

## Resistance to Empiric Antimicrobial Therapy is Associated with Prolonged Length of Stay in Patients Hospitalised with Urinary Tract Infection

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### Abstract

#### **Aim**

This study aimed to identify the prevalence of empiric antibiotic resistance in acutely hospitalized patients with urinary tract infection (UTI), and to investigate any association with hospital length of stay (LOS).

#### **Methods**

Acute hospital admissions with confirmed UTI over an 8-month period were identified. Empiric treatment was with co-amoxiclav.

#### **Results**

From 59 screened patients, 45 had confirmed UTI. The mean age was 49.2 years (SD 23.4), 80% were female and the mean LOS was 6.6 days (SD 4.8). The predominant uropathogen was *E.coli* (80%). Bacteraemia was present in 20% (n=8) of patients with blood cultures taken. Co-amoxiclav resistance was detected in 60% (n=27) of isolates. Co-amoxiclav resistance was associated with longer LOS compared to susceptible patients, mean 7.6(SD 5.5) vs. 5.1(SD 3.2) days (p=0.04).

#### **Conclusion**

Co-amoxiclav resistance was highly prevalent and associated with a prolonged LOS, highlighting the importance of surveillance of local resistance patterns and regularly reviewing empiric prescribing.

## Introduction

Empiric antimicrobial guidelines incorporate knowledge of local resistance patterns and require regular surveillance due to increasing antibiotic resistance. A review at this institute from 1999-2009 showed co-amoxiclav resistance rates for *E.coli* of 10%.<sup>1</sup> International guidelines suggest that a local antimicrobial resistance prevalence >20% should preclude use as empiric therapy.<sup>2,3</sup> A subsequent Irish study from 2005-2014 showed further increasing co-amoxiclav resistance in 48% of hospital admissions.<sup>4</sup>

We hypothesised that the prevalence of resistance to co-amoxiclav (current empiric treatment) has increased, leading to ineffective therapy at admission for some patients and significant consequences for healthcare cost-effectiveness. For example, in community-acquired pneumonia, first-line antibiotic therapies effective against a majority of community pathogens are associated with improved clinical outcomes and cost-effectiveness compared to traditional empiric choices.<sup>5</sup> To investigate the current prevalence of resistance to empirical UTI treatment with co-amoxiclav, and any association with hospital LOS, an observational study was conducted.

## Methods

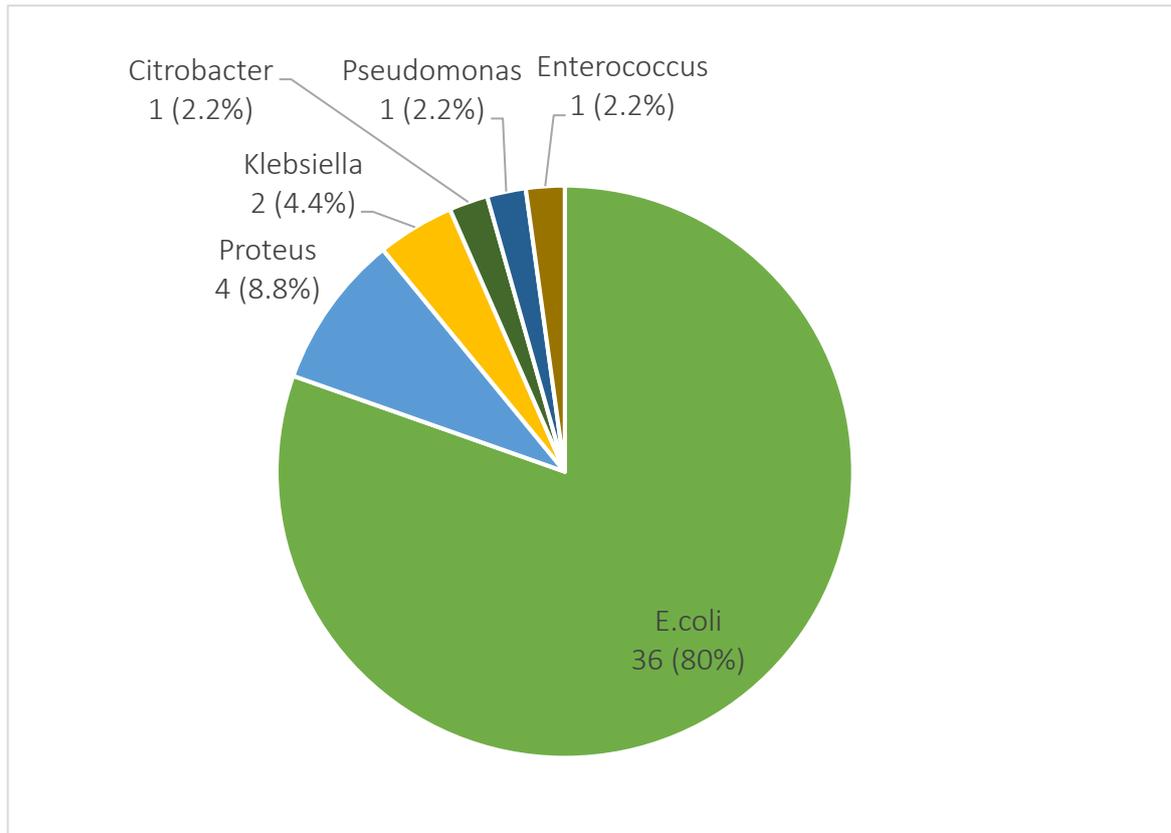
All consecutive patients under the care of the Nephrology service with a primary diagnosis of UTI were retrospectively identified over an eight-month period (July 2019 - February 2020). Inclusion was based on a single uropathogen ( $\geq 10^5$  cfu/mL) on admission culture with a clinical diagnosis of UTI, agreed by both the admitting medical consultant and subsequent consultant nephrologist (following transfer of care at a daily "decant" of acute medical admissions). Empiric treatment was with co-amoxiclav, with an additional recommendation for gentamicin if there was evidence of sepsis.

Clinical and demographic details were gathered from paper and electronic records. Primary outcomes were the proportion of patients resistant to empiric treatment and hospital LOS. Categorical variables were presented as percentages and continuous variables as means. The Fisher Exact and Mann Whitney tests were used to examine the association between categorical and continuous variables, respectively. The alpha level of significance was 0.05. Ethical approval was granted by the local Research Ethics Committee.

## Results

A total of 59 patients were screened, with 14 excluded based on urine culture results (no growth n=8, sample leaked n=4, mixed growth n=1, no sample n=1). Of the remaining 45 patients, the mean age was 49.2 years (SD 23.4), 80% were female and the mean LOS was 6.6 days (SD=4.8). The dominant uropathogen was *E.coli*, accounting for 80% of cases (n=36) (Fig.1). Of patients with an admission blood culture taken (n=40), 20% had confirmed bacteraemia, all *E.coli* isolates.

**Figure 1.** Uropathogen Frequency (total cohort n=45)



The overall proportion of patients with urine isolates resistant to co-amoxiclav was 60% (n=27). Comparing these patients to those with co-amoxiclav susceptible isolates (n=18), there was no significant difference in mean age, 51.2 vs 46.3 years ( $z=0.7$ ,  $p=0.4$ ), admission serum creatinine, 79.2 vs 103 $\mu\text{mol/l}$  ( $z=1.2$ ,  $p=0.2$ ) or incidence of bacteraemia, 25% of both groups, respectively. There was a trend towards a higher incidence of AKI at admission in patients with co-amoxiclav resistance, 25% vs 5.5% ( $p=0.12$ ).

In the overall cohort, there was a significantly longer hospital LOS in co-amoxiclav resistant patients compared to susceptible patients, mean hospital LOS of 7.6 (SD 5.5) days vs. 5.1 (SD 3.2) days ( $z=2.13$ ,  $p=0.04$ ).

## Discussion

The observed high prevalence of co-amoxiclav resistance represents an important finding for local and national policy-makers. We demonstrated continued growth in co-amoxiclav resistance compared to previous Irish studies, consistent with that seen over time internationally also.<sup>2,4,6,7</sup> Co-amoxiclav resistance was associated with an increased hospital LOS, the importance of which cannot be understated in the current environment of healthcare provision.

With efficacious first-line treatment, a more rapid clinical recovery could translate into reduced LOS for patients resistant to empiric treatment. Appropriate empiric antibiotic therapy, coupled with appropriate stewardship and structured de-escalation, has been shown to reduce patient LOS and reduce healthcare costs.<sup>8</sup> The importance of appropriate empiric therapy is highlighted in one large study of patients with bacteraemia, which demonstrated that discordant empiric therapy was associated a 46% increased mortality risk.<sup>9</sup>

This study is limited by small size and single-centre setting. However, the study provides an important insight into increasing co-amoxiclav resistance in patients hospitalized with UTI, and the potential consequence of prolonged LOS associated with ineffective empiric therapy. These findings should encourage surveillance of local resistance patterns and of empiric prescribing, in line with the Health Protection Surveillance Centre (HSPC) national guidelines.<sup>10</sup> Medical personnel should be educated on individualization of antibiotic therapy, with appropriate rationalization of therapy to select the correct drug, dose and course duration for each patient based on the individual presentation and local patterns of anti-microbial resistance.

**Declaration of Conflicts of Interest:**

The authors have no conflicts of interest to declare.

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