Pneumonia

REVIEW

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Serotype distribution and antimicrobial resistance of *Streptococcus pneumoniae* in China among children under 14 years of age post-implementation of the PCV13: a systematic review and meta-analysis (2017–2024)

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Abstract

Background *Streptococcus pneumoniae* (*S. pneumoniae*) is a major cause of morbidity and mortality in children worldwide, and its evolving serotype distribution and antibiotic resistance patterns are of global health concern. This meta-analysis aims to investigate the serotype distribution and antimicrobial resistance of *S. pneumoniae* after the introduction of pneumococcal conjugate vaccine 13-valent (PCV13) as a self-funded vaccine in Chinese pediatric populations.

Methods We systematically reviewed studies published between 2017 and 2024 that focused on *S. pneumoniae* serotypes isolated from children under 14 years old in mainland China. Data sources included PubMed, Embase, Web of Science, CNKI, Wanfang, and SinoMed. The findings were synthesized using either a fixed-effects or random-effects model.

Results Our meta-analysis included 12 studies, identifying the most common serotypes of *S. pneumoniae* were 19 F, 19 A, 23 F, 14, 6B and 6 A. Vaccine serotype coverage rates were 52.17% (95%CI: 44.91-59.42%) for PCV10, 74.77% (95%CI: 71.53-78.01%) for PCV13, 76.72% (95%CI: 75.37-78.07%) for PCV15 and 92.90% (95%CI: 92.09-93.71%) for PPSV23. Antimicrobial resistance was most pronounced for erythromycin at 93.73% (95%CI: 90.58-96.88%), followed by azithromycin, tetracycline, clindamycin, and sulfamethoxazole. Serotype prevalence and vaccine coverage varied regionally and by strain type.

Conclusion The distribution of *S. pneumoniae* serotypes and their antibiotic resistance profiles in children under 14 years in mainland China have remained relatively stable post-PCV13 introduction as a self-funded vaccine. The results

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support continued use and possible expansion of PCV13 immunization and highlight the importance of ongoing surveillance and vaccine development to cover all prevalent serotypes in China.

Keywords Streptococcus pneumoniae, Serotype distribution, Antimicrobial resistance, PCV13, Meta-analysis

Introduction

Streptococcus pneumoniae (*S. pneumoniae*), also known as pneumococcus, represents a significant public health challenge, particularly in pediatric populations. It serves as a primary causative agent in various forms of invasive pneumococcal disease (IPD), including meningitis, bacteremia, and sepsis, as well as noninvasive mucosal diseases such as otitis media (OM) and pneumonia. Annually, pneumococcal disease results in 9.2 million vaccine-preventable cases and 318,000 deaths in children under 5 worldwide [1]. China ranks fourth among countries with the highest burden of pneumococcal diseases in children under 5 years of age, comprising 3% of the total global burden [1, 2]. Given the severity and prevalence of *S. pneumoniae* infections, effective preventive and treatment strategies are imperative, highlighting the critical need for ongoing research and surveillance efforts.

Pneumococcal conjugate vaccines (PCVs), presently available as 10-valent (PCV10) or 13-valent (PCV13) formulations, have been introduced into routine infant immunization programs worldwide. These vaccines have demonstrated efficacy in reducing both nasopharyngeal carriage prevalence and incidence rates of IPD among both vaccinated individuals (direct protection) and unvaccinated individuals (indirect protection) [3, 4]. The introduction of PCVs, particularly PCV13, has led to significant changes in the epidemiological profile of *S. pneumoniae* infections. PCV13 offers broader coverage of pneumococcal serotypes compared to earlier formulations, thereby enhancing protection against pneumococcal diseases.

In China, PCV7 was made available in 2008, and PCV13(Prevnar 13; Pfizer Inc, New York, NY) replaced it in 2016, represented a strategic public health decision aimed at controlling the transmission of *S. pneumoniae* infections. PCV13, which rapidly became the primary pneumococcal vaccine for children due to its extensive serotype coverage and cost-effectiveness, is available as a non-National Immunization Program vaccine, necessitating private payment by families. The recommended vaccination schedule for PCV13 involves administering one dose at 2, 4, and 6 months of age, with a booster dose at 12 to 15 months, totaling four doses. A recent study analyzing cross-sectional data from ten provinces in China, including vaccine records for 5,294 children in 2019, found that the one-dose coverage rate for PCV13 was 7.7% (95%CI: 6.9–8.4) and the three-dose coverage rate was 5.1% (95%CI: 4.5–5.8) [5], highlighting the suboptimal vaccination coverage in the region. This shift in vaccine usage has predictably influenced the serotype distribution and resistance patterns of *S. pneumoniae* in pediatric populations, with ongoing scientific interest in the post-vaccination dynamics related to serotype distribution, serotype coverage, and antibiotic resistance among children under 14 years in China.

Higher valency vaccines, such as PCV15 and PCV20, are also being developed to cover additional serotypes. Additionally, other PCVs like Pneumosil™ (Serum Institute of India, PCV10-SII) have been introduced in various countries to address the pneumococcal disease burden. To address these concerns, we performed a comprehensive meta-analysis of studies published from 2017 to 2024. This analysis synthesized data from multiple studies to offer a comprehensive perspective on the serotype distribution, serotype coverage, and antibiotic resistance of *S. pneumoniae* and provide basic information for the pneumococcal vaccination strategy of China.

Materials and methods

Literature search

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a comprehensive and transparent reporting process [6]. We identified studies reporting pneumococcal serotypes from outpatients or hospitalised patients, or isolates from healthy children aged < 14 years in mainland China, published between 1 January 2017 and 5 February 2024. A comprehensive literature search was conducted in multiple electronic databases, including PubMed, Web of Science, Embase, China National Knowledge Infrastructure (CNKI), Wanfang and Chinese Bio-Medical Literature Service System, China (SinoMed) Data. Keywords and Medical Subject Headings (MeSH) terms related to "Streptococcus pneumoniae" "serotype distribution" "antimicrobial resistance" "PCV13" and "China" were used to identify relevant studies. Additional studies were identified by reviewing reference lists of the selected articles until no potential articles were found. The search strategy is summarized in the Supplementary File 1.

Review strategy

Using Endnote X (Thomson Reuters, Inc., Philadelphia, PA), we established a digital citation library for managing articles from database searches. We removed duplicates from PubMed, Embase, and Web of Science results via Endnote. Each article received a unique ID for efficient

tracking during the review and analysis stages. Two reviewers independently screened titles and abstracts to shortlist eligible studies. Full-text reviews were conducted for these studies to determine final inclusion. Reviewer disagreements were resolved by discussion and reaching a consensus.

Study selection criteria and exclusion criteria

The criteria for including studies in this analysis were as follows: (1) Study Period: Only studies reporting data on *S. pneumoniae* after the implementation of PCV13 were considered. (2) Population: Studies focusing on pediatric populations (age 0–14 years) residing in mainland China. (3) Study design and Outcomes: observational studies reporting serotype distribution, serotype coverage of vaccines and/or antibiotic resistance of *S. pneumoniae*.

Exclusion criteria were as follows: (1) Studies that included data on *S. pneumoniae* collected before the implementation of the PCV13 vaccine; (2) Studies involving children over 14 years of age or those residing outside of mainland China; (3) Studies categorized as reviews, case reports, prior meta-analyses, letters to the editor, commentaries, editorials, or those based on experimental models or animal studies; (4) Studies lacking specific data on serotype distribution, vaccine serotype coverage, or antibiotic resistance patterns of *S. pneumoniae*.

Data extraction

The data extraction from the selected studies was structured using a standardized form. We gathered key information, including study details like author, year of publication, design, and study period, as well as specifics on the study population, such as sample size and age groups. Additionally, serotype distribution, serotype coverage of vaccines and antibiotic resistance were recorded. This process was carried out independently by two researchers and any differences in data extraction were resolved through discussion.

Definitions

The invasive isolates were defined as *S. pneumoniae* strains isolated from normal sterile specimens, such as blood, cerebrospinal fluid, pleural effusion, etc. The non-invasive isolates were defined as *S. pneumoniae* strains isolated from non-sterile specimens, such as hypopharyngeal aspirates, bronchoalveolar lavage, nasopharyngeal swabs, etc.

Quality assessment

We rigorously evaluated the methodological quality of each article using a modified 12-point scoring system, based on Downs and Black's criteria [7]. Our evaluation focused on several essential aspects: the quality of the reporting, the study's external validity, and potential biases, including risk and confounding factors, as well as the study's statistical power. Our scoring was guided by a detailed checklist. This included the clarity of study objectives, the study design specification, how well the sample represented the target population, consistency in participant recruitment timing, justification for the sample size, effective management of missing data, and comprehensive reporting of participant demographics (age, gender, etc.). We also assessed how confounding variables, serotyping detection methods, potential biases, and defined outcomes were reported.

Statistical analysis

Statistical analysis was performed using STATA software version 14.0 (Stata Corporation, College Station, TX, USA). To analyze the spatial distribution patterns of *S. pneumoniae* serotype in China, we examined changes across different regions. The demarcation for these regions was based on the Qinling Mountain-Huaihe River line [8]. For serotype distribution, serotype coverage of vaccines and antibiotic resistance, prevalence rates were calculated. Heterogeneity among the studies was quantified using the I^2 statistic: I^2 values of ≤25% denoted low heterogeneity, values between 25% and 50% indicated moderate heterogeneity, and values between 50% and 75% suggested high heterogeneity [9]. Given that the majority of our meta-analysis results exhibited high heterogeneity (I^2>75%), the random-effects model was employed for pooled estimation and 95% confidence interval (CI). To assess potential publication bias, Begg's funnel plots [10] and Egger's test [11] were utilized. Statistical significance was established at a p-value of less than 0.05 [12].

Ethical considerations

As this meta-analysis utilized data from published studies, ethical approval was not required.

Results

Study selection

Our initial search across databases including PubMed, Web of Science, Embase, CNKI, Wanfang, and SinoMed Data yielded 1,758 research articles. The distribution of articles identified from each database is as follows: PubMed (181), Web of Science (237), Embase (212), CNKI (370), Wanfang (363), and SinoMed Data (395). Of these, 912 were excluded due to duplication. We then reviewed the titles and abstracts of the remaining 846 studies, leading to the exclusion of 802 articles for various reasons (such as being reviews, case report, case series, meta-analysis, letters, comments, or editorials, experimental or animal studies). This process resulted in 44 studies being selected for full-text review. However, 32 of these were further excluded due to the following

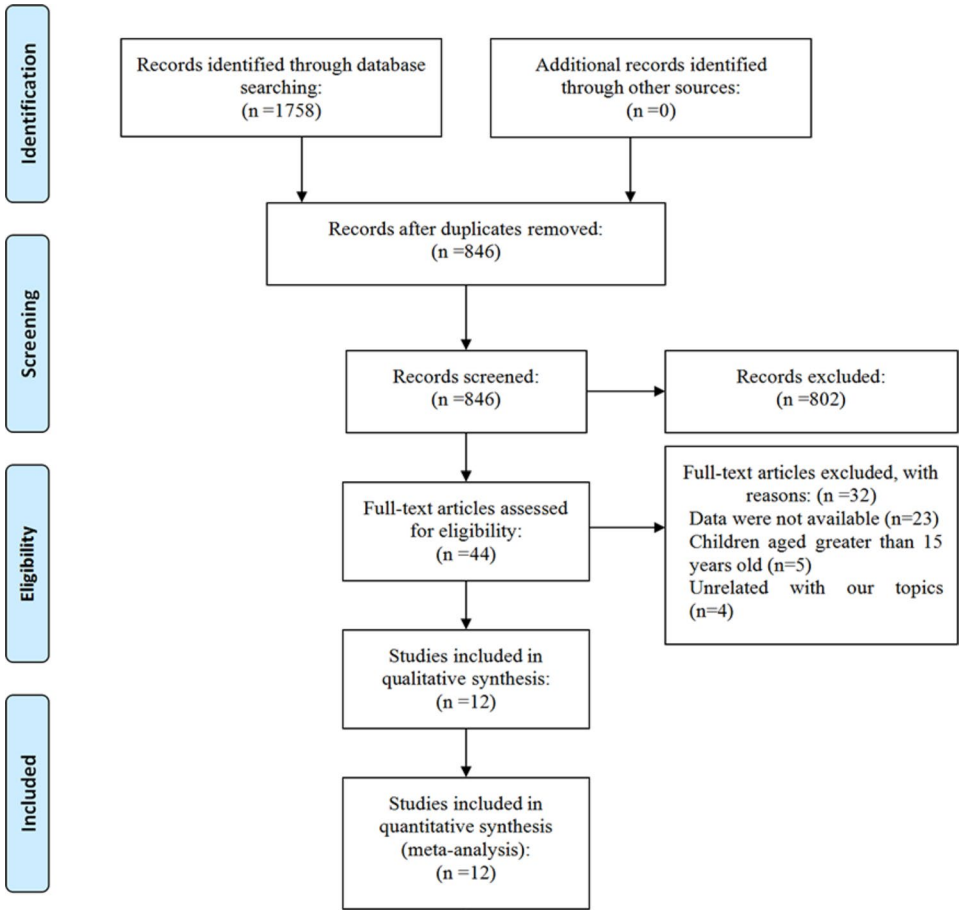

Fig. 1 Eligibility of studies for inclusion in meta-analysis

Table 1 Baseline characteristics of patients in the studies included in the meta-analysis

Study	Publication year	Study period	Study site	Age	Serotyping method	Total strains	Positive strains
Tang P [13]	2021	2018.11-2019.6	Sichuan	< 14y	Quelling reaction, E-test or disc diffusion method	192	151
Ma J [14]	2023	2019.1-2021.1	Qinghai	5 m-6y	Quelling reaction	44	39
Feng S [15]	2021	2017.1-2019.7	Jiangsu	< 14y	Quelling reaction, E-test method	3652	3652
Tian JL [16]	2020	2018.1-2018.12	Xinjiang	1 m-14y	Quelling reaction, E-test method	225	225
Zhang CH [17]	2022	2020.1-2021.12	Henan	3 m-12y	Quelling reaction, E-test method	360	343
Hu HH [18]	2021	2017.1-2019.12	Henan	< 6y	Quelling reaction, disc diffusion method	1788	1788
Zhang HY [19]	2021	2017.1-2019.12	Shandong	< 6y	Quelling reaction, E-test or disc diffusion method	106	101
Zhao YY [20]	2021	2018.1-2019.7	Zhejiang	1-12y	Quelling reaction, E-test or disc diffusion method	176	43
Li XN [21]	2022	2018.1-2018.12	Guangdong	1 m-14y	MPCR	98	45
Guan HY [22]	2023	2019.11-2020.4	Shandong	< 6 m	Quelling reaction, E-test	11	11
Yan ZY [23]	2021	2017.3-2019.11	Southwest China	< 14y	MPCR	128	110
Chen HJ [24]	2022	2019.1-2021.1	Sichuan	< 5y	MPCR	108	85

Abbreviations m, month; y, year; MPCR multiple polymerase chain reaction

reasons: unavailability of data in 23 studies, inclusion of children older than 14 years in 5 studies, and irrelevance to our research topics in 4 studies. Ultimately, 12 studies [13–24] were included in our systematic review and meta-analysis (Fig. 1).

Study characteristics and quality assessment

The characteristics and quality assessment scores of these studies are summarized in Table 1. The included studies, published between 2020 and 2023, encompassed a wide range of geographical regions within China. Six studies

were conducted in the North [16–19, 22], five studies were conducted in the South [13, 15, 20, 21, 24], and one study were from multicenter analyses [23] (Fig. 2).Notably, ten of these studies were published in Chinese language, with nine appearing in prominent Chinese core domestic journals. Of the 12 studies, a majority, 75.0% (9/12), focused on non-IPD. In terms of diagnostic methods, 75.0% (9/12) of the studies employed the Quelling reaction, E-test or disc diffusion method for serotyping *S. pneumoniae*, whereas the remaining three studies adopted the multiple polymerase chain reaction (MPCR). Eight studies were regarded as A, highlighting their relatively good quality (Supplementary File 2).

Distribution of pneumococcus serotypes

Eleven studies reported the data of serotype distributions of *S. pneumoniae* among Chinese children under 14 years old. Overall, serotypes 19 F, 19 A, 6B, 14, 6 A, and 23 F were identified as the most prevalent (Table 2). Among the IPD strains, the pooled prevalence was highest for 19 F at 27.29% (95%CI: 21.83-32.74%), followed by 19 A at 13.66% (95%CI: 9.46-17.87%), 6B at 12.10% (95%CI: 8.10-16.09%), 14 at 11.42% (95%CI: 3.79-19.05%), 6 A at 8.05% (95%CI: 4.72-11.38%), and 23 F at 3.13% (95%CI: 0.11-6.14%)(Fig. 3; Table 2).

Among the non-IPD strains, serotype 19 F was most predominant at 22.92% (95%CI: 14.13-31.72%). This was followed by serotype 19 A at 17.81% (95%CI: 8.51-27.10%), 6 A at 14.26% (95%CI: 5.73-22.78%), 23 F at 8.97% (95%CI: 7.55-10.39%), 14 at 8.95% (95%CI: 4.2-13.7%), and 6B at 8.83% (95%CI: 5.34-12.32%)(Fig. 3; Table 2). It was noted that serotypes 19 F, 14, and 6B were more common in IPD strains, whereas serotypes 19 A, 23 F and 6 A were more prevalent in non-IPD strains.

Regional subgroup analysis indicated a distinction in prevalence: in Southern China, serotype 19 F was most predominant, while in the Northern regions, serotype 19 A was most frequent (Fig. 3; Table 2).

Proportion of vaccine-type serotypes

Six studies reported the data of coverage rate of vaccine-type serotypes. The serotype coverage rates were 52.17% (95%CI: 44.91-59.42%) for PCV10, 74.77% (95%CI: 71.53-78.01%) for PCV13, 76.72% (95%CI: 75.37-78.07%) for PCV15 and 92.90% (95%CI: 92.09-93.71%) for PPSV23 (Table 3). Notably, the serotype coverage rates for PCV10 and PCV13 were lower for IPD strains than for non-IPD strains (Table 3).

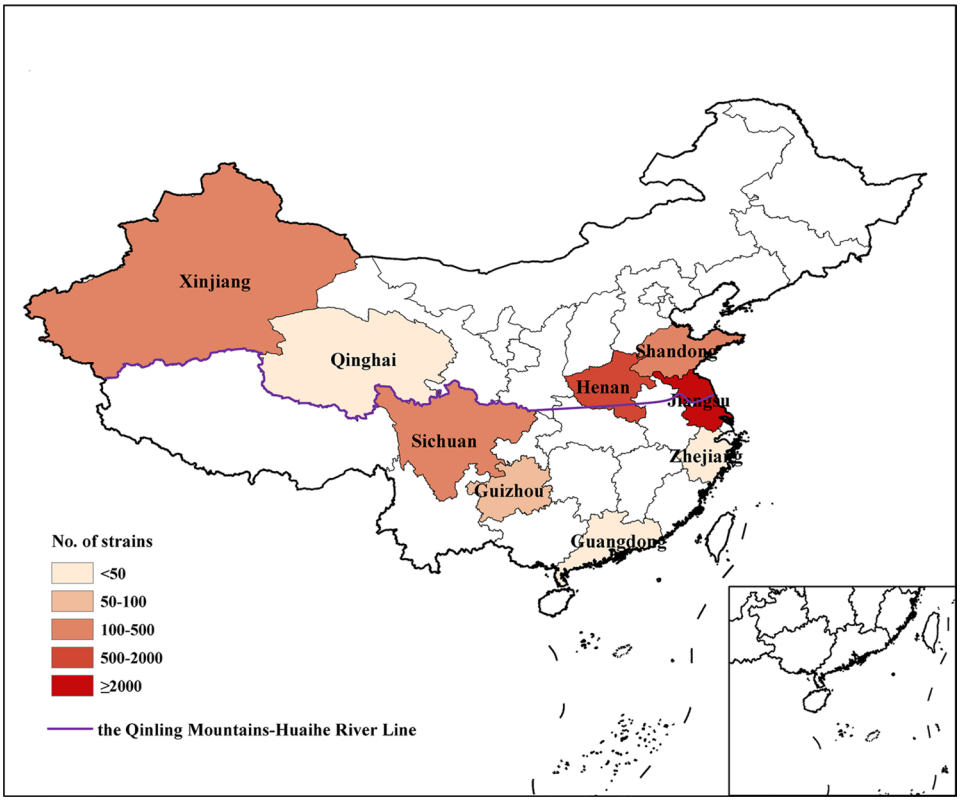

Fig. 2 Distribution of included articles by province. China's Northern region refers to the north of the Qingling Mountain-Huaihe River line, and Southern region refers to the south of the Qingling Mountain-Huaihe River line

Table 2 Pooled serotype distribution of Streptococcus pneumoniae among Chinese children under 14 years old

Serotype	Region	Strain	Rate(%)	95% CI
19 F	North	IPD	-	-
		Non-IPD	19.67	4.12–35.22
	South	IPD	27.29	21.83–32.74
		Non-IPD	24.30	18.76–29.85
	Multicenter	IPD	27.29	21.83–32.74
		Non-IPD	22.92	14.13–31.72
19 A	North	IPD	19.17	15.1-23.23
		Non-IPD	26.69	10.99–42.40
	South	IPD	13.66	9.46–17.87
		Non-IPD	12.35	6.73–17.97
	Multicenter	IPD	13.66	9.46–17.87
		Non-IPD	17.81	8.51–27.1
23 F	North	IPD	6.94	4.32–9.57
		Non-IPD	9.15	7.05–11.26
	South	IPD	3.13	0.11–6.14
		Non-IPD	8.30	5.62–10.98
	Multicenter	IPD	3.13	0.11–6.14
		Non-IPD	8.97	7.55–10.39
14	North	IPD	15.56	11.81–19.30
		Non-IPD	4.72	0.68–8.75
	South	IPD	11.42	3.79–19.05
		Non-IPD	13.94	3.15–24.73
	Multicenter	IPD	11.42	3.79–19.05
		Non-IPD	8.95	4.2–13.7
6B	North	IPD	5.56	3.19–7.92
		Non-IPD	7.31	2.39–12.23
	South	IPD	12.10	8.10-16.09
		Non-IPD	9.60	6.07–13.13
	Multicenter	IPD	12.10	8.10-16.09
		Non-IPD	8.83	5.34–12.32
6 A	North	IPD	-	-
		Non-IPD	16.36	3.43–29.28
	South	IPD	8.05	4.72–11.38
		Non-IPD	9.45	4.16–14.74
	Multicenter	IPD	8.05	4.72–11.38
		Non-IPD	14.26	5.73–22.78

Abbreviations IPD, invasive pneumococcal disease; CI, confidence interval

Distribution and prevalence of non-vaccine serotypes not covered by PCV13

Given the potential for serotype replacement, we analyzed the distribution and prevalence of non-vaccine serotypes not covered by PCV13. The most common non-vaccine serotypes identified were 6 C, 15B, 16 F and 15 A. Among these, serotype 6 C had the highest prevalence at 4.28% (95%CI: 1.66-6.90%), followed by 15B at 3.47% (95%CI: 1.21-5.74%), 16 F at 3.10% (95%CI: 2.57-8.77%), and 15 A at 3.09% (95%CI: 1.47-7.65%)(Table 4).

Prevalence of antimicrobial resistance

Eight studies reported the data of antimicrobial resistance patterns. The highest level of resistance was observed for erythromycin at 93.73% (95%CI: 90.58-96.88%), closely followed by azithromycin at 82.69% (95%CI: 65.63-99.75%), tetracycline at 80.95% (95%CI: 70.92-90.98%), clindamycin at 76.28% (95%CI: 64.74-87.83%), and sulfamethoxazole at 55.02% (95%CI: 42.73-67.32%) (Table 4). Furthermore, the rate of penicillin non-susceptible *S. pneumoniae* (PNSP) was identified to be 9.97% (95%CI: 9.02-10.93%), and the rate of resistance to penicillin was calculated at 27.74% (95%CI: 11.54-43.94%) (Table 5).

Publication Bias

Publication bias was assessed using Begg's and Egger's test. The results did not indicate significant publication bias among the included studies (Begg's: $P=0.245$; Egger's: $P=0.113$).

Discussion

This meta-analysis is performed to examine the serotype distribution and coverage and antibiotic resistance patterns of *S. pneumoniae* after the introduction of PCV13 as a self-funded vaccine in the pediatric population under 14 years of age in China. Our comprehensive analysis revealed that serotypes 19 F, 19 A, 6B, 14, 6 A, and 23 F were predominantly observed in both invasive and non-invasive strains. Significantly, the coverage rates of serotypes by PCV10, PCV13, PCV15, and PPSV23 vaccines were calculated to be 52.17%, 74.77%, 76.72%, and 92.90%, respectively. In addition, significant resistance was observed in *S. pneumoniae* to erythromycin, which was the most common, followed sequentially by azithromycin, tetracycline, clindamycin, and sulfamethoxazole, necessitating a reevaluation of current therapeutic strategies against this pathogen.

The findings of this study have several important clinical and public health implications. Firstly, the persistence of certain serotypes, such as 19 F and 19 A, despite the introduction of PCV13, underscores the need for ongoing surveillance and potential updates to vaccine formulations to include additional serotypes prevalent in the Chinese pediatric population. The high prevalence of antibiotic-resistant strains highlights the urgent need for new antibiotics and alternative treatment strategies, particularly given the limited therapeutic options available for pediatric patients.

Although PCV13 has been available since 2016 and has broader serotype coverage compared to previous formulations, its uptake in China remains low. This vaccine is an out-of-pocket expense and is not currently included in the national immunization programme, despite recommendations to do so. This limited access can have a significant impact on low socioeconomic populations and remote areas where the burden of pneumococcal disease may be higher and access to vaccines more limited. The financial burden on families in these populations may

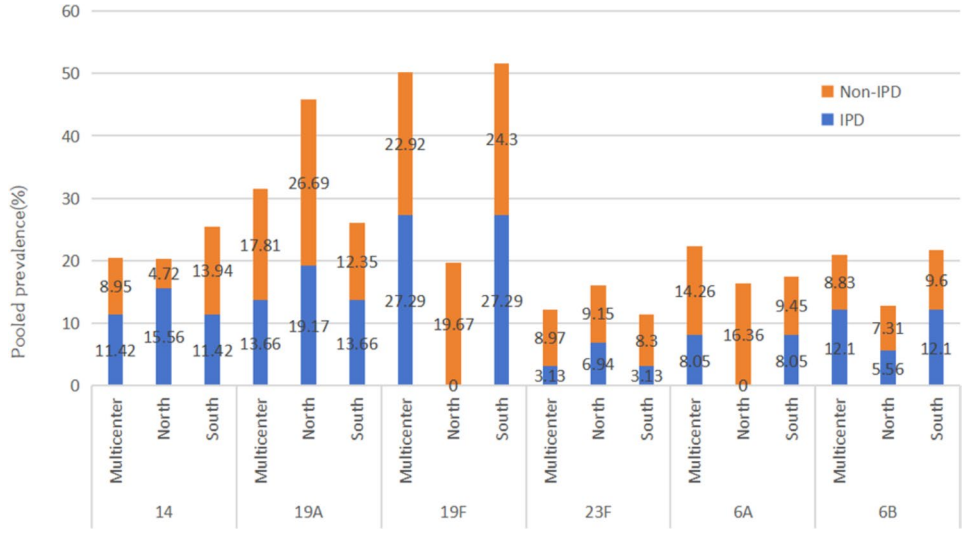

Fig. 3 Distribution of pneumococcus serotypes

Table 3 Pooled serotype coverage of *Streptococcus pneumoniae* vaccine

Vaccine	Strain	Coverage rate (%)	95% CI
PCV10	IPD	51.32	37.01–65.63
	Non-IPD	53.80	45.63–61.97
	Overall	52.17	44.91–59.42
PCV13	IPD	73.32	71.01–75.63
	Non-IPD	78.15	68.20–88.10
	Overall	74.77	71.53–78.01
PCV15	IPD	-	-
	Non-IPD	76.72	75.37–78.07
	Overall	76.72	75.37–78.07
PPSV23	IPD	-	-
	Non-IPD	92.90	92.09–93.71
	Overall	92.90	92.09–93.71

Abbreviations PCV, pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine

Table 4 Distribution and prevalence of non-vaccine serotypes not covered by PCV13

Serotype	Rate(%)	95%CI
16 F	3.10	2.57–8.77
15 A	3.09	1.47–7.65
6 C	4.28	1.66–6.90
15B	3.47	1.21–5.74
8	2.72	1.48–6.93
23 A	2.34	0.11–4.57
34	2.78	1.64–7.20
7 A	2.78	1.08–4.48
60 C	1.64	1.23–2.06
35 F	1.51	1.11–1.90
7 C	1.78	0.05–3.50
16 A	1.04	0.39–2.48

Abbreviations CI, confidence interval

Table 5 Pooled antibiotic resistance rates of *Streptococcus pneumoniae*

Antibiotics	No. of included studies	Resistance rate (%)	95% CI
Penicillin	8	27.74	11.54–43.94
Ceftriaxone	7	3.14	1.36–4.93
Clindamycin	6	76.28	64.74–87.83
Azithromycin	3	82.69	65.63–99.75
Chloramphenicol	8	6.88	4.66–9.09
Amoxicillin clavulanic acid	6	11.58	3.01–20.16
Cefotaxime	4	7.42	0.96–13.87
Cefuroxime	3	40.05	22.41–57.68
Erythromycin	8	93.73	90.58–96.88
Tetracycline	8	80.95	70.92–90.98
Levofloxacin	4	2.44	0.21–4.67
Rifampicin	3	0.30	-0.24-0.84
Meropenem	3	3.68	-0.99-8.36
Sulfamethoxazole	6	55.02	42.73–67.32
Moxifloxacin	3	0.58	-0.17-1.32
PNSP	4	9.97	9.02–10.93

Abbreviations PNSP, Penicillin-Non-susceptible *Streptococcus pneumonia;* CI, confidence interval

result in lower vaccination rates, further exacerbating health disparities.

Moreover, the study underscores the importance of integrating PCV13 into the national immunisation programme to ensure broader and more equitable access to vaccination. Achieving higher vaccination coverage rates is crucial for reducing the incidence of pneumococcal diseases and preventing the spread of antibiotic-resistant strains. This is particularly important in low socioeconomic and remote populations, where the burden of disease is often highest, and healthcare access is limited.

Our study also highlights the need for more carriage studies. Carriage studies are essential in understanding

the transmission dynamics of *S. pneumoniae* and the impact of vaccination on pneumococcal ecology. They provide critical insights into the prevalence and spread of different serotypes within communities, particularly in populations where vaccine coverage is suboptimal. Future research should prioritize these studies to inform and optimize vaccination strategies.

In the context of the post-PCV13 vaccination era, our research has shown that the predominant serotypes of *S pneumoniae* include 19 F, 19 A, 6B, 14, 6 A, and 23 F. This serotype prevalence, although with minor variations in order, is consistent with patterns observed in pre-PCV13 vaccine studies [25–27]. Fu JJ, et al. [25] conducted a meta-analysis of 16 studies published before September 2016, focusing on the serotype distribution and antibiotic resistance of *S. pneumoniae* causing IPD in China. The study reported a predominant distribution of serotypes 19 F (27.7%), 19 A (21.2%), 14 (16.5%), 6B (8.6%), and 23 F (7.3%) in children. Similarly, Lyu S, et al. [26] conducted a systematic review that included studies from 2006 to 2016 on *S. pneumoniae* serotypes isolated from children aged < 14 years in mainland China. In their review of 40 studies conducted before the licensure of PCV13, the most common serotypes were 19 F, 19 A, 23 F, 14, and 6B [26]. Taken together, these findings suggest that the primary serotype profile of *S. pneumoniae* in the Chinese pediatric population remained unchanged after the licensing of PCV13 in 2016, suggesting a negligible effect of PCV vaccine on the predominant serotype distribution of *S. pneumoniae*.

Our study found that the predominant pneumococcal serotypes in the northern and southern regions of China exhibited a remarkable uniformity, suggesting a homogenous distribution pattern of these serotypes across the nation. This observation is consistent with findings from other regions of China. For example, in the northern region, Beijing demonstrated prevalence of serotypes 19 F, 19 A, 23 F, 14, and 6 A [28], while in the southern region, Liuzhou reported 19 F, 6B, 19 A, 24 F, and 14 [29]. Similar patterns were observed in Shanghai in the eastern region (19 F, 19 A, 14, and 6B) [30] and Chongqing in the western area (19 F, 61, 6B, and 19 A) [31]. In contrast, developed countries have markedly different prevalent serotypes. For instance, in the USA, the predominant serotypes include 35B, 3, 11 A, and 11D [32], whereas in the UK and Ireland, they are 3, 8, and 15 A [33], and in Japan, they are 12 F, 3 and 23 A [34]. However, slight discrepancies were observed in developing nations. Thailand reports serotypes 6B, 23 F, and 14 [35], Malaysia 14, 6B, 19 A and 6 A [36], Mexico 19 A, 3, 15B and 19 F [37], and Northern Russia 19 F, 23 F and 6 A [38]. The variation in serotype distribution may be attributed to factors such as the divergent evolutionary trajectories of native *S. pneumoniae* across different regions, resulting in distinct capsular genotypes; differential susceptibilities among diverse racial populations to specific *S. pneumoniae* serotypes; and the disparity in PCV coverage in various populations, which arguably is the most critical determinant.

Our analysis of non-vaccine serotypes revealed that the most common serotypes not covered by PCV13 were 6 C, 15B, 16 F, and 15 A. The increasing prevalence of these non-vaccine serotypes suggests potential serotype replacement, which is a concern with the widespread use of PCVs. Understanding the dynamics of non-vaccine serotypes is crucial for monitoring the long-term effectiveness of PCV13 and informing future vaccine development strategies. Continuous surveillance and updating of vaccine formulations to cover emerging non-vaccine serotypes are essential for maintaining the efficacy of pneumococcal vaccination programs.

Serotype replacement has been observed in regions where PCVs are widely available [39, 40]. An interesting finding in our study was that the PCVs-covered serotypes decreased slightly as compared to the data before the PCV13 vaccine was introduced [25, 26]. The serotype coverage rates of PCV10 and PCV13 in our study were 52.17%, and 74.77%, as compared to that of 60.8%, 65.1% and 90.0% in the studies before the introduction of PCV13 [25, 26]. These results were also reported by Yan ZY, et al. [23] who investigated the prevalence, serotypes and antibiotic susceptibility of *S. pneumonia* isolated from Chinese children from 2017 to 2019. In that study, the authors reported that the PCVs-covered serotypes decreased slightly (PCV10: 69.7% VS.50.8%; PCV13: 93.3% VS.77.3%), as compared to their previous data obtained before the introduction of PCV13 [41]. These may attributed to the introduction of PCV13 in 2016. Although the serotype coverage of PCV13 was slightly decreased after the introduction of PCV13, our result was still higher than that in other developed countries. For example, the serotype coverage of PCV13 was 52% in Spain [42], 41.4% in USA [39], and 37.5% in Japan [40].

An interesting finding in our study was that the coverage of PCV10, and PCV13 for IPD strains was less compared to non-IPD strains. This contrasts with a previous meta-analysis covering the period before PCV13 introduction in China, which included 85 studies (2000–2016) and found higher vaccine coverage for invasive isolates [43]. Contrarily, another U.S. meta-analysis highlighted a substantial decline in IPD rates following 5-years of PCV13 licensure, predominantly due to reductions in serotype 19 A [44]. In mainland China, despite PCV7 licensure in 2008 and PCV13 in 2016, their adoption as self-paid vaccines was limited, implying that the 20-year serotype fluctuation in China was minimally influenced by PCV introduction. The primary shifts observed were increases in serotypes 19 A and 19 F from 2000 to 2004, likely driven by antibiotic selective pressure. Notably,

even with limited PCV7 usage, the rise in serotype 19 A was significant, making it a prevalent serotype across many regions in China [44]. In contrast, in the U.S., serotype 19 A, not covered by PCV7, escalated from 2.7% in 1999–2000 to 34.1% in 2010–2011 post-PCV7 licensure, a trend attributed primarily to serotype replacement post-vaccination [39, 45].

The advent of antibiotic-resistant *S. pneumonia* in recent years has precipitated novel complexities in clinical anti-infective regimens, particularly in pediatric populations whose liver and kidney functions are not fully developed, increasing their vulnerability to drug toxicity [46, 47]. This study observed a 27.74% resistance rate to penicillin, a notable decrease from the 45.1% reported prior to the PCV13 vaccine introduction [25]. This aligns with a study in Japan, which showed a reduction in penicillin resistance from 54.3 to 11.2% following the PCV13 introduction, correlating with the diminished prevalence of penicillin-resistant and intermediate genotypes, particularly in serotypes 6B, 14, 19 F, 23 F, and 6 A among children [48]. Furthermore, we noted that resistance rates for *S. pneumonia* to antibiotics such as ceftriaxone, chloramphenicol, rifampicin, moxifloxacin, meropenem, and levofloxacin were below 10.00%, consistent with previous studies [13, 14, 17, 23]. This may be linked to the lower usage of these antibiotics in treating *S. pneumonia* infections in this area. However, the high resistance rates to erythromycin, tetracycline, and azithromycin, all over 80%, are alarming and require immediate attention. The urgent need for new *S. pneumonia* vaccines is evident, with WHO recommending in 2019 the inclusion of PCVs in immunization programs to protect children's health [49].

Strengths and limitations

This study has several strengths. Firstly, it is the first meta-analytic effort to comprehensively examine the serotype distribution and antibiotic resistance patterns of *S. pneumoniae* in Chinese children post-PCV13 introduction. Secondly, the inclusion of multiple databases and rigorous selection criteria ensures a broad and representative sample of studies. Thirdly, the analysis includes data from 12 studies with a total of 6593 *S. pneumoniae* strains for serotyping, which increases the statistical power of the results.

However, this study also has limitations. Initially, a lack of adequate data precluded the execution of a subgroup analysis distinguishing between community-acquired and hospital-acquired pneumonia. Secondly, in certain instances, the delineation between data collated post-2017 and pre-2017 was unfeasible, necessitating the exclusion of these studies from our analysis, which may have introduced a degree of bias. Thirdly, the study encountered substantial heterogeneity in several outcomes. This heterogeneity could be attributable to various factors, including geographical diversity, age discrepancies among pediatric subjects, differences in the study periods, and potentially other unidentified variables. Lastly, the studies included in this meta-analysis span from 2017 to 2024, a period that overlaps with the COVID-19 pandemic. It is plausible that the pandemic may have contributed to reduced PCV13 vaccination rates, potentially influencing outcomes like the distribution of pneumococcal serotypes and antimicrobial resistance profiles. Given these considerations, our results should be interpreted with caution.

Conclusions

Our study found that serotype 19 F and 19 A the most prevalent serotype in mainland China after the introduction of PCV13. The distribution of *S. pneumoniae* serotypes and their antibiotic resistance profiles in children under 14 years in mainland China have remained relatively stable. However, the ongoing evolution of *S. pneumoniae* in response to vaccination requires continual adaptation of public health strategies. Increased efforts to integrate PCV13 into the national immunization program and to conduct more carriage studies are essential to better understand and control pneumococcal disease.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41479-024-00141-z.

Supplementary Material 1

Author contributions

LY made significant contributions to the reported work, be it in conception, study design, conduct, data collection, analysis, writing, and interpretation. WSJ, HL and XLJ participated in the methodology, statistical analysis, and modification of the final draft. WF and ZYB conceived the study, participated in its design, coordination, selection of the studies, initial and final draft of the study. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

We confirm that all materials included in this manuscript can be published.

Competing interests

The authors declare no competing interests.

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