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Clinicopathological Profile of Chronic Suppurative Otitis Media and Antimicrobial Utilization Patterns.

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Abstract

Background: Chronic Suppurative Otitis Media (CSOM) remains a primary cause of preventable hearing impairment and permanent otologic morbidity worldwide, particularly in low and middle-income countries. Effective management requires a clear understanding of its distinct clinical phenotypes, underlying tissue pathology, and microbiological etiology. However, empirical antibiotic overuse and rising antimicrobial resistance (AMR) increasingly complicate clinical outcomes. ***Objective:*** To evaluate the clinicopathological spectrum of mucosal and squamosal CSOM, characterize the predominant microbiological pathogens and their resistance profiles, and analyze real-world antimicrobial utilization patterns relative to culture-sensitivity evidence. ***Methods:*** A 36-month prospective observational cohort study was conducted with 320 adult and pediatric patients presenting with active CSOM at a tertiary academic medical center. Patients were categorized clinically into mucosal (safe) and squamosal (unsafe) CSOM. Ear discharge samples were collected for bacterial and fungal culture and antimicrobial susceptibility testing (AST). Tissue specimens obtained during tympanoplasty, ossiculoplasty, or mastoidectomy (n=176) underwent quantitative histopathological evaluation. Antimicrobial utilization was quantified using the World Health Organization Anatomical Therapeutic Chemical (ATC) classification and Defined Daily Dose (DDD) methodologies. ***Results:*** Of 320 enrolled patients, 192 (60.0%) presented with mucosal CSOM and 128 (40.0%) with squamosal CSOM. The primary clinical presentation was persistent otorrhea (100%) and conductive hearing loss (89.1%; mean pure-tone average air-bone gap 33.6±10.8 dB). Microbiological culture yielded positive growth in 284 cases (88.8%), dominated by *Pseudomonas aeruginosa* (42.3%) and *Staphylococcus aureus* (28.2%, with 32.5% MRSA). Histopathological examination revealed cholesteatoma matrix in 40.3% of surgical cases, dense granulation tissue in 52.8%, and osteitis with ossicular erosion in 35.8%. Prior to tertiary consultation, empirical antimicrobial therapy had been prescribed in 83.8% of patients, with broad-spectrum oral fluoroquinolones and oral β-lactams accounting for the highest consumption. Crucially, empirical antibiotic regimens exhibited a 45.1% discordance rate with laboratory-confirmed susceptibility patterns. Post-culture transition to targeted topical ciprofloxacin/dexamethasone drops combined with surgical ear clearance achieved an overall disease control rate of 92.5% at 6-month follow-up. ***Conclusion:*** CSOM exhibits significant tissue-level structural pathology, including osteitis and ossicular destruction, driven by refractory pathogens like *P. aeruginosa* and *S. aureus*. Widespread empirical systemic antibiotic overuse without prior culture sensitivity remains a critical driver of treatment failure and local resistance. Incorporating early microbiological profiling, targeted topical otic therapies, and timely surgical intervention is essential to optimize patient outcomes and reinforce antimicrobial stewardship.

Keywords: Chronic Suppurative Otitis Media; Cholesteatoma; Microbiological Profile; Antimicrobial Resistance; Drug Utilization; Osteitis; Tympanoplasty.

INTRODUCTION

Chronic Suppurative Otitis Media (CSOM) is defined as a chronic, persistent inflammation of the middle ear cleft and mastoid cavity, characterized by recurrent or continuous otorrhea through a perforated tympanic membrane lasting longer than 2 to 6 weeks [1]. According to World Health Organization (WHO) estimates, CSOM affects over 65 to 330 million individuals globally, with 60% suffering from significant associated hearing impairment [2]. The disease burden falls

disproportionately on developing regions due to factors such as overcrowded living conditions, poor hygiene, nutritional deficiencies, and limited access to specialized otolaryngological care [3].

Classically, CSOM is categorized into two distinct clinical phenotypes:

1. **Mucosal CSOM (Safe/Tubotympanic):** Characterized by a central tympanic membrane perforation, inflamed middle ear mucosa, and a low risk of intracranial complications [4].
2. **Squamosal CSOM (Unsafe/Atticoantral):** Characterized by marginal or attic perforations, retraction pockets, keratinizing squamous epithelium (cholesteatoma), and progressive osteolytic bone destruction that poses a severe risk of intra- and extracranial complications (e.g., facial nerve palsy, labyrinthitis, brain abscess, and lateral sinus thrombosis) [5].

Pathologically, chronic middle ear inflammation induces profound tissue alterations, including mucosal hyperplasia, submucosal fibrosis, cholesterol granuloma formation, dense granulation tissue, and osteitis of the temporal bone and ossicular chain [6]. These structural changes create sheltered microenvironments that impair local blood flow, impede drug delivery, and foster polymicrobial biofilm formation [7].

The microbiological landscape of CSOM is complex and differs substantially from acute otitis media. Aerobic organisms such as *Pseudomonas aeruginosa* and *Staphylococcus aureus* predominate, alongside secondary facultative anaerobes and fungi [8]. Because *P. aeruginosa* produces protective extracellular polymeric substances (biofilms) and possesses intrinsic resistance mechanisms, eradicating these infections requires high local concentrations of antimicrobial agents [9].

Despite international consensus recommending topical otic drops (such as fluoroquinolones) as first-line medical therapy [10], real-world clinical management is frequently characterized by the empirical over-prescription of oral and systemic antibiotics [11]. Unguided systemic antimicrobial administration not only achieves poor drug concentrations within the avascular, osteotic middle ear microenvironment, but also accelerates the emergence of antimicrobial resistance (AMR), including methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant *Pseudomonas* species [12].

To date, few studies have comprehensively linked real-world drug utilization metrics with quantitative histopathological patterns and local microbiological resistance profiles in CSOM. This study was undertaken to evaluate the clinicopathological spectrum of CSOM, identify the predominant microbiological flora and their susceptibility profiles, and analyze drug utilization patterns to foster evidence-based antimicrobial stewardship and surgical decision-making.

MATERIALS AND METHODS

Study Design and Patient Selection

This prospective observational cohort study was conducted in the Department of Otorhinolaryngology, in collaboration with the Departments of Pharmacology and Pathology, at multiple tertiary care academic hospital over a 36-month period (January 2023 to December 2025). The protocol was approved by the Institutional Ethics Committee, and written informed consent was secured from all participants or their legal guardians prior to enrollment in accordance with the Declaration of Helsinki.

Inclusion Criteria:

- Patients of all ages presenting with active CSOM (continuous or intermittent otorrhea through a perforated tympanic membrane for >6 weeks).
- Patients scheduled for definitive medical therapy or surgical intervention (tympanoplasty, cortical mastoidectomy, or canal wall down/up mastoidectomy).
- Provision of informed consent and agreement to complete a 6-month follow-up schedule.

Exclusion Criteria:

- Acute otitis media or otitis externa without tympanic membrane perforation.
- Active malignant disease of the temporal bone or head and neck.
- Prior history of temporal bone radiation therapy.
- Systemic immunosuppression (e.g., end-stage renal disease, active chemotherapy, advanced HIV/AIDS).

Clinical and Otoneurological Evaluation

All patients underwent a standardized evaluation including detailed medical history, microscopic ear examination, rigid high-definition otoscopy (0° and 30°, 2.7 mm sinus scopes), and pure-tone audiometry (PTA). Air conduction (AC) and bone conduction (BC) thresholds were measured across standard frequencies (250 Hz to 8000 Hz), and the average Air-Bone Gap (ABG) was calculated for frequencies 500, 1000, 2000, and 4000 Hz. High-Resolution Computed

Tomography (HRCT) of the temporal bone was performed in all squamosal cases and select refractory mucosal cases to grade soft-tissue opacification, scutum erosion, ossicular chain status, and tegmental/sigmoid plate integrity.

Microbiological Sampling and Antimicrobial Susceptibility Testing

Prior to administering any fresh topical or systemic antimicrobial agents at our facility, active ear discharge was sampled under direct microscopic visualization using sterile fine-tipped Dacron swabs. To avoid contamination from the outer ear canal, care was taken not to touch the external auditory canal walls.

Swabs were immediately transported in Amies transport medium for processing:

- **Direct Microscopy:** Gram staining and Potassium Hydroxide (KOH) wet mounts for cellular and fungal evaluation.
- **Culture Isolation:** Inoculation onto Blood Agar, MacConkey Agar, and Sabouraud Dextrose Agar (SDA). Aerobic plates were incubated at **37°C** for 24–48 hours; SDA plates were incubated at **28°C** for up to 7 days.
- **Identification & Sensitivity:** Bacterial isolates were identified using standard biochemical methods and automated VITEK 2 systems. Antimicrobial susceptibility testing (AST) was performed via Kirby-Bauer disk diffusion method in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines [13].

Histopathological Evaluation

In patients undergoing surgical intervention (n = 176), tissue specimens (middle ear mucosa, granulation tissue, retraction pocket matrices, and diseased bone/ossicles) were preserved in 10% neutral buffered formalin, processed routinely, embedded in paraffin, sectioned at 4\ \mu\text{m}, and stained with Hematoxylin and Eosin (H&E). Masson's trichrome staining was utilized to assess fibrosis, and Verhoeff-Van Gieson stain was used for vascular structures.

Pathologists blinded to clinical prescription histories evaluated:

1. **Epithelial Changes:** Presence of keratinizing stratified squamous epithelium (cholesteatoma), glandular metaplasia, mucosal hyperplasia, or ulceration.
2. **Inflammatory Infiltrate:** Semi-quantitative scoring (0 = absent, 1 = mild, 2 = moderate, 3 = severe) of lymphocytes, plasma cells, neutrophils, and histiocytes.
3. **Submucosal Pathology:** Presence of foreign body giant cell reaction, cholesterol granuloma, fibrosis, and microvascular proliferation.
4. **Bone & Ossicular Remodeling (Osteitis):** Presence of osteoclastic activity, lacunar resorption, periosteal thickening, and avascular necrosis.

Drug Utilization Analysis

Complete pharmacological histories for the 6 months prior to tertiary presentation and throughout the 6-month postoperative follow-up were recorded [14]. Prescriptions were classified using the WHO Anatomical Therapeutic Chemical (ATC) classification system. Drug consumption patterns were evaluated for route of administration (topical vs. systemic), antibiotic spectrum, duration, and concordance with microbiological sensitivity results. Concordance was defined as the administration of an antimicrobial agent to which the isolated pathogen demonstrated *in vitro* susceptibility on AST.

Statistical Analysis

Sample size estimation indicated that 295 patients were required to detect a 15% difference in treatment response between concordant and discordant antimicrobial groups at 80% power ($\beta = 0.20$) and $\alpha = 0.05$.

Data were entered into Microsoft Excel and analyzed using SPSS version 28.0 (IBM Corp., Armonk, NY). Categorical variables were presented as frequencies and percentages and compared using the Pearson Chi-Square (χ^2) test or Fisher's exact test. Continuous variables were presented as mean ± standard deviation (SD) and compared using Independent Student's t-tests or Mann-Whitney U tests depending on distribution normality. Bivariate correlations were evaluated using Spearman's rank coefficient. Logistic regression models were built to identify independent clinical and histopathological risk factors for treatment failure and ossicular destruction. Adjusted Odds Ratios (aOR) with 95% Confidence Intervals (95% CI) were reported. p-values < 0.05 were considered statistically significant.

RESULTS

Patient Baseline Characteristics and Clinical Spectrum

A total of 320 patients were enrolled (178 males [55.6%], 142 females [44.4%]; age range 7 to 71 years, mean age 35.1 ± 14.8 years). Based on otoscopic and radiological features, 192 patients (60.0%) were diagnosed with Mucosal CSOM and 128 patients (40.0%) with Squamosal CSOM.

The baseline demographic, clinical, and radiological findings are summarized in Table 1. Unilateral disease was present in 248 patients (77.5%), while 72 (22.5%) had bilateral involvement. Otalgia was reported significantly more frequently in the squamosal group (43.0% vs. 18.8%; $p < 0.001$). The baseline mean pure-tone average Air-Bone Gap was 33.6 ± 10.8dB, with squamosal cases exhibiting significantly greater conductive hearing loss (39.8 ± 9.8dB) than mucosal cases

(29.4 ± 9.1 dB; $p < 0.001$). HRCT demonstrated bone erosion (scutum, ossicular chain, or mastoid air cells) in 112 out of 128 squamosal cases (87.5%) and in 21 out of 192 mucosal cases (10.9%).

Table 1. Baseline Demographics and Clinical Presentations Stratified by CSOM Subtype (N = 320)

Clinical Parameter	Total Cohort (N=320)	Mucosal CSOM (n=192)	Squamosal CSOM (n = 128)	p-value
Age (years), Mean ± SD	35.1 ± 14.8	33.6 ± 15.2	37.3 ± 13.9	0.026
Sex (Male / Female), n (%)	178 (55.6) / 142 (44.4)	104 (54.2) / 88 (45.8)	74 (57.8) / 54 (42.2)	0.521
Duration of Symptoms (years), Mean±SD	5.6 ± 4.2	5.0 ± 4.0	6.5 ± 4.4	0.002
Otorrhea Profile, n (%)				< 0.001
• Profuse / Mucopurulent / Inodorous	180 (56.3)	168 (87.5)	12 (9.4)	
• Scanty / Purulent / Foul-smelling	140 (43.8)	24 (12.5)	116 (90.6)	
Associated Otalgia, n (%)	91 (28.4)	36 (18.8)	55 (43.0)	< 0.001
Tympanic Perforation Pattern, n (%)				< 0.001
• Central (Small / Medium / Subtotal)	185 (57.8)	185 (96.4)	0 (0.0)	
• Marginal / Attic Retraction / Perforation	135 (42.2)	7 (3.6)	128 (100.0)	
Mean Air-Bone Gap (dB), Mean ± SD	33.6 ± 10.8	29.4 ± 9.1	39.8 ± 9.8	< 0.001
HRCT Bone Erosion Present, n (%)	133 (41.6)	21 (10.9)	112 (87.5)	< 0.001

Microbiological Isolation and Sensitivity Profiling

Microbiological analysis of ear swabs yielded positive cultures in 284 of 320 cases (88.8%). Monomicrobial growth was identified in 232 samples (72.5%), polymicrobial growth in 52 samples (16.3%), and 36 samples (11.3%) yielded no growth or normal skin flora.

As detailed in Table 2, *Pseudomonas aeruginosa* was the most frequently isolated pathogen (135 isolates, 42.2%), followed by *Staphylococcus aureus* (90 isolates, 28.1%). Among *S. aureus* isolates, 29 (32.2%) were confirmed as Methicillin-Resistant *S. aureus* (MRSA). Other gram-negative bacilli included *Proteus mirabilis* (8.1%), *Klebsiella pneumoniae* (5.3%), and *Escherichia coli* (3.4%). Fungal pathogens predominantly *Aspergillus niger* and *Candida albicans* were isolated in 32 cases (10.0%), primarily in patients with prolonged prior systemic antibiotic usage.

Antimicrobial Susceptibility Testing (AST) Highlights:

- ***Pseudomonas aeruginosa*:** Highest susceptibility was observed to Amikacin (91.9%), Piperacillin-Tazobactam (88.1%), and Ceftazidime (83.0%). Resistance to oral Ciprofloxacin was present in 28.9% of isolates.
- ***Staphylococcus aureus*:** Showed high susceptibility to Vancomycin (100%), Linezolid (100%), and Co-trimoxazole (78.9%). High rates of resistance were observed for Penicillin G (91.1%), Erythromycin (54.4%), and Ciprofloxacin (42.2%).

Table 2. Microbiological Profile and Resistance Rates of Isolated Pathogens (N = 320)

Microorganism Isolated	Frequency (n)	Percentage (%)	Key Resistance Profiles
Aerobic Gram-Negative Bacilli			
• Pseudomonas aeruginosa	135	42.20%	Ciprofloxacin R: 28.9%; Gentamicin R: 24.4%
• Proteus mirabilis	26	8.10%	Ampicillin R: 65.4%; Co-trimoxazole R: 42.3%
• Klebsiella pneumoniae	17	5.30%	Ceftriaxone R: 41.2%; Amoxicillin-Clavulanate R: 35.3%
• Escherichia coli	11	3.40%	Ciprofloxacin R: 54.5%; Ampicillin R: 81.8%
Aerobic Gram-Positive Cocci			
• Staphylococcus aureus (MSSA)	61	19.10%	Penicillin R: 88.5%; Erythromycin R: 45.9%
• Staphylococcus aureus (MRSA)	29	9.10%	Oxacillin/Cefoxitin R: 100%; Ciprofloxacin R: 65.5%
• Coagulase-Negative Staphylococci	14	4.40%	Erythromycin R: 57.1%
Fungal Pathogens			
• Aspergillus niger / flavus	23	7.20%	Amphotericin B Sensitive: 95.7%
• Candida albicans	9	2.80%	Fluconazole Sensitive: 88.9%
Sterile / Normal Skin Flora	36	11.30%	N/A

Abbreviations: *MSSA, Methicillin-Susceptible Staphylococcus aureus; MRSA, Methicillin-Resistant Staphylococcus aureus; R, Resistant.*

Histopathological Findings and Structural Correlates

A total of 176 surgical tissue sets (122 squamosal, 54 mucosal refractory cases) were processed for formal histopathology. As presented in Table 3, distinct structural patterns were identified across surgical specimens.

Squamous keratogenic matrix (cholesteatoma) was confirmed in 71 cases (40.3% of all surgical cases; 58.2% of squamosal surgical cases). Dense inflammatory granulation tissue characterized by marked microvascular proliferation and intense lymphoplasmacytic infiltration was observed in 93 cases (52.8%). Submucosal cholesterol granulomas—featuring foreign body giant cells surrounding lipid clefts—were present in 30 cases (17.0%).

Histopathological osteitis (bone erosion, osteoclastic resorption lacunae, and fibrous replacement of haversian canals) was present in 63 surgical cases (35.8%). Osteitis was strongly associated with ossicular chain destruction (incus long process erosion or stapes superstructure destruction), occurring in 84.1% of osteotic specimens compared to 19.5% of non-osteotic specimens ($p < 0.001$).

Table 3. Histopathological Profile of Middle Ear and Mastoid Tissue Specimens (n = 176 Surgical Cases)

Histopathological Feature	Frequency (n)	Percentage (%)	Primary Clinical Correlate
Keratinizing Stratified Squamous Epithelium	71	40.30%	Squamosal CSOM / Cholesteatoma
Submucosal Granulation Tissue	93	52.80%	Active, Persistent Otorrhea
• *Moderate-to-Severe Lymphoplasmacytic Infiltrate*	78	44.30%	Chronicity > 5 years
• *Neutrophilic Microabscesses*	36	20.50%	Active Bacterial Superinfection
Cholesterol Granuloma	30	17.00%	Impaired Mastoid Air Clearance
Glandular Metaplasia / Goblet Cell Hyperplasia	48	27.30%	Mucosal Hypersecretion
Histopathological Osteitis & Bone Erosion	63	35.80%	Ossicular Destruction & HRCT Scutum Erosion
• *Incus Long Process Necrosis*	56	31.80%	Conductive ABG > 35 dB
• *Malleus Handle / Stapes Superstructure Erosion*	34	19.30%	Severe ABG > 45 dB

Antimicrobial Utilization Patterns and Drug-Culture Concordance

Prior to entering our tertiary care facility, 268 of the 320 patients (83.8%) had received one or more courses of systemic antimicrobial therapy within the preceding 6 months.

As summarized in Table 4, oral broad-spectrum fluoroquinolones (ATC code J01MA; e.g., Ciprofloxacin, Levofloxacin) were the most frequently prescribed systemic agents (59.4% of patients), followed by oral β-lactams (ATC code J01CR; e.g., Amoxicillin-Clavulanate; 43.8%). Topical ear drops had been used by 208 patients (65.0%), though 39.4% of those users reported irregular application or premature treatment cessation.

Evaluation of Antimicrobial Concordance:

When empirical pre-referral systemic prescriptions were evaluated against laboratory-confirmed culture sensitivity results, 121 out of 268 empirical regimens (45.1%) were discordant—meaning the patient was taking a systemic antibiotic to which the primary pathogen was resistant *in vitro*. Discordance was highest for empirical Amoxicillin-Clavulanate against *P. aeruginosa* (100% intrinsic discordance) and empirical Ciprofloxacin against MRSA and resistant *Pseudomonas* strains (42.5% discordance).

Following baseline culture and sensitivity testing, patients were managed with culture-guided topical therapy (0.3% Ciprofloxacin + 0.1% Dexamethasone otic drops; 4 drops twice daily for 14 days) combined with mechanical aural toilet. Systemic antibiotics were reserved strictly for cases with invasive soft tissue extension, acute osteitis, or immediate perioperative surgical coverage.

At 6-month follow-up post-medical/surgical intervention:

- Overall dry ear rate (complete clearance of otorrhea) was achieved in 296 of 320 patients (92.5%).
- Antimicrobial discordance was successfully reduced from 45.1% at baseline to 3.1% post-intervention ($p < 0.001$).
- Overuse of systemic antibiotics dropped from 83.8% pre-referral to 13.8% post-referral ($p < 0.001$).

Table 4. Pre-Referral vs. Post-Intervention Antimicrobial Utilization Patterns (ATC Classification) and Concordance (N = 320)

Antimicrobial Category (ATC Code)	Pre-Referral Utilization (n = 320)	Post-Intervention Utilization (n = 320)	Pre-Referral Sensitivity Concordance	Post-Intervention Sensitivity Concordance	p-value (Concordance Improvement)
Systemic Fluoroquinolones (J01MA)	190 (59.4%)	24 (7.5%)	57.90%	95.80%	< 0.001
Systemic β-Lactams / Augmentin (J01CR)	140 (43.8%)	20 (6.3%)	41.40%	95.00%	< 0.001
Systemic Aminoglycosides (J01GB)	16 (5.0%)	10 (3.1%)	87.50%	100.00%	0.38
Topical Otic Fluoroquinolones (S02CA)	208 (65.0%)	298 (93.1%)	67.30%	97.30%	< 0.001
Topical Antifungals (S02AA)	14 (4.4%)	32 (10.0%)	50.00%	96.90%	0.001
Overall Regimen Discordance Rate	**45.10%**	**3.10%**	-	-	< 0.001

Predictors of Treatment Failure and Ossicular Erosion

Multivariate logistic regression analysis was conducted to establish independent clinical, microbiological, and pathological risk factors for primary treatment failure (persistent otorrhea at 6 months) and severe ossicular erosion (Table 5).

After adjusting for age, disease duration, and smoking status:

- **Presence of Histopathological Osteitis** was the strongest independent predictor of ossicular chain destruction (aOR = 5.64, 95CI: 2.82–11.28, $p < 0.001$).
- **Pre-referral Antimicrobial Discordance** independently tripled the risk of medical treatment failure (aOR = 3.25, 95CI: 1.61–6.58, $p = 0.001$).
- **Isolation of *P. aeruginosa* with Ciprofloxacin Resistance** doubled the risk of persistent otorrhea requiring surgical intervention (aOR = 2.84, 95CI: 1.38–5.85, $p = 0.005$).

Table 5. Multivariate Logistic Regression for Risk Factors Associated with Ossicular Erosion and Treatment Failure

Risk Factor / Variable	Unadjusted OR (95% CI)	Adjusted OR (aOR)* (95% CI)	p-value
Histopathological Osteitis	7.12 (3.68 – 13.80)	5.64 (2.82 – 11.28)	< 0.001
Pre-referral Antimicrobial Discordance	4.05 (2.10 – 7.82)	3.25 (1.61 – 6.58)	0.001
Ciprofloxacin-Resistant *P. aeruginosa*	3.22 (1.62 – 6.40)	2.84 (1.38 – 5.85)	0.005
Squamosal CSOM Phenotype	4.92 (2.61 – 9.28)	3.72 (1.88 – 7.36)	< 0.001
Disease Duration > 5 years	2.18 (1.20 – 3.94)	1.65 (0.86 – 3.16)	0.132

**Adjusted for age, sex, smoking status, and baseline pure-tone average.*

DISCUSSION

Chronic Suppurative Otitis Media continues to pose a formidable challenge to otolaryngologists and public health practitioners [15]. This study offers a comprehensive appraisal of CSOM by bridging clinical presentation, microbiological isolates, tissue-level histopathology, and real-world drug utilization. Our findings demonstrate that while CSOM produces extensive structural pathology including osteitis, granulation tissue, and cholesteatoma treatment success is severely hampered by inappropriate empirical systemic antimicrobial usage and a high rate of drug-culture discordance [16].

Microbiological Dynamics and the Pitfalls of Empirical Systemic Therapy

In our cohort, *Pseudomonas aeruginosa* (42.2%) and *Staphylococcus aureus* (28.1%) were the dominant pathogens, matching global epidemiological trends in chronic otitis media [17]. The pathogenicity of *P. aeruginosa* in the middle ear is driven by pili-mediated epithelial adherence, exotoxin A production, and its pronounced capacity for biofilm formation [18]. Biofilms shield bacteria from host immune clearance and reduce antibiotic penetration by up to 1,000-fold compared to planktonic forms [19].

Crucially, our study identified significant resistance among isolated strains: 28.9% of *P. aeruginosa* isolates were resistant to Ciprofloxacin, and 32.2% of *S. aureus* isolates were MRSA. These rates directly reflect local drug selection pressure driven by widespread, unguided oral fluoroquinolone and β-lactam administration in primary care settings [20].

Analysis of pre-referral drug utilization revealed that over 83% of patients had received systemic antibiotics, with an overall drug-culture discordance rate of 45.1%. Oral β-lactams such as Amoxicillin-Clavulanate are entirely ineffective against *P. aeruginosa* due to intrinsic resistance mechanisms. Furthermore, oral administration achieves relatively low serum and tissue concentrations in the middle ear cleft, especially when avascular granulation tissue or dense osteitic bone is present [21]. This sub-therapeutic tissue penetration accelerates the development of acquired resistance without eradicating the infection.

Superiority of Targeted Topical Otic Pharmacotherapy

In contrast to systemic therapy, topical administration of non-ototoxic fluoroquinolone drops (e.g., Ciprofloxacin or Ofloxacin, often combined with a mild corticosteroid) delivers antibiotic concentrations directly to the middle ear mucosa that are hundreds of times higher than the Minimum Inhibitory Concentration (MIC) of most pseudomonal and staphylococcal strains [22].

Following our intervention protocol which replaced unguided systemic antibiotics with culture-targeted topical ciprofloxacin/dexamethasone drops and routine mechanical aural clearing—regimen discordance fell to 3.1%, and the overall dry ear rate reached 92.5% at 6 months. This confirms that topical fluoroquinolones, when combined with proper aural toilet, should remain the cornerstone of non-invasive CSOM management, reserving systemic antibiotics for soft tissue complications or perioperative surgical prophylaxis [23].

Histopathological Insights: Osteitis as a Driver of Disease Recalcitrance

Histopathological examination of surgical tissue specimens provided valuable mechanistic insights into disease chronicity. Bone erosion and osteitis were documented in 35.8% of surgical specimens and were strongly correlated with ossicular chain necrosis (predominantly the long process of the incus).

Osteitis in CSOM is triggered by persistent bacterial lipopolysaccharide (LPS) exposure, which upregulates Prostaglandin E_2(PGE_2), Interleukin-1β (IL-1β), and Tumor Necrosis Factor-alpha (TNF-α) within the submucosa [24]. These pro-inflammatory cytokines activate the RANKL (Receptor Activator of Nuclear Factor-κB Ligand) pathway, stimulating osteoclast differentiation and active bone resorption [22].

Our multivariate analysis identified histopathological osteitis as the strongest independent predictor of ossicular destruction (aOR = 5.64). When osteitis and dense granulation tissue are established within the mastoid air cells and attic, medical therapy alone is rarely sufficient to clear the infection. Surgical clearance via tympanoplasty with or without mastoidectomy is necessary to remove the osteotic bone bed, eradicate sequestration, and reconstruct the hearing mechanism [25].

Clinical Implications and Antimicrobial Stewardship

The findings of this study advocate for a structured, evidence-based algorithm for CSOM management:

1. **Routine Microbiological Profiling:** Prior to initiating prolonged antimicrobial courses, ear swabs should be obtained for culture and sensitivity testing, particularly in recurrent or refractory cases.
2. **Prioritizing Topical Therapy:** Topical ciprofloxacin/dexamethasone drops combined with regular microscopic aural douching must be prioritized over empirical oral systemic antibiotics.

3. **Curtailing Systemic Antibiotic Overuse:** Primary care prescribers should avoid routine empirical oral Augmentin or fluoroquinolones for uncomplicated mucosal CSOM.
4. **Timely Surgical Escalation:** Patients presenting with squamosal disease, osteitis on HRCT, or persistent otorrhea despite culture-guided topical therapy should be promptly referred for surgical intervention (tympanomastoidectomy) to prevent disease progression and irreversible ossicular damage.

LIMITATIONS

Several limitations should be noted. First, as a single-center study conducted at a tertiary referral center, our cohort may reflect a higher proportion of complex, refractory, or squamosal cases than encountered in primary care practices. Second, anaerobic cultures were not systematically performed due to technical constraints, potentially underestimating the contribution of strict anaerobes in polymicrobial squamosal infections. Third, while VITEK 2 and disk diffusion provided comprehensive resistance profiles, molecular genotyping of resistance genes (e.g., *mecA* or metallo-β-lactamase genes) was not conducted.

CONCLUSION

Chronic Suppurative Otitis Media presents a complex clinicopathological spectrum where chronic inflammation, tissue osteitis, and ossicular erosion are driven by persistent bacterial pathogens like *P. aeruginosa* and *S. aureus*. Unguided empirical prescription of systemic antibiotics remains widespread prior to specialist consultation, resulting in high rates of drug-culture discordance (45.1%) and fostering local antimicrobial resistance.

Transitioning to evidence-based management combining early microbiological culture, targeted topical otic fluoroquinolones, mechanical aural toilet, and timely surgical eradication of osteotic bone significantly improves clinical cure rates (92.5%) while curbing unnecessary systemic antibiotic exposure. Adopting these stewardship principles is crucial to preserving hearing, preventing intracranial complications, and safeguarding global antimicrobial efficacy.

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