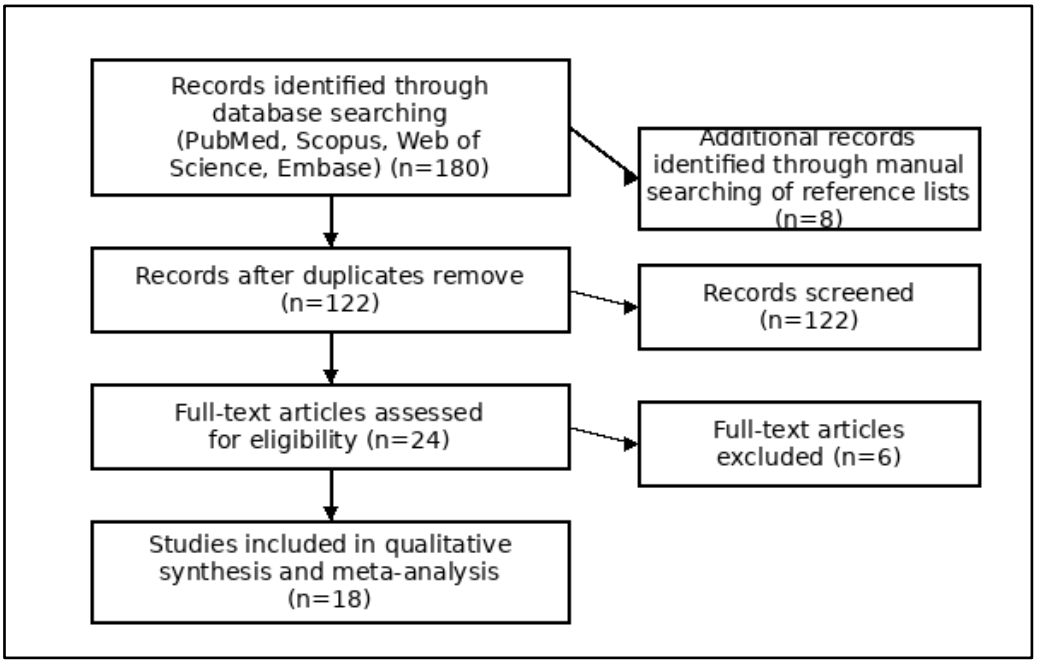

Figure 1. Flow chart for study search and selection methods

As depicted in Table 1, wide variations were observed in the patterns of bacterial susceptibility to antibiotics between different studies. Despite variation in geographic locations, study populations, and antimicrobial panels some trends did emerge. Frequent reporting of gram-negative pathogens as major causative organisms were seen in the present study and highlighted multiple reports on particular Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae and Proteus spp. Pathogens were generally highly susceptible to most aminoglycosides (amikacin and gentamicin), fluoroquinolones (ciprofloxacin and levofloxacin) carbapenems and colistin. There was however high degree of resistance to commonly-prescribed antibiotics such as ampicillin, penicillin, tetracycline and some cephalosporins. Likewise, significant resistance to penicillins and related β-lactam antibiotics was also evaluated by Gram-positive bacteria. Several reports had noted methicillin-resistant S. aureus (MRSA) strains. However, susceptibility to aminoglycosides and some broad-spectrum agents remained relatively preserved in multiple studies. The results have also shown that Haemophilus influenzae and Streptococcus pneumoniae showed increasing resistance, especially to drug classes such as ampicillin and penicillin respectively. A major point of interest is the emergence of multidrug-resistant (MDR) isolates, which have been frequently reported across multiple studies. Resistance mainly occurred to commonly used first-line antibiotics and reserve antibiotics (eg, colistin, carbapenems, amikacin) remained highly efficacious. Such patterns suggest that needless or prolonged use of antibiotics may be playing a role in the selection and spread of resistant strains of bacteria.

Table 1. Main Characteristics of Eligible Studies indicating the antibiotic used in the studies, the sensitive bacteria and the resistance bacteria

Ref.	Antibiotic Used	Sensitive Bacteria	Resistant Bacteria
[35]	Ciprofloxacin, Amikacin, Gentamicin, Penicillins, Tetracyclines, Sulfonamides	*S. aureus*, *P. aeruginosa*	All isolates showed mixed resistance to Penicillins, Tetracyclines, and Sulfonamides
[36]	Ciprofloxacin, Gentamicin, Ampicillin, Ceftriaxone, Amoxicillin, Tetracycline	Majority of isolates (including *Proteus* spp. and *S. aureus*)	*Proteus* spp., *S. aureus*, *Pseudomonas* spp. (to Ampicillin, Ceftriaxone, Amoxicillin, Tetracycline)

[37]	Tetracycline, Penicillins, Erythromycin, Co-trimoxazole, Fluoroquinolones, Aminoglycosides	GPB (Vancomycin, Gentamicin); GNB (Ciprofloxacin, Norfloxacin, Ceftriaxone)	*S. aureus*, *Proteus* spp., *Pseudomonas* spp. (to Tetracycline, Penicillins, Macrolides)
[38]	Amikacin, Levofloxacin, Amoxicillin-clavulanate, Penicillin, Erythromycin, Cloxacillin	All tested isolates	*S. aureus* (Penicillin, Erythromycin, Cloxacillin); *P. aeruginosa* (Ceftazidime)
[39]	Piperacillin-tazobactam, Tobramycin, Ampicillin, Tetracycline, Penicillin	*E. coli*, *P. aeruginosa*, *K. pneumoniae*	*S. aureus* (MRSA), *E. coli* (to Ampicillin, Tetracycline, Penicillin)
[40]	Ampicillin, Amoxicillin, Amoxicillin-clavulanic acid	*H. influenzae*, *S. pneumoniae*	*H. influenzae* (Ampicillin); *S. pneumoniae* (intermediate Penicillin resistance)
[41]	Ciprofloxacin, Gentamicin, Chloramphenicol, Ampicillin, Penicillin, TMP-SMX	*S. aureus*, *P. mirabilis*, *S. pneumoniae*	*S. aureus*, *E. coli*, *Klebsiella* spp. (to Ampicillin, Penicillin, TMP-SMX)
[42]	Amikacin, Levofloxacin, Ciprofloxacin, Amoxyclav, 3rd Gen Cephalosporins	*P. aeruginosa*, *S. aureus*, *K. pneumoniae*	Majority of common isolates (to Amoxyclav, 3rd Gen Cephalosporins, Ciprofloxacin)
[43]	Common first-line antibiotics	*P. aeruginosa* (predominant)	Majority of isolates (high resistance to common first-line antibiotics)
[44]	Quinolones	OME, COM, and Chole OM isolates	*S. aureus* (MRSA) and *P. aeruginosa* (resistance to Quinolones increased)
[45]	Amikacin, Cefepime, Ciprofloxacin, Meropenem, Ampicillin, Cefuroxime	*P. aeruginosa*, *K. pneumoniae*, *P. mirabilis*, *S. aureus*	*E. coli*, *M. morganii*, *S. marcescens*, *Citrobacter* spp. (to Ampicillin, Cefuroxime, Amc)
[46]	Colistin, Ceftazidime, Cefepime, Imipenem, Ceftriaxone, Cefpodoxime	*P. aeruginosa*	*P. aeruginosa* (to Ceftriaxone, Cefpodoxime)
[47]	Tobramycin, Ciprofloxacin, Cefuroxime, Ceftazidime, TMP-SMX, Penicillin, Ampicillin	Majority of isolates	*S. aureus*, *P. aeruginosa*, *Enterococcus* spp. (to TMP-SMX, Penicillin, Ampicillin)
[48]	Colistin, Imipenem, Meropenem, Piperacillin, Ceftazidime, Cefepime	*P. aeruginosa* (Colistin, Carbapenems)	*P. aeruginosa* (to Piperacillin, Ceftazidime, Cefepime)
[49]	Ciprofloxacin, Ceftriaxone, Chloramphenicol, Amoxicillin-clavulanic acid, Ampicillin	*P. aeruginosa*, *S. aureus*, *Proteus* spp.	*P. aeruginosa*, *S. aureus*, *Proteus* spp. (to Amc, Ampicillin, Penicillin, Oxacillin)
[50]	Ceftazidime, Ciprofloxacin, Gentamicin, Amikacin, Penicillin, Tetracycline	Gram-negative isolates (majority)	*S. aureus* (Penicillin, Tetracycline); GNB (Amoxicillin/Clavulanic acid, Ampicillin)
[51]	Gentamicin, Amikacin, Amoxyclav, Ceftazidime, Oxacillin, Ampicillin	*Pseudomonas* sp., *Klebsiella* sp., *E. coli*, *Proteus* sp., *MRSA*	*Pseudomonas* (Ceftazidime); *K. pneumoniae* / *E. coli* (Amoxyclav); *MRSA* (Oxacillin)
[52]	Piperacillin/Tazobactam, Amikacin, Penicillin, Ciprofloxacin	*P. aeruginosa*, *S. aureus*, *Pneumococci*	*S. aureus* (Penicillins, 1st gen Cephalosporins); *P. aeruginosa* (Fluoroquinolones)

The pathogenic bacteria to be included in the studies above, is represented through their association with antimicrobial resistance constitute Pseudomonas aeruginosa (Table 2). The finding supports its well-established intrinsic and acquired resistance mechanisms such as efflux pumps,

biofilm formation and outer membrane permeability factors. Staphylococcus aureus, notably methicillin-resistant strains (MRSA), was similarly associated with resistance, indicative of its endemic β-lactam and multi-class antibiotic resistance. Among Gram-negative non fermenters, Escherichia coli and Klebsiella pneumoniae exhibited significant resistance rates, particularly to ampicillin, amoxicillin-clavulanic acid and the selected cephalosporins. Compared with Lactobacillus and Bacteroides, Proteus species showed intermediate degrees of resistance; on the other hand, Haemophilus influenzae and Streptococcus pneumoniae were significantly less resistant (still significant) than non fermenters (amoxicillin-clavulanate-aciduric and penicillin-based agents). Of the pathogens reported, Enterococcus species had the weakest association with resistance but still displayed resistance to many traditional antibiotics.

Table 2. Association between the diagnosed bacterial species and antibiotic resistance

Bacterial Species		Unstandardized β Estimate (95% CI)	p-value
Pseudomonas aeruginosa	0.78	0.84 (0.69–0.99)	<0.001
Staphylococcus aureus	0.74	0.79 (0.63–0.95)	<0.001
Escherichia coli	0.68	0.71 (0.54–0.88)	0.002
Klebsiella pneumoniae	0.63	0.65 (0.48–0.82)	0.004
Proteus spp.	0.59	0.58 (0.40–0.76)	0.008
Haemophilus influenzae	0.47	0.46 (0.24–0.68)	0.021
Streptococcus pneumoniae	0.42	0.39 (0.18–0.60)	0.034
Enterococcus spp.	0.38	0.34 (0.11–0.57)	0.047

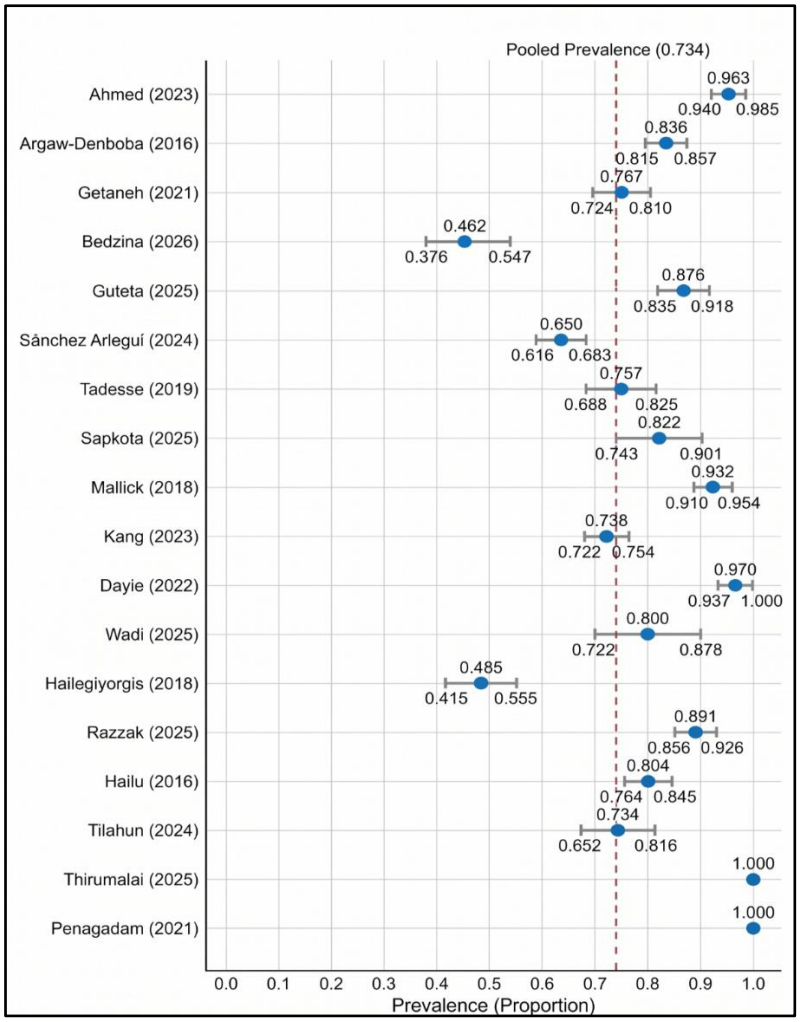

Figure 2. Forest plot of individual study effect sizes showing the rate of antibiotic resistance in otitis media

Table 3 shows the pooled meta-analysis resulted in a statistically significant overall antibiotic resistance rate of bacterial isolates related to otitis media. The pooled meta-analysis demonstrated that the overall prevalence of antibiotic resistance among bacterial isolates associated with otitis media was 61% (pooled prevalence = 0.61; 95% CI: 0.54–0.68; P < 0.001). Such analysis concluded that around 61% of bacterial pathogens found across the studies investigated showed resistance to typically-used antimicrobial agents. There was substantial between-study heterogeneity (I^2 = 72.4%) in the analysis of subpopulations, likely due to geographic locations, distribution of bacterial species, antibiotic prescribing practices and laboratory methods among studies included. This heterogeneous distribution resulted in a non-significant overall median resistance burden, which nevertheless highlights the consistent nature of the observed burden across sites. Moreover, Egger's test did not provide statistically significant evidence of funnel plot asymmetry; however, the ability of the test to detect publication bias was limited by the small number of studies and substantial heterogeneity.

Table 3. Summary of pooled meta-analysis results for the rate of antibiotic resistance in otitis media

	Egger's Test (p-value)	Pooled Prevalence	95% Confidence Interval	Heterogeneity (I^2)	P-value for Overall Effect
Antibiotic Resistance	0.184	0.61	[0.54–0.68]	72.40%	<0.001 (HS)

HS : High Significant at P value <0.01

Discussion

This systematic review and meta-analysis synthesized evidence from different geographical settings investigating antibiotic resistance among bacterial pathogens associated with otitis media. The pooled analysis showed a high overall antibiotic resistance rate of 61% (95% CI: 54%–68%), which means more than half of the bacterial isolates recovered from cases of otitis media are resistant to commonly prescribed antimicrobial agents. Similarly, high heterogeneity (I^2 = 72.4%) between studies indicates a wide variation in resistance profiles among populations, bacterial species and levels of healthcare.

The high incidence of the antimicrobial resistance observed in this review conforms with global apprehensions with reference to the declining efficacy of traditional antibiotics for treating ear infections [53]. Many included studies reported high prevalence of resistance to penicillins, tetracyclines, sulfonamides, and first-generation cephalosporins. With regard to other antibiotics, Ahmed [35] found that all isolates from chicken faeces showed a mixed susceptibility pattern to the penicillins, tetracyclines and sulfonamides. found high level of resistance for *Staphylococcus aureus* [44][54], *Proteus* species and *Pseudomonas* species against tetracycline–based and penicillin–based therapies [41][37]. found that *S. aureus, Escherichia coli* and *Klebsiella* species demonstrated elevated resistance levels against ampicillin, penicillin and trimethoprim-sulfamethoxazole. Overall, these findings indicate that the antibiotics long considered first-line therapies are on a downward trajectory of efficacy [6].

Only two bacterial pathogens were designated in this study, which included *Staphylococcus aureus* and *Pseudomonas aeruginosa* as the most reported resistant organisms [55]. Multiple studies in the review emphasized that S. aureus including MRSA has multidrug resistance (MDR) capabilities against several classes of antibiotics. Also, the increase in beta-lactam antibiotic resistance was recurrently described among S. aureus isolates in other studies and is consistent with the global spread of MRSA strains [39][51]. Similarly, *P. aeruginosa* showed high resistance to ceftazidime, cefepime and piperacillin (Table 1). Findings similar to those of other researchers including [48][46] were confirmed by 74.7-100% carbapenems resistance in *P. aeruginosa* isolates although colistin and carbapenems still remained the most efficient antimicrobials agent against them. The relentless emergence of multidrug-resistant P. aeruginosa is particularly alarming due to its inherent resistance

mechanisms and ability to obtain additional resistance determinants from environmental reservoirs by horizontal gene transfer.

While, in contrast, multiple studies showed retained susceptibility to aminoglycosides and fluoroquinolones. The overall higher efficacy was consistent for all concentrations against Gram-positive organisms and the similarly resistant Gram-negative organisms where amikacin, gentamicin ciprofloxacin and levofloxacin were found more active than moxifloxacin. High sensitivity rates to amikacin and fluoroquinolones in prevalent otitis media pathogens have been reported [56][47][45][42][38]. Likewise, also retained ciprofloxacin and tobramycin as some of the most active agents against bacterial isolates. It can be concluded that aminoglycosides and fluoroquinolones still remain good alternatives in the treatment of these infections, but their use must be cautious so as to avoid emergence of resistance [57].

The heterogeneity observed among studies is probably due to differences in bacterial epidemiology, local prescribing practices, healthcare infrastructure and antimicrobial stewardship programs. Significant variation between studies may also be due to differences in laboratory methods, clinical characteristics of the patient populations, and disease classification. This is consistent with the previously reported similar high levels of heterogeneity in systematic reviews targeting antimicrobial resistance in respiratory infections and ear infections, underlining their multivariate nature and the difficulty determining where resistance arises [58][13][59].

The Egger statistic did not indicate significant publication bias ($p = 0.184$) which adds to the confidence in the pooled estimate This finding confirms that both positive and negative studies were well represented in the analysis, suggesting a likely absence of publication bias inflating the overall effect size via selective reporting. Thus, the pooled resistance estimate should reflect current trends in resistance among pathogens of otitis media.

These results have important clinical implications. The significantly high resistance rates found for the most commonly prescribed antibiotics indicate that, whenever possible, empirical treatment strategies should be informed by local susceptibility data. Laboratory protocols to characterize pathogens associated with infection and antibiotic susceptibility testing (AST) should be standard practice, especially for recurrent or chronically symptomatic cases that show no improvement after initial treatment [60]. Furthermore, ASPs should target the reduction of unnecessary antibiotic prescribing along with promoting evidence-based prescribing. These types of interventions are important to reduce the selective pressure and delay the emergence of resistant strains.

This review has numerous strengths, including the consideration of studies from multiple regions and employing quantitative meta-analytic methods to calculate pooled resistance rates. But there are few limitations that have to be kept in minds. There was wide heterogeneity between studies, and not all studies examined the same bacterial types or antibiotic panels. In addition, resistance patterns can evolve over time and findings from older studies may not be generalizable. Standardization of surveillance systems and longitudinal follow-up of resistance trends in otitis media pathogens should be priorities for future work.

Conclusion

This meta-analysis shows the considerable burden of antibiotic resistance in bacterial pathogens causing otitis media. *Staphylococcus aureus* and *Pseudomonas aeruginosa* were identified as the most common resistant organisms, whereas aminoglycosides and fluoroquinolones retained higher efficacy in general. These findings highlight the urgent need for ongoing resistance surveillance, appropriate empirical antibiotic prescribing practices and more robust antimicrobial stewardship strategies to ensure the continued clinical efficacy of these important therapeutic agents and for optimizing patient outcomes.

REFERENCES

[1] A. A. Elmanama, N. E. A. Tayyem, and S. A. N. Allah, “The bacterial etiology of otitis media and their antibiogram among children in Gaza Strip, Palestine,” Egypt. J. Ear Nose Throat Allied Sci., vol. 15, no. 2, pp. 87–91, 2014.

[2] F. Prestinaci, P. Pezzotti, and A. Pantosti, “Antimicrobial resistance: A global multifaceted phenomenon,” Pathog. Glob. Health, vol. 109, no. 7, pp. 309–318, 2015.

[3] L. Hall-Stoodley, J. W. Costerton, and P. Stoodley, “Bacterial biofilms: From the natural environment to infectious diseases,” Nat. Rev. Microbiol., vol. 2, no. 2, pp. 95–108, 2004.

[4] E. Leibovitz and D. Greenberg, “Acute otitis media in children: Current epidemiology, microbiology, clinical manifestations, and treatment,” Chang Gung Med. J., vol. 27, no. 7, pp. 475–488, 2004.

[5] M. Khairkar, P. Deshmukh, H. Maity, V. Deotale, and N. V. Maggon, “Chronic suppurative otitis media: A comprehensive review of epidemiology, pathogenesis, microbiology, and complications,” Cureus, vol. 15, no. 8, 2023.

[6] E. C. Schuts, M. E. Hulscher, J. W. Mouton, C. M. Verduin, J. W. C. Stuart, H. W. Overdiek, P. D. van der Linden, S. Natsch, C. M. Hertogh, and T. F. Wolfs, “Current evidence on hospital antimicrobial stewardship objectives: A systematic review and meta-analysis,” Lancet Infect. Dis., vol. 16, no. 7, pp. 847–856, 2016.

[7] J. R. Casey and M. E. Pichichero, “Changes in frequency and pathogens causing acute otitis media in 1995–2003,” Pediatr. Infect. Dis. J., vol. 23, no. 9, pp. 824–828, 2004.

[8] A. Schafenacker and J. Singh, “Hematuria in a 7-year-old internationally adopted male,” Pediatr. Infect. Dis. J., vol. 39, no. 10, pp. 979–981, 2020.

[9] R. Kaur, M. Morris, and M. E. Pichichero, “Epidemiology of acute otitis media in the postpneumococcal conjugate vaccine era,” Pediatrics, vol. 140, no. 3, Art. no. e20170181, 2017.

[10] V. K. Leung et al., “Influenza vaccination responses: Evaluating impact of repeat vaccination among health care workers,” Vaccine, vol. 35, no. 19, pp. 2558–2568, 2017.

[11] R. E. Lewis et al., “Comparative analysis of amphotericin B lipid complex and liposomal amphotericin B kinetics of lung accumulation and fungal clearance in a murine model of acute invasive pulmonary aspergillosis,” Antimicrob. Agents Chemother., vol. 51, no. 4, pp. 1253–1258, 2007.

[12] S. Hullegie et al., “Prevalence and antimicrobial resistance of bacteria in children with acute otitis media and ear discharge: A systematic review,” Pediatr. Infect. Dis. J., vol. 40, no. 8, pp. 756–762, 2021.

[13] G. Fernandez, “Turning the juggernaut,” Lancet Microbe, vol. 3, no. 6, p. E75, 2022.

[14] N. Umoh, B. Osibu, A. Eyo, V. Usanga, M. Mbah, and A. Asuquo, "Prevalence and antibiotic-resistance indices of bacterial pathogens of otitis media among patients attending a tertiary hospital in Calabar, Nigeria," Int. J. Trop. Dis. Health, vol. 44, no. 12, pp. 16–23, 2023.

[15] World Health Organization, Antimicrobial Resistance: Global Report on Surveillance. Geneva, Switzerland: WHO, 2021. Available: https://www.who.int/publications/i/item/9789241564748.

[16] L. Monasta et al., “Burden of disease caused by otitis media: Systematic review and global estimates,” PLoS One, vol. 7, no. 4, Art. no. e36226, 2012.

[17] J. O'Neill, *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. London, U.K.: Review on Antimicrobial Resistance, 2016.

[18] N. D. Dombrowski et al., “Mucoepidermoid carcinoma of the head and neck in children,” Int. J. Pediatr. Otorhinolaryngol., vol. 120, pp. 93–99, 2019.

[19] A. Vergison et al., "Otitis media and its consequences: Beyond the earache," Lancet Infect. Dis., vol. 10, no. 3, pp. 195–203, 2010.

[20] S. Tristram, M. R. Jacobs, and P. C. Appelbaum, "Antimicrobial resistance in Haemophilus influenzae," Clin. Microbiol. Rev., vol. 20, no. 2, pp. 368–389, 2007.

[21] P. S. Stewart and J. W. Costerton, “Antibiotic resistance of bacteria in biofilms,” Lancet, vol. 358, no. 9276, pp. 135–138, 2001.

[22] T. T. Lao, M. K. Chung, T. Cheung, and L. W. Law, "Antenatal hepatitis B and increased risk of gestational diabetes mellitus: Implications for obstetric care," J. Infect., vol. 72, no. 5, pp. 625–626, 2016.

[23] L. Onorato, M. Macera, F. Calò, C. Monari, F. Russo, M. R. Iovene, G. Signoriello, R. Annibale, M. C. Pace, and C. Aurilio, "The effect of an antimicrobial stewardship programme in two intensive care units of a teaching hospital: An interrupted time series analysis," Clin. Microbiol. Infect., vol. 26, no. 6, pp. 782.e1–782.e6, 2020.

[24] P. D. Tamma et al., "Comparing the activity of novel antibiotic agents against carbapenem-resistant Enterobacterales clinical isolates," Infect. Control Hosp. Epidemiol., vol. 44, no. 5, pp. 762–767, 2023.

[25] A. Hoberman et al., "Treatment of acute otitis media in children under 2 years of age," N. Engl. J. Med., vol. 364, no. 2, pp. 105–115, 2011.

[26] T. Chonmaitree et al., "Acute otitis media and other complications of viral respiratory infection," Pediatrics, vol. 137, no. 4, Art. no. e20153555, 2016.

[27] M. L. Wernroth et al., "Early childhood antibiotic treatment for otitis media and other respiratory tract infections is associated with risk of type 1 diabetes: A nationwide register-based study with sibling analysis," Diabetes Care, vol. 43, no. 5, pp. 991–999, 2020.

[28] S. I. Pelton and E. Leibovitz, "Recent advances in otitis media," Pediatr. Infect. Dis. J., vol. 28, no. 10, pp. S133–S137, 2009.

[29] R. E. El Feghaly, A. Nedved, S. E. Katz, and H. M. Frost, "New insights into the treatment of acute otitis media," Expert Rev. Anti Infect. Ther., vol. 21, no. 5, pp. 523–534, 2023.

[30] M. J. Page, J. E. McKenzie, P. M. Bossuyt, I. Boutron, T. C. Hoffmann, C. D. Mulrow, L. Shamseer, J. M. Tetzlaff, E. A. Akl, and S. E. Brennan, "The PRISMA 2020 statement: An updated guideline for reporting systematic reviews," BMJ, vol. 372, p. n71, 2021.

[31] E. Gualdi-Russo and L. Zaccagni, "The Newcastle–Ottawa Scale for Assessing the Quality of Studies in Systematic Reviews," Publications, vol. 14, no. 1, p. 4, 2026.

[32] J. P. Higgins, S. G. Thompson, J. J. Deeks, and D. G. Altman, "Measuring inconsistency in meta-analyses," BMJ, vol. 327, no. 7414, pp. 557–560, 2003.

[33] M. Egger, G. Davey Smith, M. Schneider, and C. Minder, "Bias in meta-analysis detected by a simple, graphical test," BMJ, vol. 315, no. 7109, pp. 629–634, 1997.

[34] J. A. Sterne, A. J. Sutton, J. P. Ioannidis, N. Terrin, D. R. Jones, J. Lau, J. Carpenter, G. Rücker, R. M. Harbord, and C. H. Schmid, "Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials," BMJ, vol. 343, p. d4002, 2011.

[35] S. Ahmed, "Antibiotic susceptibility patterns of isolated bacteria from otitis media in children at Mohamed Aden Sheikh Children Teaching Hospital in Hargeisa, Somaliland," J. Biosci. Med., vol. 11, no. 6, 2023, Art. no. 10.4236.

[36] A. Argaw-Denboba, A. A. Abejew, and A. G. Mekonnen, "Antibiotic-resistant bacteria are major threats of otitis media in Wollo Area, Northeastern Ethiopia: A ten-year retrospective analysis," Int. J. Microbiol., vol. 2016, Art. no. 8724671, 2016.

[37] A. Getaneh, G. Ayalew, D. Belete, M. Jemal, and S. Biset, "Bacterial etiologies of ear infection and their antimicrobial susceptibility pattern at the University of Gondar Comprehensive Specialized Hospital, Gondar, Northwest Ethiopia: A six-year retrospective study," Infect. Drug Resist., vol. 14, pp. 4313–4322, 2021.

[38] I. Bedzina et al., "Bacterial agents of otitis media and their antibiotic resistance profile: A retrospective clinical presentation at St. Dominic Hospital, Akwatia, Ghana," BMC Microbiol., vol. 26, no. 1, p. 98, 2026.

[39] E. T. Guteta, F. A. Abdi, S. G. Feyisa, B. S. Kinfu, and T. B. Tafesse, "Bacterial etiologies, antimicrobial susceptibility profiles and associated factors among patients with otitis media referred to Nekemte Public Health Research and Referral Laboratory Center, Western Ethiopia: A cross-sectional study," BMC Microbiol., vol. 25, no. 1, p. 6, 2025.

[40] A. S. Arlegui, J. D. A. Rodríguez, X. D. V. Vázquez, M. G. Rodrigo, I. Gangoiti, and S. Mintegi, "Bacterial pathogens and antimicrobial resistance in acute otitis media," An. Pediatr. (Engl. Ed.), vol. 100, no. 3, pp. 173–179, 2024.

[41] B. Tadesse, T. Shimelis, and M. Worku, “Bacterial profile and antibacterial susceptibility of otitis media among pediatric patients in Hawassa, Southern Ethiopia: Cross-sectional study,” BMC Pediatr., vol. 19, no. 1, p. 398, 2019.

[42] A. Sapkota, B. Aryal, R. Bhandari, S. Lohani, S. S. Panta, and A. Sapkota, “Bacteriological profile of chronic suppurative otitis media and antibiotic susceptibility in a tertiary care centre of Central Nepal,” J. Bharatpur Hosp., vol. 1, no. 2, pp. 112–118, 2025.

[43] A. Mallick, H. Sharma, A. K. Mishra, N. V. Maggon, and A. Sethi, “Bacteriological profile and antibiotic resistance in cases of chronic otitis media and its clinical implications,” Int. J. Otorhinolaryngol. Head Neck Surg., vol. 4, no. 4, pp. 918–922, 2018.

[44] M. Z. David and R. S. Daum, “Community-associated methicillin-resistant Staphylococcus aureus: Epidemiology and clinical consequences of an emerging epidemic,” Clin. Microbiol. Rev., vol. 23, no. 3, pp. 616–687, 2010.

[45] N. T. Dayie, V. Bannah, F. P. Dwomoh, F. C. Kotey, and E. S. Donkor, “Distribution and antimicrobial resistance profiles of bacterial aetiologies of childhood otitis media in Accra, Ghana,” Microbiol. Insights, vol. 15, Art. no. 11786361221104446, 2022.

[46] F. R. Wadi and M. K. Ali, "Isolation and antibiotic sensitivity testing of Pseudomonas aeruginosa isolates from patients with chronic suppurative otitis media in Baghdad," Ibn Al-Haitham J. Pure Appl. Sci., vol. 38, no. 1, pp. 27–36, 2025.

[47] T. T. Hailegiyorgis, W. D. Sarhie, and H. M. Workie, “Isolation and antimicrobial drug susceptibility pattern of bacterial pathogens from pediatric patients with otitis media in selected health institutions, Addis Ababa, Ethiopia: A prospective cross-sectional study,” BMC Ear Nose Throat Disord., vol. 18, no. 1, p. 8, 2018.

[48] S. Razzak, M. Sohail, F. Uddin, and M. R. Dogar, “Antimicrobial resistance patterns in Pseudomonas aeruginosa isolated from chronic suppurative otitis media,” J. Coll. Physicians Surg. Pak., vol. 35, no. 7, pp. 866–871, 2025.

[49] D. Hailu, D. Mekonnen, A. Derbie, W. Mulu, and B. Abera, “Pathogenic bacteria profile and antimicrobial susceptibility patterns of ear infection at Bahir Dar Regional Health Research Laboratory Center, Ethiopia,” SpringerPlus, vol. 5, no. 1, p. 466, 2016.

[50] M. Tilahun et al., "Prevalence of bacterial ear infections and multidrug resistance patterns among ear infection suspected patients in Ethiopia: A systematic review and meta-analysis," BMC Infect. Dis., vol. 24, no. 1, p. 1358, 2024.

[51] K. Thirumalai, S. Rajalakshmi, S. Rani, M. Pharm, and B. Swaminathan, "Prescribing pattern versus antibiotic sensitivity and outcome of antibiotic usage in patients with chronic suppurative otitis media at tertiary care hospital," Int. J. Pharm. Res. Appl., vol. 10, no. 3, pp. 930–938, 2025.

[52] C. Penagadam, Y. D. C. Yadav, and C. Srinivasarao, “Prevalence and antibiotic susceptibility of bacterial pathogens in children with acute otitis media: A retrospective study at a tertiary care teaching hospital, India,” Schol. Acad. J. Pharm., vol. 10, no. 4, pp. 77–81, 2021.

[53] M. Umar, R. M. Orakzai, A. Khan, M. Idrees, A. A. Khan, and R. Syed, "Prevalent bacteria and antibiotic resistance patterns in otitis media cases: A retrospective analysis from a tertiary care hospital in Islamabad," Indian J. Otolaryngol. Head Neck Surg., pp. 1–8, 2026.

[54] S. Y. Tong, J. S. Davis, E. Eichenberger, T. L. Holland, and V. G. Fowler Jr., "Staphylococcus aureus infections: Epidemiology, pathophysiology, clinical manifestations, and management," Clin. Microbiol. Rev., vol. 28, no. 3, pp. 603–661, 2015.

[55] Z. Pang, R. Raudonis, B. R. Glick, T. J. Lin, and Z. Cheng, “Antibiotic resistance in Pseudomonas aeruginosa: Mechanisms and alternative therapeutic strategies,” Biotechnol. Adv., vol. 37, no. 1, pp. 177–192, 2019.

[56] K. Drlica and X. Zhao, “DNA gyrase, topoisomerase IV, and the 4-quinolones,” Microbiol. Mol. Biol. Rev., vol. 61, no. 3, pp. 377–392, 1997.

[57] D. C. Hooper and G. A. Jacoby, “Mechanisms of drug resistance: Quinolone resistance,” Ann. N. Y. Acad. Sci., vol. 1354, no. 1, pp. 12–31, 2015.

[58] Antimicrobial Resistance Collaborators, “Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis,” Lancet, vol. 399, no. 10325, pp. 629–655, 2022.

[59] I. Khan, M. Osama, I. Ullah, and I. U. Haq, "Microbiological spectrum and antibiotics sensitivity pattern of chronic suppurative otitis media (CSOM) patients: A prospective study from a tertiary care hospital in Peshawar," Pak. J. Med. Sci., vol. 41, no. 1, p. 194, 2025.

[60] M. A. Wikler, Performance Standards for Antimicrobial Susceptibility Testing: Seventeenth Informational Supplement. Wayne, PA, USA: Clinical and Laboratory Standards Institute, 2007.