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Trends of Antimicrobial Resistance Markers of Clinical Streptococcus Pneumoniae in Niger, 2018–2025

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Abstract **Original Research Article**

Background: *Streptococcus pneumoniae* remains a leading cause of morbidity and mortality worldwide, with antimicrobial resistance (AMR) posing a significant threat to effective treatment. This study aimed to analyze the demographic characteristics, temporal trends, and molecular resistance profiles of *S. pneumoniae* detected in cerebrospinal fluid in Niger from 2018 to 2025. ***Methods:*** A retrospective analysis was conducted on 714 *S. pneumoniae*-positive cerebrospinal fluid (CSF) samples collected across various regions. Resistance markers were detected by PCR, and patient sociodemographic data were extracted from the National Reference Laboratory database of Centre de Recherche Médicale et Sanitaire (CERMES). ***Results:*** The study population had a median age of 10 years, with a male predominance (63.1%). The 0-2 years age group was the most affected (18.0%). Geographically, the Zinder region accounted for the highest number of cases (31.7%). A notable increase in detected cases was observed from 2020 onwards, peaking in 2024. The overall prevalence of resistance genes was highest for PRSP (*Streptococcus pneumoniae* with reduced Sensitivity to Penicillin, 33.0%) and *tetM* (28.0%). A striking temporal trend was the dramatic increase in *tetM* prevalence, rising from 3.8% in 2019 to 43.9% in 2024. Conversely, PSDP prevalence peaked in 2020 (72.7%) before declining ***Conclusion:*** Our findings reveal a shifting landscape of *S. pneumoniae* AMR in Niger, characterized by a concerning and rapid emergence of tetracycline resistance mediated by the *tetM* gene. The sustained burden of disease, particularly in young children and specific geographic hotspots like Zinder, underscores the urgent need for enhanced molecular surveillance, robust antimicrobial stewardship programs, and targeted public health interventions to mitigate the spread of resistant strains.

Keywords: Antimicrobial resistance, Molecular surveillance, Niger, Streptococcus pneumoniae, *tetM*.

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1. INTRODUCTION

Streptococcus pneumoniae (the pneumococcus) is a major human pathogen responsible for a wide spectrum of diseases, ranging from non-invasive infections like otitis media and sinusitis to life-threatening invasive pneumococcal diseases (IPD) such as pneumonia, meningitis, and sepsis , (Gergova *et al.,* 2021; Mahdi and Abed 2024; Mokupi 2021; O'brien *et al.,* 2009; Zia 2014). It remains a leading cause of mortality and morbidity globally, particularly affecting young children and the elderly. The burden of pneumococcal disease is disproportionately high in low- and middle-income countries, where access to healthcare and vaccination may be limited (Chen et al. 2019; Niyibitegeka *et al.,* 2024).

The advent of antibiotics revolutionized the treatment of bacterial infections, but their widespread use has driven the selection and spread of antimicrobial resistance (AMR) (Baker *et al.,* 2018; Tarín-Pelló *et al.,* 2022) Pneumococcal resistance to commonly used antibiotics, including penicillins, macrolides, and tetracyclines, is a growing public health crisis that complicates treatment, increases healthcare costs, and worsens clinical outcomes (WHO, 2022). Monitoring the evolution of AMR is therefore essential for updating treatment guidelines and implementing effective control strategies.

Molecular methods, such as polymerase chain reaction (PCR), provide a rapid and sensitive means to detect the genetic determinants of resistance. Key resistance mechanisms in *S. pneumoniae* include alterations in penicillin-binding proteins (conferring beta-lactam resistance, detectable via markers like PBP2b), ribosomal modification by the *ermB* gene, and

drug efflux mediated by the *mefA* gene (both causing macrolide resistance), and ribosomal protection by the *tetM* gene (causing tetracycline resistance) (Anjum *et al.,* 2017, 2018; Fluit *et al.,* 2001; Sundsfjord *et al.,* 2004). Tracking the prevalence of these genes provides critical insights into the circulating resistance mechanisms within a population.

In Niger, a country within the African meningitis belt, surveillance of pathogens like *S. pneumoniae* is of paramount importance. However, comprehensive, long-term data on the molecular epidemiology and AMR trends of pneumococcus are often scarce. This study aims to fill this gap by analyzing a large dataset of *S. pneumoniae* samples collected across Niger between 2018 and 2025. The primary objectives were: (1) to describe the demographic characteristics of the patient population; (2) to analyze the temporal trends of *S. pneumoniae* detection; (3) to determine the prevalence and temporal trends of key resistance genes (*ermB*, *mefA*, *tetM*, and PBP2b/PSDP); and (4) to explore associations between demographic factors and resistance profiles. The findings are intended to provide evidence-based recommendations for public health policy and clinical practice in the region.

2. METHODS

2.1. Study Design and Data Source

A retrospective observational study was conducted using laboratory surveillance data collected from January 2018 to early 2025. The dataset was compiled from results of PCR tests performed on Cerebrospinal Fluid (CSF) samples that tested positive for *S. pneumoniae*, sent from various health facilities across Niger during meningitis epidemics. All analyses were based on anonymized data, and the study was performed in accordance with institutional ethical guidelines (WO, 2012).

2.2. Study Population and Data Collection

The study included all patients whose CSF were available and tested positive for *S. pneumoniae* by PCR as part of national meningitis surveillance and case confirmation. A total of 900 positive cases were identified during the period, out of which 714 with available samples were included in the final analysis. Sociodemographic data were extracted from the meningitis database of the National Reference Laboratory for meningitis at the Centre de Recherche Médicale et Sanitaire (CERMES). For each case, information collected included a unique patient identifier (PID), date of sample collection, geographical region, age, and sex. Available CSF were processed by PCR as described by Velusamy et al. (2020) (Velusamy *et al.,* 2020) for detection of the *lytA* gene and four resistance determinants: *ermB*, *mefA*, *tetM*, and PBP2b. CSF testing negative for the PBP2b gene were considered positive for *S. pneumoniae* with reduced susceptibility to Penicillin (SPRSP), here referred to as PSDP. Those testing positive (cycle threshold or Ct < 35) for *lytA* and for *ermB*, *mefA*, or *tetM* genes were considered resistant to Macrolides, Erythromycin, and Tetracycline, respectively (Velusamy *et al.,* 2020) .

2.3. Statistical Analysis

All data were cleaned and analyzed using EpiInfo version 7.2. Descriptive statistics were used to summarize the demographic characteristics of the study population. Continuous variables like age were described using mean, standard deviation (SD), median, and interquartile range (IQR). Categorical variables (sex, region, age group, presence of resistance genes) were described using frequencies and percentages. Temporal trend analysis was performed by aggregating the number of positive cases and the prevalence of each resistance gene by year. The prevalence of a resistance gene was calculated as the number of cases positive for that gene divided by the total number of cases with a valid test result for that gene in a given year. Associations between demographic variables (age group, sex, region) and the prevalence of resistance genes were assessed using cross-tabulations.

3. RESULTS

3.1. Characteristics of the Study Population

From January 2018 to December 2025, 900 CSF samples were tested positive for *S. pneumoniae* and recorded in the LNR database of CERMES. A total of 714 available in the biobank were considered in the present analysis by PCR for the detection of resistance genes. The demographic characteristics of the patient population (Table 1) showed that the mean age of patients was 13.5 ± 14.5 years, with a median age of 10 years (IQR: 3–17). The majority of patients with sex reported were male (370/586, 63.1%). The Zinder region (Fig. 1) contributed the highest number of cases (226, 31.7%), followed by Tahoua (149, 20.9%) and Niamey (109, 15.3%). When stratified by age group, the 0-2 years group was the most represented, accounting for 18.0% of all cases (128/714).

Table 1. Characteristics of 714 pneumococcal meningitis patients considered in the study.

Characteristic	Value
Total Cases	714
Age (years)	
Mean ± SD	13.5 ± 14.5
Median (IQR)	10 (3 - 17)
Sex (n=586)	
Male, n (%)	370 (63.1%)
Female, n (%)	216 (36.9%)
Most Common Age Group, n (%)	
0-2 years	128 (18.0%)

Legend: SD: Standard Deviation; IQR: Interquartile Range. Percentages for sex are based on non-missing data.

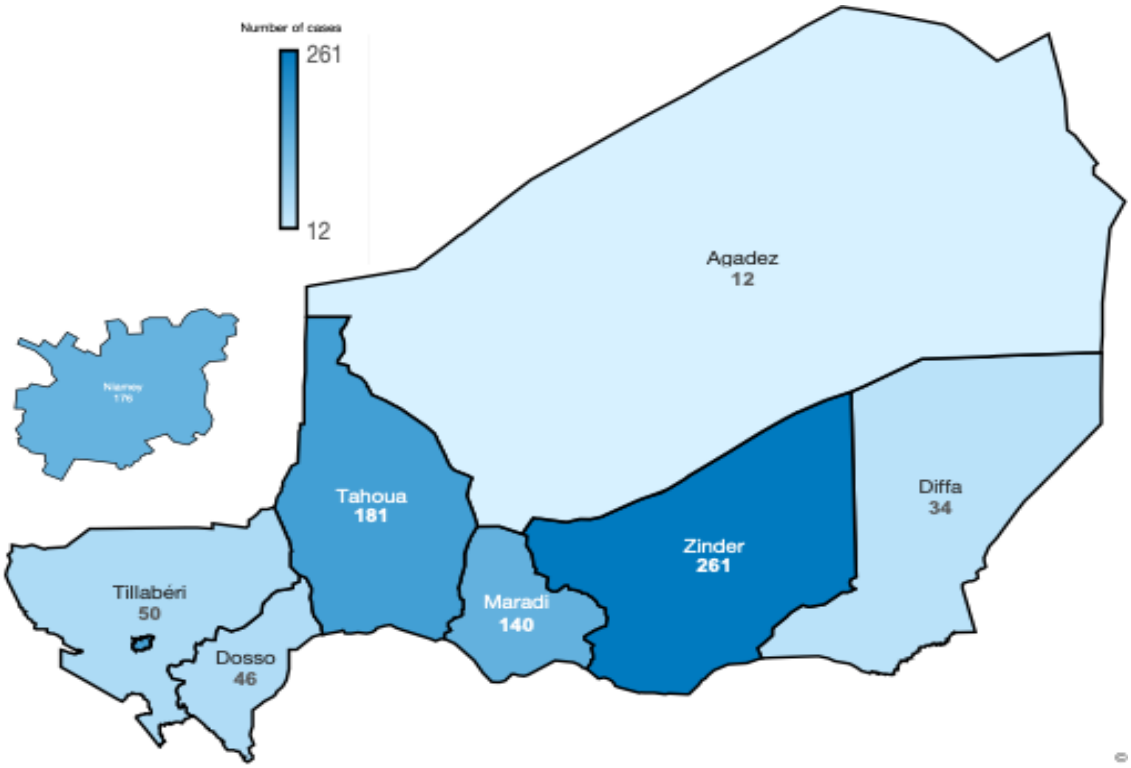

Fig. 1. Spatial distribution of pneumococcal meningitis cases from 2018 to 2025.

3.2. Temporal Trends of S. pneumoniae Cases

The annual distribution of *S. pneumoniae* cases showed significant fluctuation over the study period (Table 2). After an initial period of high detection in 2018 and 2019, the number of cases dropped to its lowest point in 2020 (34 cases). Following this decline, a steady and significant increase was observed, with the number of cases rising each year to a peak of 139 cases in 2024.

Table 2. Temporal trend of S. pneumoniae positive cases detected annual

Period	Number of cases	Percent
2018	77	10.8%
2019	53	7.4%
2020	34	4.8%
2021	95	13.3%
2022	95	13.3%
2023	105	14.7%
2024	139	19.5%
2025	116	16.2%
Cumulative Total (N)	**714**	**100%**

3.3. Prevalence and Trends of Antimicrobial Resistance Genes

The overall prevalence of the four resistance determinants is shown in Fig. 2. The most frequently detected marker was PSDP (PBP2b), found in 33.0% (231/700) of isolates, followed closely by *tetM* at 28.0% (199/711). Macrolide resistance genes were less common, with *mefA* detected in 9.3% (66/711) and *ermB* in 6.5% (46/711) of isolates.

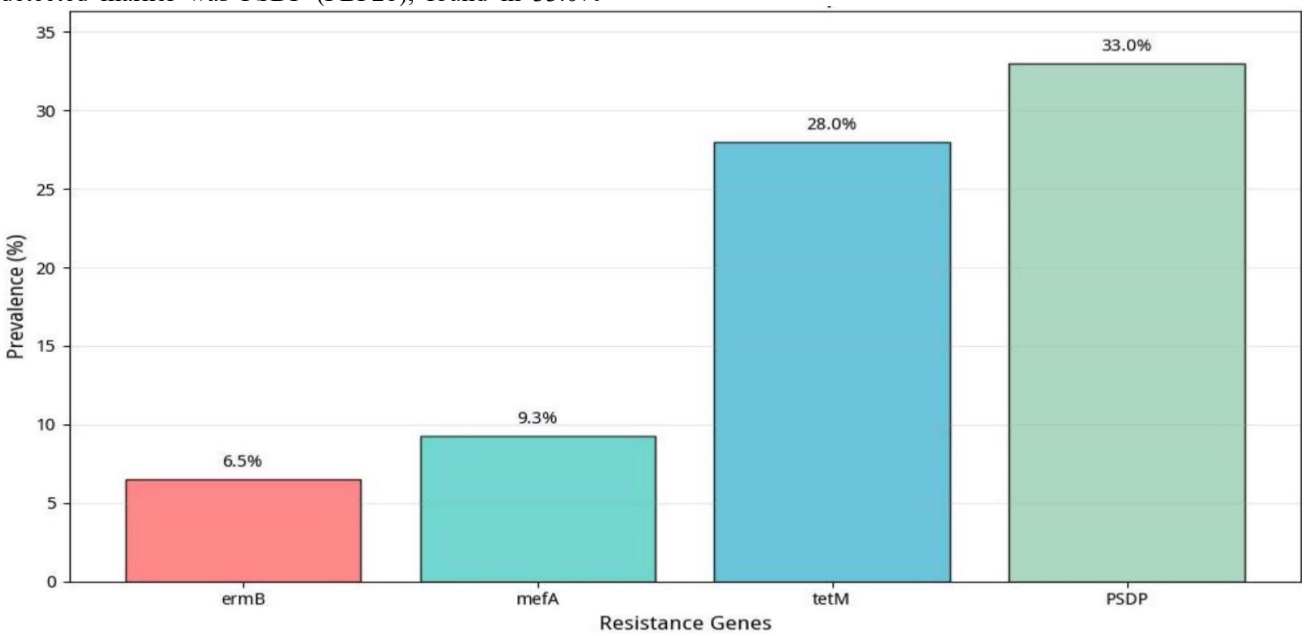

Fig. 2. Overall prevalence of antimicrobial resistance genes among S. pneumoniae isolates (2018–2025). SPRSP and tetM are the most prevalent markers.

Analysis of temporal trends revealed dramatic shifts in resistance gene prevalence (Table 3). Most notably, the prevalence of the *tetM* gene increased alarmingly, from just 3.8% in 2019 to 43.9% in 2024. In contrast, the prevalence of SPRSP was highly variable, peaking at 72.7% in 2020 before decreasing substantially in subsequent years. The prevalence of macrolide resistance genes *mefA* and *ermB* remained relatively low and stable throughout the study period, with minor fluctuations.

Table 3. Proportion per year of positive cases for antimicrobial resistance genes detected in CSF tested positive for S. pneumoniae 2018-2025 in Niger

Year	Beta lactams	Tetracyclin	Macrolide resistance	
	SPRSP (%)	tetM (%)	mefA (%)	ermB (%)
2018	35.7	21.4	2.9	5.7
2029	48.1	3.8	6.4	1.9
2020	72.7	15.2	9.1	3.0
2021	6.9	21.2	9.6	8.7
2022	21.5	29.9	10.3	8.4
2023	19.0	37.1	15.2	8.6
2024	5.9	43.9	7.9	4.3
2025	19.0	28.01	9.37	6.57

3.4. Association between Demographics and Resistance

Resistance patterns varied across different demographic groups. Analysis by age group revealed that isolates from patients in the 0-2 years age group had the highest prevalence of the SPRSP marker (45.1%). There were no significant differences in resistance prevalence between males and females. Geographically, notable variations were observed. The Agadez region, despite having few cases overall, showed the highest PSDP prevalence (60.0%). The Tillabery region had the highest prevalence of *ermB* (12.8%). The widespread and rapidly increasing *tetM* gene was prevalent across multiple regions, indicating broad dissemination.

4. DISCUSSION

This study provides a comprehensive overview of the molecular epidemiology and antimicrobial resistance trends of *Streptococcus pneumoniae* in Niger from 2018 to 2025. Our analysis reveals several critical findings, most notably a resurgence in detected cases post-2020 and a dramatic, concerning rise in the prevalence of the tetracycline resistance gene, *tetM*.

4.1. Principal Findings and Interpretation

The demographic profile of our cohort, with a high burden of disease in children under two years old, is consistent with global patterns of pneumococcal disease (Mahdi and Abed, 2024). This age group's immature immune system makes them particularly vulnerable. The geographical clustering of cases in the Zinder region suggests it may be a hotspot for transmission, warranting focused public health investigation and intervention.

The temporal trend of case detection is particularly insightful. The sharp drop in cases in 2020 likely does not reflect a true decrease in disease incidence but rather the profound impact of the COVID-19 pandemic on healthcare-seeking behaviors, surveillance activities, and laboratory capacity. The subsequent and sustained increase from 2021 to 2024 is alarming and may indicate a rebound effect, a true increase in transmission, or improved surveillance capacity post-pandemic. This underscores the importance of maintaining robust surveillance systems, even during public health emergencies (Mokupi, 2021).

The most striking finding of this study is the rapid emergence and dissemination of the *tetM* gene. Its prevalence skyrocketed from a negligible level in 2019 to affecting nearly half of all isolates by 2024. This indicates a powerful selective pressure, likely driven by the widespread use of tetracycline-class antibiotics in the region for human and/or veterinary medicine. The rise of *tetM* signals a significant shift in the pneumococcal resistance landscape in Niger and poses a serious threat to the utility of an entire class of affordable, broad-spectrum antibiotics.

In contrast, the trend for the penicillin non-susceptibility marker PSDP was more volatile, with a sharp peak in 2020 followed by a decline. This fluctuation could be multifactorial, potentially related to changes in circulating pneumococcal serotypes (some of which are more prone to developing resistance) or shifts in beta-lactam antibiotic prescribing practices. The decline post-2020 is a positive sign but requires continued monitoring. The prevalence of macrolide resistance genes (*ermB* and *mefA*) remained relatively low and stable, suggesting that macrolides may still be a viable treatment option in many cases, although local stewardship is crucial to preserve their efficacy.

4.2. Strategic Recommendations

Based on these findings, we propose the following strategic recommendations:

1. **Enhance Molecular Surveillance:** The rapid evolution of resistance profiles highlights the need for a robust, real-time molecular surveillance system. This system should continue to monitor not only the prevalence of known resistance genes but also be capable of detecting new or emerging resistance mechanisms. Integrating genomic sequencing would provide higher-resolution data on circulating clones and transmission dynamics.
2. **Implement Targeted Interventions:** Public health resources should be prioritized for high-burden areas and populations. The Zinder region should be a focus for intensified surveillance, infection prevention and control measures, and potentially vaccination campaigns. The high prevalence of PSDP in infants underscores the critical importance of on-time vaccination with pneumococcal conjugate vaccines (PCVs) to reduce the burden of disease and the need for antibiotics in this vulnerable group.
3. **Strengthen Antimicrobial Stewardship (AMR):** The dramatic rise of *tetM* is a clear call to action for AMR. Urgent reviews of antibiotic prescribing guidelines are needed. Educational campaigns for healthcare providers and the public on the appropriate use of antibiotics, particularly tetracyclines, are essential to reduce selective pressure. Data on antibiotic consumption should be collected and correlated with resistance trends to guide AMR policies.
4. **Conduct Further Research:** This study raises important questions that warrant further investigation. Research is needed to identify the specific pneumococcal serotypes associated with the rise in *tetM*. Understanding the drivers of the geographical disparity in case distribution, particularly the high burden in Zinder, is also crucial for designing effective local interventions.

4.3. Limitations

This study has several limitations. First, its retrospective nature relies on data collected for routine surveillance, which may lead to inconsistencies or missing information (e.g., for sex and age in some records). Second, the dataset lacks clinical outcome data, preventing any correlation between resistance genotypes and disease severity or treatment failure. Third, information on patient vaccination status and antibiotic consumption was not available, which limits our ability to fully interpret the drivers of the observed resistance trends. Finally, the data does not include pneumococcal serotype information, which is a key factor in understanding the epidemiology and impact of vaccination programs.

5. CONCLUSION

In conclusion, this study provides critical insights into the evolving epidemiology of *Streptococcus pneumoniae* in Niger. We document a concerning increase in detected cases since 2020 and a rapid, alarming emergence of tetracycline resistance mediated by the *tetM* gene. These findings highlight a dynamic and challenging AMR landscape. There is an urgent need for a coordinated public health response, including strengthened molecular surveillance, targeted regional interventions, and aggressive antimicrobial stewardship, to preserve the effectiveness of essential medicines and combat the threat of pneumococcal disease in the region.

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