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Risk factors for resistance in urinary tract infections in women in general practice: A cross-sectional survey

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Accepted 19 May 2015

Available online ■ ■ ■

KEYWORDS

Urinary tract infection;
Epidemiology;
Antibiotic resistance;
Risk factors;
General population;
General practitioner

Summary Objectives: In 2012 and 2013, a cross-sectional survey was conducted in women visiting a general practitioner for a urinary tract infection (UTI) to i) describe the patterns of antibiotic resistance of Enterobacteriaceae involved in community-acquired UTIs and ii) identify the factors associated with UTIs due to a multi-drug-resistant Enterobacteriaceae (MDREB).

Methods: Urine analyses were performed systematically for all adult women presenting with signs of UTI. Characteristics of women with UTI due to MDREB were compared to those with UTI due to non-MDREB. Weighted logistic regressions were performed to adjust for the sampling design of the survey.

Results: Significant factors associated with MDREB included the use of penicillin by the patient in the last three months (OR = 3.1; [1.2–8.0]); having provided accommodation in the previous 12 months to a resident from a country at high risk for drug resistance (OR = 4.0; [1.2

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<http://dx.doi.org/10.1016/j.jinf.2015.05.012>

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–15.1]); and the consumption of raw meat within the previous three months (OR = 0.3; [0.1–0.9]).

Conclusions: In the community, antibiotic use and exposure to a person returning from an area with a high risk of drug resistance are associated with UTIs due to MDREB. The potentially protective role of raw meat consumption warrants further study.

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Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections. In the United States, one-third of all women have had at least one physician-diagnosed presumed UTI by the age of 26 years.¹ UTIs are typically caused by Enterobacteriaceae, such as *Escherichia coli* (*E. coli*), which are involved in 70–80% of cases.²

The epidemiology of antimicrobial resistance varies among countries, particularly due to the impact of antibiotic prescriptions.^{3–5} In France, in 2009, the resistance rates of *E. coli* reached 55% for amoxicillin, 18% for fluoroquinolone, 8% for aminoglycoside and 10% for third-generation cephalosporin in healthcare-related infections.⁶ In 2011, the incidence of patients with at least one diagnostic sample testing positive for extended-spectrum β -lactamase Enterobacteriaceae (ESBLE) was 0.46 per 1000 days of hospitalization in French acute care hospitals.⁷ Data are scant for community-onset UTIs, as urine analysis is not mandatory in the treatment of uncomplicated cystitis. Thus, in previous epidemiological studies, urine cultures were not obtained for all women presenting with symptoms of UTI, but rather for women with complicated UTIs or UTIs seen in healthcare settings.

The empirical therapy of UTIs should be guided by knowledge of antimicrobial resistance and by identifying risk factors for resistance.⁸ Known risk factors include previous hospitalization, previous antibiotic use, urinary catheterization and recurrent UTIs.^{9,10} Other risk factors have been suspected, although they are less clearly established, such as international travel, living with pets, eating fish or raw meat, and swimming.^{11–13} Almost all of these risk factors have been identified in hospitalized patients. However, most UTIs occur in the community and are frequently treated in the absence of urine analysis. Data on the epidemiology of drug resistance in this setting are scant. Therefore, to identify factors associated with antimicrobial resistance in UTIs caused by Enterobacteriaceae in the French community, we conducted a cross-sectional survey in women visiting a general practitioner (GP) for a suspected UTI. Urine analysis was performed for all included individuals.

Materials and methods

Design and study population

The study population was derived from a national cross-sectional prospective survey, titled Drug resistant Urinary Tract Infection (Druti), that was conducted in France in 2012 and 2013 by general practitioners (GPs) of the Sentinelles network¹⁴ to estimate the annual incidence of

UTIs due to antibiotic-resistant Enterobacteriaceae in women visiting a GP for a suspected UTI (the results were pending at the time that this manuscript was written). In brief, a two-step sampling design was performed. For the first step, GPs of the Sentinelles network were randomly selected for participation and stratified into five groups according to five regions of France: north, east, west, southwest, and southeast. For the second step, the GPs prospectively included all female patients 18 years of age and older who had presented in the last seven days with at least one of the following UTI symptoms: dysuria, frequent urination, or urgency of urination. Those patients who agreed to participate and had not taken an antibiotic in the last seven days were included. A urine sample was collected from all participants, and urine culture performed on all samples at the same laboratory. The GPs were blinded to the urine culture results.

For each included patient, the GP administered a questionnaire that was completed during the consultation. It included questions regarding the patient's demographic characteristics (age, household members, and nationality), clinical status (chronic diseases and comorbidities, particularly pregnancy, urinary tract disorder, previous UTIs, and urinary catheterization), history of pharmacological treatments before consultation (especially antibiotic use by the patient or a member of the patient's household), previous hospitalization, contact with a professional or personal healthcare worker by the patient or a member of the patient's household, international travel, contact with an animal (with information on possible antibiotic treatments administered to this animal) and the consumption of raw meat. To recover any missing data, a trained investigator telephoned the GP and the patient to verify the information within two weeks of inclusion.

According to French recommendations, complicated UTI was defined as UTI occurring in a woman with urinary tract anomalies, pregnant, aged 65 years and older or treated for a chronic disease (diabetes, cancer, renal insufficiency). To define countries at high risk of drug resistance, a wide definition was chosen based on previous publications^{2,15,16}; if a country was located in Central/South America, Eastern/Southern Europe, Africa or Asia, it was considered to be high risk.

Sample size

The sample size of the Druti study was calculated for the objective of incidence. A total of 280 *E. coli*-positive samples was calculated to estimate the incidence rate of UTIs caused by fluoroquinolone-resistant *E. coli*, according to an expected proportion of fluoroquinolone resistance of 18% and a precision of 4.5%.⁶ Based on the assumption of 70% positive urine cultures for suspected UTIs and 77%

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