Journal of Infection (2015) 70, 247—254

BIAMM
British Infection Association

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Risk factors for severe sepsis in community-onset bacteraemic urinary tract infection: Impact of antimicrobial resistance in a large hospitalised cohort

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Accepted 15 September 2014
Available online 12 October 2014

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http://dx.doi.org/10.1016/j.jinf.2014.09.011

KEYWORDS
Bacteraemia;
Urinary tract infection;
Severe sepsis or septic shock;
Multidrug resistance;
Risk factors

Summary *Objective:* To determine risks factors associated with severe sepsis or septic shock (SS) at admission in patients with community-onset bacteraemic urinary tract infection (CO-BUTI) including the impact of multidrug-resistant (MDR) bacteria.
Methods: We analysed a prospective cohort of all consecutive episodes of CO-BUTI requiring hospitalisation in 8 tertiary hospitals of Spain between October 2010 and June 2011.
Results: Of an overall of 525 CO-BUTI episodes, 175 (33%) presented with SS at admission. MDR bacteria were isolated in 29% (51/175) of episodes with SS and in 33% (117/350) of those without SS ($p = 0.32$). The main MDR microorganism was *Escherichia coli* in both groups (25% and 28% respectively). Independent risk factors associated with SS at admission were: having fatal underlying conditions, McCabe score II/III (OR 1.90; 95%CI 1.23–2.92; $p = 0.004$), presence of an indwelling urethral catheter (OR 3.01; 95%CI 1.50–6.03; $p = 0.002$) and a history of urinary tract obstruction (OR 1.56; 95%CI 1.03–2.34; $p = 0.03$). After considering interactions, indwelling urethral catheters were a risk factor only for patients without fatal underlying conditions.
Conclusions: SS at hospital admission occurred in a third of CO-BUTI. Mainly host factors, and not the causative microorganisms or antimicrobial resistance patterns had an impact on the presence of SS.

Introduction

Urinary tract infection (UTI) is considered to be the most common bacterial infection in the community and has recently been recognized as a major cause of community-acquired bacteraemia, accounting for 30–35% of episodes in the adult population.[1–3] The incidence of severe sepsis or septic shock (SS) associated with this infection is not well reported in the literature; furthermore, most studies are retrospective, and some of these include cases without microbiological confirmation.[4–6] UTI, however, has been identified as the third leading cause of SS,[7,8] a condition associated with high morbidity and whose mortality rates can exceed 35%.[9,10]

Although bacteraemic infections caused by MDR bacteria have been associated with higher mortality, it is far from clear whether MDR microorganisms are more virulent; some studies, in fact, have suggested that the fitness of bacteria, especially *Escherichia coli*, could be reduced when acquiring certain mechanisms of resistance.[11,12] Few clinical studies have assessed the impact of MDR on the development of SS in patients with CO-BUTI; this is a particularly important issue since it is the leading cause of CO-bacteraemia in adults, and antimicrobial resistance in *Enterobacteriaceae*—the most common cause of UTI—has been dramatically increasing over the last two decades.[13,14]

The purpose of this study was to investigate the risk factors for SS, more specifically, to analyse the impact of bacterial aetiology and antimicrobial resistance patterns on SS at admission in patients with CO-BUTI.

Material and methods

Design, setting and patients

A prospective surveillance of all consecutive BUTI episodes of adult patients (≥18 years) were conducted in 8 tertiary care hospitals in Spain (total number of beds 6500, and serving a population of 3,701,600) between October 2010 and June 2011. As described elsewhere,[15] BUTI episodes were identified from clinical chart review of all patients with potential uropathogens isolated in blood cultures in microbiology laboratories of each hospital which were daily reported to principal investigators. Based on a protocol with standardised definitions, local investigators verified BUTI criteria and collected epidemiological and clinical data, including presence of severe sepsis or septic shock at admission. Information required was obtained from clinical chart or by direct interview with patients or their relatives. Patients were followed for 30 days after diagnosis of bacteraemia. For the purposes of this study we selected BUTI with a community-onset (CO). Fig. 1 shows the flow chart of selected episodes.

Study variables

The main variable was presence of severe sepsis or septic shock at admission (both). Length of hospital stay and mortality at 48 h, day 7 and day 30 were also analysed.

Explanatory variables included: age, sex, site of acquisition (community-acquired or healthcare-associated), severity of underlying diseases according to the Charlson comorbidity index and the McCabe classification, urological history, clinical symptoms, Pitt Score[16] assessed when the positive blood culture was collected, causative microorganisms, antibiotic susceptibility, and treatment.

Definitions

Bacteraemia associated with symptomatic UTI, following the Center for Disease Control (CDC)/National Healthcare Safety Network (NHSN) definitions,[17] was considered bacteraemic urinary tract infection (BUTI). In patients with no urinary symptoms, BUTI was diagnosed when the same uropathogen was isolated in urine and blood samples and there was no