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Review

Risk factors for aquiring multidrug-resistant organisms in urinary tract infections: A systematic literature review

Justin Tenney [a,*], Nicholas Hudson [b], Hazar Alnifaidy [c], Justin Ting Cheung Li [a], Kathy Harriet Fung [a]

[a] School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong
[b] Elkhart General Hospital, Department of Pharmacy, Elkhart, IN, USA
[c] Sidra Medical and Research Center, Department of Pharmacy, Doha, Qatar

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ABSTRACT

Background: This is the first review to analyze literature identifying risk factors for a multidrug-resistant urinary tract infection (MDR UTI). Risk factors for other infections involving multidrug-resistant organisms have been evaluated in other reviews, but they do not assess urinary tract infections. The purpose of this study is to collect currently published data to determine the most commonly and consistently identified risk factors for UTIs.

Material and methods: For this study, 3 independent researchers searched PubMed, Embase, and Cochrane database from 1966 to February 2016 for articles identifying risk factors for MDR UTI.

Results: A total of 25 studies including 31,284 patients with positive cultures provide evidence for 12 possible risk factors for MDR UTI . The most commonly identified risk factor was previous antibiotic usage as evidenced in 16 of the 20 studies that evaluated this possible risk factor. The time range utilized to define previous antibiotic usage ranged from 2 days to 365 days. Other risk factors with the strongest supporting data were urinary catheterization, previous hospitalization, and nursing home residence.

Conclusion: We identified 12 different possible risk factors for a MDR UTI, however several risk factors have minimal or conflicting evidence. The definitions of the risk factors varied widely among the studies, and should be standardized for future studies.

Contents

* Corresponding author at: School of Pharmacy, Rm 801J, 8/F, Lo Kwee-Seong Integrated Biomedical Sciences Building, Area 39, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong.
E-mail address: jten@pharmacy.cuhk.edu.hk (J. Tenney).

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1. Introduction

Urinary tract infections (UTIs) are the most frequently reported infections and drive antibiotic use around the world (Anthony, 2002; Klevens et al., 2002). UTIs are the fourth most common type of healthcare-associated infection (Magill et al., 2014). Multidrug-resistant organisms (MDRO) are predominantly bacteria, that are resistant to one or more classes of antimicrobial agents. Sulfamethoxazole-trimethoprim resistance has been shown throughout the world for *E. coli* and has led to expanded use of fluoroquinolones and cephalosporins. Gram negative extended-spectrum beta lactamase producing enterobacteriaceae are an increasing concern in regards to antibiotic resistance and their potential cause of serious infections which are difficult to treat (Shaikh et al., 2015). Throughout the world there is increasing antimicrobial drug resistance, therefore it is important to identify factors that place patients at increased risk for a multidrug-resistant infection, so that broad spectrum antibiotics can be reserved for use in these patients. Limiting broad spectrum empiric antibiotics to patients with proven risk factors can help slow the prevalence of resistance to these antibiotics. The concern that our study addresses is how to define and identify the patients who are at increased risk of infection by these multidrug-resistant organisms in regards to a UTI.

This is the first review to analyze the literature identifying risk factors for a multidrug-resistant (MDR) urinary tract infections (UTIs). Risk factors for other infections involving multidrug-resistant organisms have been evaluated in other reviews, but these studies do not assess infections of the urinary tract system. The objective of our study is to identify and appraise the current literature to determine what are the possible risk factors for developing a MDR UTI's and which risk factors have the strongest supporting data.

2. Material and methods

2.1. Data sources and search strategy

A literature search was completed independently by three authors using PubMed, Embase, and Cochrane databases. Search was conducted from January 1966 up to February 31st 2016. The following keywords were used as search terms: ([drug AND resistance AND multiple] OR [multidrug AND resistance]) AND ([urinary AND tract AND infection] OR pyelonephritis OR cystitis) AND (risk AND factors). Reference lists of included articles were also reviewed for eligible studies. We categorized the risk factors evaluated in the studies into 3 categories: Probable risk factor, possible risk factor, and unlikely risk factor or further research needed Table 2). Due to the likeliness of variable definitions of multidrug resistance those studies that follow the 2011 international consensus panel's expert proposal definition for acquired resistance were also assessed (Magiorakos et al., 2012).

2.2. Study selection

Studies were considered eligible for inclusion if the study identified and reported any risk factors associated or not associated with MDR UTIs in patients with positive cultures. Studies were eligible for inclusion only if published in English. Studies were limited to those reporting on human adult or pediatric patients. Titles and abstracts were reviewed for identification of risk factors for MDR UTIs. Articles deemed relevant were reviewed in full to determine inclusion in our analysis. All articles were evaluated for inclusion by three authors and a consensus was achieved whenever there was a disagreement on inclusion. The primary outcome assessed was the association of different risk factors with MDR UTIs.

2.3. Data extraction and quality assessment

The three reviewers independently extracted data from all eligible studies and agreed on any discrepancies by consensus. The extracted data for each study when available was placed into an Excel spreadsheet and included the country, study type, year of publication, number of patients, type of UTI (pyelonephritis vs. cystitis, complicated vs. uncomplicated), organism cultured, study setting (community, inpatient hospital, emergency department), drugs of focus in study, and all risk factors reviewed for association. No uniform use of a specified definition was utilized. Studies were included regardless of how the information that was collected was defined.

Studies included for analysis were rated using the Newcastle-Ottawa Quality Assessment Scale (NOS) (O'Connell, 2002). The NOS contains eight items, categorized into three dimensions including selection, comparability, and outcome. The NOS ranges between zero and nine. Each study was reviewed independently by two of the authors and assessed for quality using the NOS. Authors discussed any discrepancies in quality assessment and came to a consensus with the assistance of a third reviewer.

Descriptive statistics were used to quantitatively describe features of the studies when analyzed collectively. Studies were chronologically assessed by the age of the study to determine relevance and/or changes in MDR UTI risk factors.

3. Results

The review identified 25 studies including 31,284 patients with positive cultures that identify possible risk factors for multidrug-resistant UTI (Allen et al., 1999; Arslan et al., 2005; Brown et al., 2002; Burman et al., 2003; Colgan et al., 2008; Colodner et al., 2004; Ena et al., 1995; Eshetie et al., 2015; Faine et al., 2015; Gangcuangco et al., 2015; Hertz et al., 2016; Ho et al., 2007; Ikram et al., 2015; Jadoon et al., 2015; Johnson et al., 2008; Kang et al., 2015; Khawcharoenporn et al., 2013; Killgore et al., 2004; Lee et al., 2010; Metlay et al., 2003; Osthoff et al., 2015; Yoon, 2014; Talan et al., 2008; Toner et al., 2015; Wright et al., 1999). There has been an increasing trend in the number of articles published regarding risk factors for developing an MDR UTI in recent years. Individual study characteristics are described in Table 1. There were 13 retrospective studies, 11 prospective studies, and 1 study with both retrospective and prospective components. 14 studies took place in the inpatient setting, 7 in the community setting, and 4 had mixed settings. Study sizes ranged from 66 to 21,414 and 23 of the 25 studies had less than 1000 participants. The percent of positive cultures in the studies included that identified *E. coli* as the causative pathogen ranged from 29.2 to 100%.

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