Risk factors for antibiotic-resistant *Escherichia coli* isolated from community-acquired urinary tract infections in Dakar, Senegal

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**Objectives:** To assess overall resistance rates and risk factors for resistance to ampicillin, co-amoxiclav, nalidixic acid, fluoroquinolones and trimethoprim/sulfamethoxazole in *Escherichia coli* strains isolated from outpatients with acute urinary tract infection in Dakar (Senegal).

**Patients and methods:** From June 2001 to June 2003, a prospective study was performed among Senegalese outpatients consulting at the Institut Pasteur of Dakar for urine analysis. Evaluated risk factors were: age, gender, prior hospitalization, antibiotic exposure, urinary tract infection and urinary catheter.

**Results:** A total of 398 non-duplicate, consecutive, biologically significant *E. coli* were isolated. The levels of antibiotic resistance in Dakar appeared dramatic and worrisome with resistance rates ranging from 18.6% for fluoroquinolones to 73.6% for ampicillin. With the exception of the presence of urinary catheter, the risk factors identified were consistent with data previously reported in developed countries.

**Conclusions:** We hope our results will assist medical authorities in the development of appropriate control strategies.

Keywords: antimicrobial resistance, multivariate analysis, Enterobacteriaceae

**Introduction**

Urinary tract infection is a common community-acquired bacterial disease which frequently affects female outpatients.1 *Escherichia coli*, the most common member of the family Enterobacteriaceae, accounts for 75–90% of all urinary tract infections in both inpatients and outpatients.2 Increasing rates of resistance among bacterial uropathogens has caused growing concern in both developed and developing countries.2 A limited number of studies conducted in developed countries have analysed demographic and epidemiological data in order to determine the risk factors associated with resistant isolates from urine cultures,1,3,4 but to our knowledge, no such research has been done in developing countries.

**Materials and methods**

To determine the risk factors for urinary tract infection due to *E. coli* strains that are resistant to commonly used antimicrobial agents, we performed a prospective study from June 2001 to June 2003 among Senegalese outpatients consulting at the Institut Pasteur of Dakar (Senegal) for urine analysis. The majority of these patients (~75%) were civil servants or middle class workers who were insured through a special agreement with the Senegalese government or through private health insurance. After obtaining informed consent, each study participant was asked to complete a brief questionnaire requesting demographic data and medical history. The risk factors for *E. coli* resistance to ampicillin, co-amoxiclav, nalidixic acid, fluoroquinolones and trimethoprim/sulfamethoxazole—the most commonly used antimicrobial agents in Dakar—were determined according to the following variables: age group (<15 years, between 15 and 45 years and >45 years), gender, hospitalization and antibiotic exposure during the previous 6 months, and urinary tract infection and presence of urinary catheter during the previous year. The biological criteria for inclusion were a pure bacterial culture with a colony count of ≥10^4 cfu/mL and a leucocyte count of ≥10^4 cells/mL. *E. coli* was biochemically identified using API 20E system (bioMérieux, Marcy l’Étoile, France). Susceptibility testing was performed by disc diffusion method as recommended by...
the Antibiogram Committee of the French Society for Microbiology. The antibiotics tested were supplied by Bio-Rad (Marne la Coquette, France) with respective quantities (µg/disc) of active compounds: ampicillin (10), co-amoxiclav (20/10), ticarcillin (30), cefoxitin (30), imipenem (10), nalidixic acid (30), fluoroquinolones [including pefloxacin (5), norfloxacin (5) and ciprofloxacin (5)], gentamicin (15), tobramycin (10), amikacin (30), tetracycline (30), chloramphenicol (30) and trimethoprim/sulfamethoxazole (1.25/23.75). Extended-spectrum β-lactamase (ESBL) strains were systematically detected by double disc synergy test with cefotaxime or ceftazidime and co-amoxiclav as recommended. Isolates producing an ESBL were classified as resistant to cephalosporins. Zones of inhibition were measured by an automatic reader (Sirscan I2A, Pérols, France) and classified according to criteria of the Antibiogram Committee of the French Society for Microbiology. Intermediate and resistant strains were grouped together and classified as resistant. Repeat isolates from the same patients with the same resistance pattern were excluded. E. coli isolates displaying resistance to one of the three fluoroquinolones tested were classified as fluoroquinolone-resistant. Appropriate ATCC control strains were used and tested weekly. Statistical analyses were performed using STATA software version 6.0. Risk factors predicting E. coli resistance were estimated by univariate analysis and tested where appropriate by χ² or Fisher’s exact test. Variables with P < 0.25 in the univariate analysis were then included in a multivariable logistic regression model. Variables with an adjusted odds ratio of P < 0.05 were considered risk factors.

Results and discussion

During the study period, 8221 urine samples were analysed by the microbiology unit of the clinical laboratory. Of 695 uropathogen strains collected, a total of 398 non-duplicate, consecutive, biologically significant E. coli were isolated from 282 female and 116 male patients with a mean age of 39.1 years (95% CI: 38.2–42.1). The majority of our patients (72.9%) were uncomplicated urinary tract infections and 39% admitted to have taken an antibiotic treatment during the last 6 months. Table 1 shows the rates of resistance by year to selected antimicrobial agents. Resistance to trimethoprim/sulfamethoxazole, ampicillin and tetracycline—the most commonly used drugs in Senegal—was highest, with respective resistance rates of 67.8%, 73.6% and 75.9%. Among β-lactams, imipenem and cefotaxime appeared to be the most effective drugs, with resistance rates of 0% and 6.5%, respectively. Resistance rates to nalidixic acid and fluoroquinolones were < 20%. Compared with the other classes of drugs, aminoglycosides were the most effective, and in particular, the rate of resistance to amikacin was less than 1%. During the study, 25 ESBL-producing strains were isolated. Among the five antimicrobial agents most commonly used for the treatment of urinary tract infections (ampicillin, co-amoxiclav, trimethoprim/sulfamethoxazole, nalidixic acid and fluoroquinolones), resistance phenotype rates to ampicillin + trimethoprim/sulfamethoxazole, ampicillin + co-amoxiclav + trimethoprim/sulfamethoxazole, ampicillin + co-amoxiclav + trimethoprim/sulfamethoxazole + nalidixic acid and ampicillin + co-amoxiclav + trimethoprim/sulfamethoxazole + nalidixic acid + fluoroquinolones were 60%, 47%, 15% and 12%, respectively. Only 10.6% of the E. coli isolates were susceptible to all of the tested antibiotics prescribed either for short course therapy (trimethoprim/sulfamethoxazole and fluoroquinolones for 3 days) or for a 7 day course (ampicillin, co-amoxiclav).
Table 2. Multivariate analysis of independent risk factors for *E. coli* resistance to ampicillin, co-amoxiclav, nalidixic acid, fluoroquinolones and trimethoprim/sulfamethoxazole

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>AMP OR [95% CI]</th>
<th>P value</th>
<th>AMC OR [95% CI]</th>
<th>P value</th>
<th>NAL OR [95% CI]</th>
<th>P value</th>
<th>FQs OR [95% CI]</th>
<th>P value</th>
<th>SXT OR [95% CI]</th>
<th>P value</th>
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<tbody>
<tr>
<td>Sex</td>
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<td>female</td>
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<tr>
<td>male</td>
<td>2.1* [1.2–3.7]</td>
<td>0.01*</td>
<td>1.20.8–1.9</td>
<td>0.42</td>
<td>1.2 [0.6–2.1]</td>
<td>0.62</td>
<td>1.4 [0.8–2.7]</td>
<td>0.28</td>
<td>1.3 [0.8–2.2]</td>
<td>0.32</td>
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<td>Age category (years)</td>
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<td>Prior (6 months) hospitalization</td>
<td>1.9 [0.8–4.9]</td>
<td>0.16</td>
<td>1.1 [0.5–2.4]</td>
<td>0.72</td>
<td>3.1* [1.1–8.7]</td>
<td>0.03*</td>
<td>1.7 [0.5–6.3]</td>
<td>0.39</td>
<td>0.7 [0.3–1.4]</td>
<td>0.29</td>
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<td>Prior (1 year) urinary catheter</td>
<td>1.4 [0.7–2.6]</td>
<td>0.36</td>
<td>2.3 [0.9–6.3]</td>
<td>0.22</td>
<td>2.9 [0.9–4.7]</td>
<td>0.08</td>
<td>2.1 [0.6–2.8]</td>
<td>0.43</td>
<td>Ref</td>
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<tr>
<td>Prior (1 year) UTI</td>
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<tr>
<td>Prior (6 months) antibiotic exposure</td>
<td>3.7* [2.0–6.8]</td>
<td>&lt;0.001*</td>
<td>2.5 [1.6–4.0]</td>
<td>&lt;0.001*</td>
<td>3.0 [1.7–5.3]</td>
<td>&lt;0.001*</td>
<td>4.1 [2.2–7.6]</td>
<td>&lt;0.001*</td>
<td>1.1 [0.6–1.9]</td>
<td>0.77</td>
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</table>

According to univariate analysis, age groups for ampicillin and co-amoxiclav and prior urinary catheter for ampicillin and trimethoprim/sulfamethoxazole were not entered into the logistic regression model (P > 0.25). UTI, urinary tract infection; OR, odds ratio; AMP, ampicillin; AMC, co-amoxiclav; NAL, nalidixic acid; FQs, fluoroquinolones including pefloxacin, norfloxacin and ciprofloxacin; SXT, trimethoprim/sulfamethoxazole.

*Significant difference (P < 0.05).
45 years was associated with urinary tract infection caused by nalidixic acid and fluoroquinolone-resistant \textit{E. coli}.\textsuperscript{3,4}

Our study is the first to provide information from a developing country concerning risk factors for urinary tract infection due to \textit{E. coli} strains that are resistant to commonly used antimicrobial agents. Despite a possible bias due to the recruitment of patients in a laboratory setting, the overall resistance rates of \textit{E. coli} in Dakar appeared notably high with the confirmation of the emergence of multidrug-resistant strains. Multivariate analysis showed that previous antibiotic treatment and prior urinary tract infection were the strongest determinants of urinary tract infection due to resistant \textit{E. coli}. We hope that our results will contribute to the development of strategies aimed at limiting the evolution of antimicrobial resistance in Dakar. Possible strategies include a better control of the distribution of antimicrobial drugs in pharmacies and among street sellers, the reinforcement of therapeutic guidelines and infection control strategies, the distribution of information about antibiotic use and drug resistance and the continued support of large antimicrobial susceptibility studies.

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\section*{References}