



Letter to the Editor

Antimicrobial resistance in *Streptococcus pneumoniae* isolates from invasive pneumococcal infections in Iran



Sir,

Throughout the past three decades, the rates of resistance to penicillin and other antimicrobial agents have been increasing rapidly in *Streptococcus pneumoniae* in many parts of the world [1]. The emergence of multidrug resistance has complicated the empirical treatment of pneumococcal infections [2]. Drug resistance surveillance of *S. pneumoniae* isolates from different populations and countries is very important for establishing treatment protocols. The present study was conducted to determine the antimicrobial resistance patterns and minimum inhibitory concentrations (MICs) of *S. pneumoniae* isolates causing invasive pneumococcal disease (IPD) in the Islamic Republic of Iran. The study was performed from June 2012 to September 2016 in Milad Hospital (Tehran, Iran) among patients with suspected IPD. Specimens were cultured on sheep blood agar and were incubated for 48 h at 35 °C in the presence of 5% CO₂. All positive samples were tested by phenotypic and biochemical tests. *S. pneumoniae* isolates were identified by Gram staining, α-haemolysis, catalase, optochin susceptibility and bile solubility testing. Duplicate isolates from the same patient were excluded unless the second isolate was isolated >30 days after the first isolation. All confirmed pneumococcal isolates were serotyped by the Quellung reaction using pneumococcal capsular antisera obtained from Statens Serum Institut (Copenhagen, Denmark) according to the manufacturer's instructions. Antimicrobial susceptibility testing for levofloxacin, trimethoprim/sulfamethoxazole (SXT), clindamycin, azithromycin, erythromycin, vancomycin, chloramphenicol and tetracycline was performed by the gradient test method in accordance with Clinical and Laboratory Standards Institute (CLSI)

2017 guidelines. MICs of antibiotics were determined by Etest (bioMérieux, Marcy-l'Étoile, France). Mueller–Hinton agar plates supplemented with 5% sheep blood was inoculated with a 0.5 McFarland standard of suspension harvested from plates and then Etest strips were placed on each plate. *S. pneumoniae* ATCC 49619 was used as the control strain. The results were interpreted according to the current breakpoints recommended by the CLSI. During the 52-month study period (June 2012 to September 2016), 50 *S. pneumoniae* isolates were collected from patients (age range 3–77 years) with clinical signs of IPD. The youngest patient was a 3-year-old girl from whom *S. pneumoniae* was isolated from the cerebrospinal fluid (CSF), and the oldest patient was an elderly man (age 77 years) from whom *S. pneumoniae* was isolated from a tracheal aspirate. Most of the isolates were obtained from bloodstream infections (40%), and the remaining isolates were cultured from CSF (14%), sputum (14%), bronchoalveolar lavage (14%), tracheal aspirate (12%) and pleural fluid (6%). Serotype 19 was the most prevalent serotype (30%), followed by serotypes 23 (16%) and 14 (10%). Fifteen pneumococcal isolates (30%) were penicillin-non-susceptible, including nine (18%) penicillin-resistant strains (MIC ≥ 8 µg/mL for non-meningeal isolates and MIC ≥ 0.12 µg/mL for meningeal isolates) and six (12%) penicillin-intermediate-resistant strains (MIC = 4 µg/mL). The MIC₅₀ and MIC₉₀ values (MICs required to inhibit the growth of 50% and 90% of the isolates, respectively) of penicillin were 1 µg/mL and 3 µg/mL, respectively, for non-meningeal isolates, and 1 µg/mL and 2 µg/mL, respectively, for meningeal isolates. Forty-four pneumococcal isolates (88%) were susceptible to vancomycin (MIC₅₀, 0.75 µg/mL; MIC₉₀ 1.5 µg/mL) and six (12%) were non-susceptible to vancomycin. A high resistance rate among pneumococcal isolates was observed for erythromycin (72%), followed by azithromycin (70%), SXT (64%), tetracycline (56%) and clindamycin (52%). The greatest susceptibility was observed for levofloxacin (98%). Table 1 shows the antimicrobial susceptibility of the pneumococcal strains. The results of the present study show that

Table 1
Minimum inhibitory concentrations (MICs) of tested antibiotics among *Streptococcus pneumoniae* isolated in Tehran, Iran (June 2012 to September 2016).

Antibiotic	Breakpoint (µg/mL)	N	%S/I/R			MIC (µg/mL)	
			S	I	R	MIC ₅₀	MIC ₉₀
Penicillin, non-meningitis	S, ≤2; I, 4; R, ≥8	43	82.2	13.3	4.4	1	3
Penicillin, meningitis	S, ≤0.06; R, ≥0.12	7	0	0	100	1	2
Levofloxacin	S, ≤2; I, 4; R, ≥8	50	98	0	2	0.75	1.5
SXT	S, ≤0.5/9.5; I, 1/19–2/38; R, ≥4/76	50	2	34	64	2	8
Clindamycin	S, ≤0.25; I, 0.5; R, ≥1	50	46	2	52	0.125	3
Azithromycin	S, ≤0.5; I, 1; R, ≥2	50	26	4	70	0.75	16
Erythromycin	S, ≤0.25; I, 0.5; R, ≥1	50	28	0	72	0.19	6
Vancomycin	S, ≤1	50	88	0	0	0.75	1.5
Chloramphenicol	S, ≤4; R, ≥8	50	74	0	26	3	24
Tetracycline	S, ≤1; I, 2; R, ≥4	50	44	0	56	12	32

S, susceptible; I, intermediate; R, resistant; MIC_{50/90}, MICs required to inhibit the growth of 50% and 90% of the isolates, respectively; SXT, trimethoprim/sulfamethoxazole.

the rates of antimicrobial resistance among *S. pneumoniae* isolates in Iran continue to increase. In this study, the rate of penicillin-non-susceptible pneumococcal isolates was 30%, whereas Houri et al. reported a rate of 20.8% [2] and Tabatabaei et al. reported 21.9% [3]. This difference may be due to the small number of CSF specimens (pneumococcal meningitis) in the current study. Kohanteb and Sadeghi [4] and Jahanmehr et al. [5] have reported similar results. Erythromycin, azithromycin and SXT were antibiotics for which a high rates of resistance were found. High levels of resistance to erythromycin (71.4%) and sulfamethoxazole (57.1%) were also observed by Houri et al. [2]. Tabatabaei et al. also reported 83.6% resistance to erythromycin [3]. In the current study, susceptibility to vancomycin was 88%. In similar studies, susceptibility to vancomycin has been reported as 93% by Tabatabaei et al. [3] and 98% by Jahanmehr et al. [5]. Similar to other studies [2], high susceptibility to levofloxacin (98%) was observed in the current study. This shows that the most resistant strains of *S. pneumoniae* remain susceptible to this antibiotic. However, most studies conducted in Iran have evaluated pneumococcal isolates from nasopharyngeal carriers. Further studies focusing on invasive pneumococcal isolates are needed. In conclusion, this study revealed a high rate of resistance among *S. pneumoniae* isolates to commonly used antibiotics such as penicillin and erythromycin. The most effective antibiotics for treatment of invasive pneumococcal infection were levofloxacin and vancomycin.

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Competing interests

None declared.

Ethical approval

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