

## State of the Globe: Rising Antimicrobial Resistance of Pathogens in Urinary Tract Infection

Antimicrobial resistance is a rising ominous threat to patient management all over the world. This is leading to escalating costs in patient care, more hospital stays, and also more mortality. Almost, all the common pathogens in the clinical practice have been reported to demonstrate significant levels of resistance to the common antimicrobial agents. Many organisms are reported to be multidrug resistant.

Urinary tract infections (UTIs) are among the most common infections leading to clinic or emergency visits or indoor admissions all over the world.<sup>[1]</sup> In the USA alone, UTI-related symptoms lead to almost 10 million office visits and around 3 million emergency visits per year.<sup>[1]</sup> In the UK, 1%–3% of all medical consultations are due to UTI.<sup>[2]</sup> It is the second most common reason for prescribing antibiotics in the UK. UTI may sometimes lead to serious complications such as pyelonephritis, sepsis, or renal abscess.<sup>[1]</sup> Especially in the immunocompromised hosts and extremes of age, UTI may lead to significant mortality and morbidity. However, if drug-resistant organisms are present, any urinary infection in otherwise normal persons may cause havoc. UTI is more common in women than men.<sup>[2]</sup> However, urinary infections in men are often complicated and thus require more attention.

UTI is caused mainly by *Escherichia coli* and *Klebsiella*, although other bacteria including Gram-positive organisms and even fungi have been isolated in many cases.<sup>[1]</sup> In complicated UTI, especially in the male, the microbiology may vary slightly, with virulent strains such as enterococci and *Proteus* being isolated more often.<sup>[1]</sup>

There is an ominously rising trend of antimicrobial resistance in urinary pathogens. Earlier, this phenomenon was noticed mainly in patients with comorbidities such as diabetes or reflux nephropathy. Furthermore, resistance was more common in the nosocomial pathogens. However now, antimicrobial resistance is noted in a significant number of community-acquired infections too.<sup>[3]</sup> This is not limited to any particular country but is a global phenomenon.

This ominous trend has been noted in all age groups. In a recent meta-analysis, significant levels of antimicrobial resistance were noted for *E. coli* in pediatric UTI.<sup>[4]</sup> The level of resistance was noted to be higher in the regions of the world where antimicrobial agents are freely available over the counter.<sup>[4]</sup> However, besides such misuse of antimicrobial agents, other factors such as the unregulated use of antimicrobials in livestock are also a factor in this rising resistance phenomenon. In another Norwegian study, in the elderly population, it was noted that the antibiotic resistance patterns did not differ between nursing home residents and those who lived in the

community.<sup>[5]</sup> There were very high-levels of resistance to commonly used antimicrobial agents such as ampicillin and nitrofurantoin in both patient groups. UTI is often treated empirically. Hence, the guidelines for treatment of UTI must take into consideration these changing patterns of resistance.

In the present issue of this journal, Erdem *et al.* have presented a study on community-acquired UTI from Turkey.<sup>[6]</sup> In it, they found *E. coli* to be the most common organism and 32% of them were extended-spectrum beta-lactamase (ESBL) producing.<sup>[6]</sup> In their study, fosfomycin and nitrofurantoin were found to be the drugs with least resistance and highest eradication rate. However, in the Norwegian study, nitrofurantoin resistance was quite high.<sup>[5]</sup> Fosfomycin is one drug whose level of resistance is quite low, as depicted in various studies.<sup>[3]</sup> Thus, this can be a sound choice in the empirical therapy.

ESBL producing organisms are an important cause of drug-resistant UTI, especially in some parts of low and middle income countries. In a recent study from India targeting ESBL producing strains in urinary pathogens, it was found that 40% of the *E. coli* strains and 45% of the *Klebsiella* strains were ESBL producing.<sup>[7]</sup> Such findings limit the choice of antibiotics even further.

There are various reasons for this rising antimicrobial resistance.<sup>[8]</sup> Overuse and abuse of these drugs are very common, especially in those parts of the world where over-the-counter sales are allowed.<sup>[8]</sup> Furthermore, antibiotics are often prescribed without indications. Even in the USA, up to 60% of antimicrobial prescriptions in the ICU are found to be inappropriate or suboptimal.<sup>[8]</sup> Another major source of antibiotic resistance is its unregulated use in livestock.<sup>[8]</sup> The USA estimate showed that out of all the antibiotic sold more than 80% is actually used to rear animals.<sup>[8]</sup> When human beings consume these food products, daily small dose of antibiotics enter the body and help foster resistance in the commensal bacteria.

Analysis of the pharmaceutical industry has revealed that development of new antimicrobial agents is not on the priority list of many major companies.<sup>[8]</sup> Furthermore, in the academic world, the interest to develop the new agents has waned considerably. Thus, as the levels of resistance are rising, there are very few new weapons to fight the threat. Hence, judicious use of antibiotics is an urgent need of the day and must be enforced at all levels of health care. There can never be one single guideline for geographically distant regions. Local levels of antimicrobial resistance (as the present study depicts) must be documented to help decide the best choice of drugs.

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