

Antimicrobial resistance patterns of respiratory pathogens: a local report from Turkey

Several surveillance studies have shown that antimicrobial resistance of the three major respiratory pathogens, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*, is an increasing problem throughout the world [1].

In this study, commonly used antimicrobial agents were tested against 142 *S. pneumoniae*, 79 *H. influenzae* and 18 *M. catarrhalis* strains isolated from community-acquired infections in 1999 and 2000. All the isolates were identified according to standard microbiologic criteria. The Etest (AB Biodisk, Solna, Sweden) was performed according to the manufacturer's recommendations and the MIC results were evaluated according to the NCCLS guidelines [2]. For *M. catarrhalis* strains, breakpoints for *H. influenzae* were applied. *S. pneumoniae* strains were tested against penicillin G, clarithromycin, trimethoprim-sulfamethoxazole (TMP-SMX) and levofloxacin. *H. influenzae* and *M. catarrhalis* strains were tested against ampicillin, ampicillin-sulbactam, clarithromycin, TMP-SMX, ciprofloxacin and levofloxacin and also tested for beta-lactamase production by using cefinase discs (Becton Dickinson, Cockeysville, MD, USA). The control strains included were *S. pneumoniae* ATCC 49619 and *H. influenzae* ATCC 49766 on each set of testing.

The specimens included in the study were sputum ($n = 123$), bronchioalveolar lavage ($n = 38$), blood ($n = 26$), deep tracheal aspirate ($n = 17$), cerebrospinal fluid (CSF) ($n = 3$), ear aspirate ($n = 11$) and conjunctival smears ($n = 21$) received from adult ($n = 104$) and pediatric ($n = 135$) patients. Of the 142 *S. pneumoniae* strains, 65 (45.7%) were isolated from adults and 77 (54.2%) from children. Twenty-one (26.5%) *H. influenzae* strains were isolated from adults and 58 (73.4%) from children, whereas *M. catarrhalis* strains were exclusively isolated from adults. Overall, 24 of the *S. pneumoniae* isolates were from blood, five from conjunctiva and two from CSF. Only one *H. influenzae* isolate was from CSF, two were from blood and 16 were from conjunctiva. The remaining isolates were from respiratory tract specimens.

Of the 142 *S. pneumoniae* isolates, only one sputum isolate was highly resistant to penicillin

(MIC = 1.5 mg/L). The rate of intermediate-level penicillin resistance was 38.7%. The highest rate of resistance was observed against TMP-SMX. There were four isolates susceptible to penicillin, but resistant to clarithromycin. The rate of resistance to clarithromycin was higher (32.7%) among *S. pneumoniae* strains showing intermediate-level penicillin resistance than penicillin susceptible strains (5.8%). TMP-SMX resistance was present in 92.7% of penicillin-resistant strains and 70.9% of penicillin-susceptible strains. The rate of penicillin resistance was 40.7% among strains isolated from children and 36.3% among those isolated from adults. The rate of susceptibilities to clarithromycin and TMP-SMX among children and adult patients were not statistically significant ($P = 0.84$, $P = 0.93$, respectively). Of the blood isolates 30.7% showed intermediate-level penicillin resistance (Table 1).

The first penicillin resistant *S. pneumoniae* strain from Turkey was reported in 1994 [3]. In another study, there was 23.4% intermediate level resistance among 132 strains isolated from children and adults, but there was no isolate with high-level resistance to penicillin [4]. Later, Gur et al. reported 29% intermediate- and 3% high-level resistance among 750 strains. The rate of penicillin resistance was 36% and 25% among strains isolated from children and adults, respectively [5].

In this study, the rate of beta-lactamase production among *H. influenzae* and *M. catarrhalis* strains was lower than the rates reported previously [6]. All beta-lactamase-producing *H. influenzae* strains were from children. TMP-SMX resistance of *H. influenzae* strains was as high as 31.6% compared to the macrolide resistance of 7.5% (Table 1). Sener et al. showed that the rate of beta-lactamase production of the strains isolated between 1992 and 1996 was 14.6% whereas the rate of resistance to azithromycin and TMP-SMX were 0% and 15%, respectively [7]. The beta-lactamase positive *M. catarrhalis* strains were resistant to ampicillin as expected and susceptible to other agents tested. In another study from Turkey, the rate of beta-lactamase production was 73% among 93 strains isolated between 1992 and 1995 and all were susceptible to amoxicillin-clavulanic acid, cephalosporins and clarithromycin [8].

Our results were similar to the previous observations regarding the higher, emerging rates of penicillin and TMP-SMX resistance in *S. pneumo-*

Table 1 Activity of commonly used antibiotics against *S. pneumoniae*, *H. influenzae* and *M. catarrhalis* isolated in 1999 and 2000 (from 2 centers, Turkey)

Bacteria/Antibiotics	Range	MIC		Intermediate <i>n</i> (%)	Resistant <i>n</i> (%)
		MIC50	MIC90		
<i>S. pneumoniae</i> (<i>n</i> = 142)					
Penicillin G	0.002–1.5	0.023	0.380	55 (38.7)	1 (0.7)
Clarithromycin	0.016–256	0.064	6.0	4 (2.8)	19 (13.3)
TMP-SMX*	0.008–32	1.5	32	23 (16.1)	91 (64.0)
Levofloxacin	0.047–2	0.750	2	0	0
<i>H. influenzae</i> (<i>n</i> = 79)					
Ampicillin	0.064–1.5	0.190	0.5	2 (2.5)	0
Ampicillin + sulbactam	0.064–1.5	0.190	0.5	0	0
Clarithromycin	1.5–256	8	16	24 (30.3)	6 (7.5)
TMP-SMX*	0.032–32	0.190	32	0	25 (31.6)
Levofloxacin	0.006–0.16	0.012	0.023	0	0
Beta lactamase production: 3/79 (3.8%)					
<i>M. catarrhalis</i> (<i>n</i> = 18)					
Ampicillin	0.125–3	0.75	2	6 (33.3)	1 (5.5)
Ampicillin + sulbactam	0.016–0.032	0.047	0.064	0	0
Clarithromycin	0.064–0.75	0.125	0.250	0	0
TMP-SMX*	0.250–6	0.5	4.0	0	3 (16.6)
Levofloxacin	0.023–0.064	0.032	0.047	0	0
Beta lactamase production: 8/18 (44.4%)					

*TMP-SMX: Trimethoprim-sulfamethoxazole

niae worldwide. There was an increase in the macrolide resistance over the years and fluoroquinolone resistance was low as expected. Although the rate of beta-lactamase production among *H. influenzae* and *M. catarrhalis* strains was lower than the rates reported previously, the rate of resistance against other antimicrobial agents showed an increase over time.

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