Science for Communities

Antimicrobial susceptibility of invasive *Haemophilus influenzae*, 2019

The antimicrobial susceptibility of 62 invasive isolates of *H. influenzae* referred to ESR in 2018 was tested. Ampicillin, amoxicillin-clavulanic acid, cefaclor and cefuroxime minimum inhibitory concentrations (MICs) were determined by gradient strip on Mueller-Hinton Fastidious (MH-F) agar. Cefotaxime, ciprofloxacin, co-trimoxazole, erythromycin, rifampicin and tetracycline susceptibilities were determined by disc diffusion on MH-F agar. Except for cefaclor, MICs and disc diffusion zone diameters were interpreted using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints.[1] Cefaclor MICs were interpreted using the Clinical and Laboratory Standards Institute (CLSI) breakpoints.[2] Two (3.2%) of the 62 isolates were serotype b.

Nine (14.5%) isolates produced β-lactamase. In addition to the nine β-lactamase-positive isolates, a further six isolates were ampicillin resistant, giving a total rate of 24.2% ampicillin resistance (see table).

Three 2019 isolates (4.8%) were found to be cefotaxime resistant by routine disc testing. Further testing with gradient strips confirmed these isolates were resistant to cefotaxime (MICs 1-2 mg/L) and ceftriaxone (MICs 0.25 mg/L). All three isolates were resistant to cefuroxime (MICs ≥256 mg/L), amoxicillin-clavulanic acid resistant (MICs ≥4 mg/L), and one produced β-lactamase. Resistance to 3rd-generation cephalosporins was detected for the first time among invasive *H. influenzae* isolates in 2017 and was found in four isolates.

Antimicrobial resistance among *Haemophilus influenzae* isolates from invasive disease, 2018

Antibiotic[1]	Number tested	Number resistant	Percent resistant
Ampicillin	62	15[2]	24.2
Amoxicillin-clavulanic acid	62	6	9.7
Cefaclor	62	7	11.3
Cefuroxime (IV(4.8%))[3]	62	10	16.1
Cefuroxime (oral)[3]	62	17	27.4
Cefotaxime	62	3	4.8
Ciprofloxacin	62	1	1.6
Co-trimoxazole	62	5	8.1
Erythromycin	62	0	-
Rifampicin	62	0	-
Tetracycline	62	0	-

1 Results for the full range of antibiotics tested are presented. Many are not appropriate for the treatment of invasive *H. influenzae* disease or the chemoprophylaxis of contacts.
2 9 of the 15 ampicillin-resistant isolates produced β-lactamase.
3 The EUCAST breakpoints for cefuroxime are variable depending on whether the drug is administered parenterally or orally.

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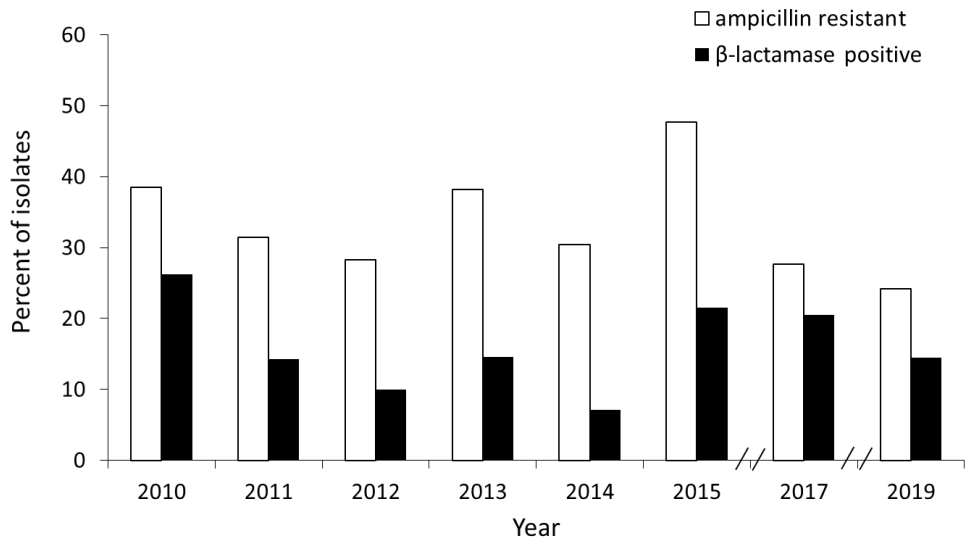
One (1.6%) isolate was ciprofloxacin-resistant by routine disc testing, and further testing with gradient strips confirmed this isolate was resistant to ciprofloxacin with an MIC of ≥32 mg/L. The first two ciprofloxacin-resistant *H. influenzae* isolates were found in 2017. None of the ciprofloxacin-resistant found in New Zealand have been resistant to 3rd-generation cephalosporins and none were group B.

Trends in ampicillin resistance and β-lactamase production among invasive *H. influenzae* over the last 10 years are shown in the figure below. However, due to changes in antimicrobial susceptibility testing methods, the rate of ampicillin resistance in 2017 and 2019 is not directly comparable with the rates for earlier years (see footnote 2 to the figure). In 2019, 60% (9/15) of ampicillin-resistant isolates were β-lactamase producers. This is lower than that observed in 2017, when 74% (17/24) of ampicillin-resistant isolates were β-lactamase producers.

Ampicillin resistance and β-lactamase production among invasive *Haemophilus influenzae*, 2010-2019



1 There is no data for 2016 and 2018 as the antimicrobial susceptibility of invasive *H. influenzae* isolates referred to ESR that year was not tested.

2 **The rates of ampicillin resistance estimated for the years 2008 to 2015 are not directly comparable with the rate for 2017 and 2019, due to changes in test methods used.** Before 2017, CLSI susceptibility testing standards were used, and isolates determined to have a mechanism of β-lactam resistance other than β-lactamase production were categorised as ampicillin resistant irrespective of the results of the actual ampicillin susceptibility test. In 2017 and 2019, EUCAST susceptibility testing standards were used, and the ampicillin susceptibility of isolates, determined to have a mechanism of β-lactam resistance other than β-lactamase production (eg, in the 1 unit penicillin disc screening test for β-lactam resistance), is reported according to the actual results obtained in the ampicillin susceptibility test. However conversely, the EUCAST breakpoint for ampicillin resistance is lower (MIC ≥2 mg/L) than the CLSI breakpoint (MIC ≥4 mg/L).

References:

1 European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 9.0; 2019 Jan. Available from http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_9.0_Breakpoint_Tables.pdf.

2 Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 29th ed. Wayne, USA: CLSI; 2019. CLSI supplement M100.