e AMR 3 WEBINAR NEWSLETTER

Date: 16th October, 2019

Topic: Redefining approach in management of LUTS, including E. coli resistance in UTIs

Passi Publications, in association with Boston University School of Medicine, USA presented its third webinar as a part of CME Program on Antimicrobial Resistance. The present report summarizes key comments from the webinar.

Dr. Nahid Bhadelia
MD, MA, Assistant Professor,
Infectious Diseases Physician,
Boston University School of Medicine, USA

The third webinar of the "Antimicrobial Resistance (AMR) series" was broadcasted on 16th of October, 2019 with the speaker Dr. Nahid Bhadelia, MD, MA, Assistant Professor, Infectious Diseases Physician, Boston University School of Medicine, USA giving a didactic presentation on the topic "Redefining approach in management of LUTS, including E. coli resistance in UTIs".

Dr. Nahid's presentation focused on the spectrum of symptomatology related to lower urinary tract, particularly in conditions such as cystitis and lower urinary tract infection along with the complications associated with these pathologies.

The major learning objectives of Dr. Nahid's presentation were to understand the epidemiology, risk factors and microbiology of lower urinary tract infections; differentiate between complicated and uncomplicated urinary tract infections; discuss the diagnostic and management approach to lower urinary tract infections, and explore guideline recommendations regarding management of lower urinary tract symptoms in special patient groups posing challenges at the therapeutic level. The presentation concluded with a Q&A session wherein participants posted questions pertaining to UTI and several antibiotic regimens used in its management.

Brought by PASSI PUBLICATIONS (L.L.C.)

Educational Support by SANOFI

In association with BOSTON UNIVERSITY

Epidemiology and pathophysiology of UTIs

Dr. Nahid started her presentation by briefly discussing the epidemiology of UTIs wherein she mentioned the global annual prevalence of UTIs estimated to be approximately 150 million. She further highlighted the self-reported annual incidence of UTI in women estimated as 12% with 50% incidence of at least one UTI by the age of 32 years and recurrence rates of 20-30%. She also spoke about the immense impact on the healthcare utilization and costs related to lower urinary tract symptoms. She further stated the incidence rates of healthcare-associated UTIs in the US, Europe and developing countries estimated to be 12.9%, 19.6% and 24%, respectively.

In terms of pathophysiology, Dr. Nahid stated the presence of a balance between several host- and pathogen-associated factors linked with the occurrence of lower urinary tract symptoms (Table 1, Figure 1). She enumerated different routes of lower urinary tract infections such as the common ascending and hematogenous routes as well as the less common lymphatic route. Furthermore, she discussed the several risk factors associated with UTI development based on age and gender.

Symptoms of acute uncomplicated cystitis

Dr. Nahid proceeded to discuss the clinical features associated with acute uncomplicated cystitis, including dysuria, urinary frequency, urinary urgency, and suprapubic pain with or without hematuria. She further mentioned the factors distinguishing acute uncomplicated cystitis from upper tract infection or urosepsis such as fever, flank pain, costovertebral angle tenderness, and other signs of systemic infection. Dr. Nahid discussed the several inflammatory and non-inflammatory components in terms of differential diagnoses of dysuria in adults.

Table 1: Host- and pathogen-associated factors linked with lower urinary tract symptoms

Host factors	Pathogen factors
• Factors of innate immunity • Composition of urine (pH, osmolality, urea concentration) • Flushing mechanism of bladder • Antimicrobial qualities of epithelial surface	Chromosomal virulence factors contributing to uropathogenic nature of certain serogroups of bacteria, including surface molecules/ adhesions such as P fimbriae and type I fimbriae

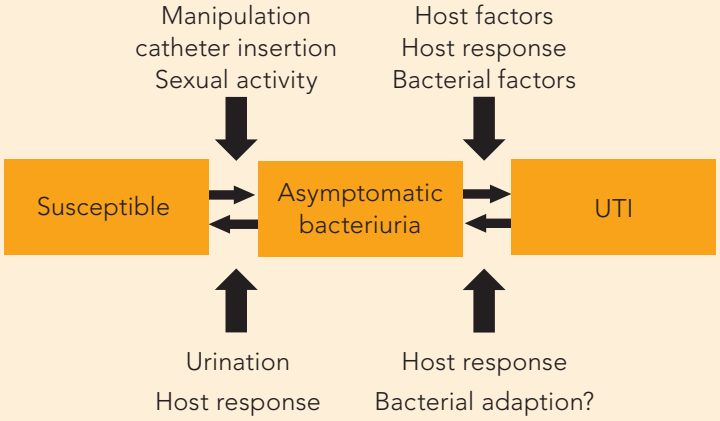
Microbiology of cystitis

Dr. Nahid touched upon the major pathogenic organisms responsible for causing cystitis wherein she stated the most important organism to be *E. coli* accounting for 80% infections along with other common microorganisms such as *Klebsiella pneumoniae*, *Proteus mirabilis* and *Staphylococcus saprophyticus*. She further marked the importance of considering few normal colonizers such as Lactobacilli, Group B streptococcus and other coagulase-negative staphylococci as uropathogenic in certain populations if isolated in clean void at high concentration in patients with lower urinary tract symptoms.

Antibiotic resistance patterns of uropathogens

Dr. Nahid described the antibiotic resistance patterns of uropathogens as per the IDSA 2011 guidelines (Box 1). She further discussed data from newer evidences which showed increased rate of culture-proven UTI due to ESBL-producing Enterobacteriaceae; higher resistance to trimethoprim-

Figure 1: Interaction between host and pathogen factors in UTI occurrence



Box 1: Antibiotic resistance patterns of uropathogens as per IDSA 2011 guidelines

- ≥20% resistance to ampicillin
- ≥20% resistance to trimethoprim (with or without sulfamethoxazole) in many regions
- <10% fluoroquinolone resistance in North America and Europe (but rising)
- <10% resistance to 1st and 2nd generation oral cephalosporins and amoxicillin-clavulanic acid (with regional variations)
- Overall good in vitro activity of nitrofurantoin, fosfomycin, and mecillinam in all countries

sulfamethoxazole and amoxicillin/clavulanate and increased ESBL-producing Enterobacteriaceae rates in pregnant or post partum women in different regions of the world.

Diagnosis and treatment principles

In terms of diagnosis, Dr. Nahid discussed the characteristics and interpretations associated with urine dipstick/urinalysis and urine culture. She further elaborated the treatment principles, including checking of local antimicrobial resistance data; ruling out sepsis and signs and symptoms pointing to extension of infection beyond the bladder; consideration of other concurrent or differential diagnoses; consideration of tolerance, renal and liver function, and allergies when prescribing antibiotics; and referring to prior urine cultures and susceptibility in recurrent infections.

Regarding treatment, Dr. Nahid discussed the NICE (Table 2) and IDSA guideline recommendations for the management of UTIs. She further explained the diagnostic and therapeutic considerations in patients with complicated disease due to systemic symptoms (such as pyelonephritis, prostatitis and urosepsis) or due to host anatomic and physiologic features (such as urogenital anatomic abnormalities, history of renal transplant, presence of chronic urinary catheter, and immunosuppression). She mentioned the special considerations for UTI in men and different clinical forms of prostatitis presenting in males with treatment options.

Table 2: NICE guideline recommendations for management of UTIs in women (≥16 years old)

Non-pregnant women	
Antibiotic	**Dose and duration**
FIRST LINE	
Nitrofurantoin - if eGFR ≥45	100 mg BID for 3 days
Trimethoprim - if low risk of resistance	200 mg BID for 3 days
SECOND LINE (if no improvement on first line after 48 hours)	
Nitrofurantoin - if eGFR ≥45	100 mg BID for 3 days
Pivmecillinam	400 mg x 1, then 200 mg TID for 3 days
Fosfomycin	3 g single dose sachet
Pregnant women	
FIRST LINE	
Nitrofurantoin - if eGFR ≥45	100 mg BID for 7 days
SECOND LINE (if no improvement on first line after 48 hours)	
Amoxicillin	500 mg TID for 7 days
Cefalexin	500 mg BID for 7 days
Asymptomatic bacteriuria	Nitrofurantoin, amoxicillin, cefalexin or other

Considerations in asymptomatic bacteriuria and recurrent UTI

Dr. Nahid discussed regarding asymptomatic bacteriuria represented by individuals having $>10^5$ colony forming units (CFUs) of bacteria in urine culture with no UTI symptoms. In terms of diagnosis and management of this condition, she cited recommendations from NICE and IDSA guidelines suggesting no routine screening or treatment for asymptomatic bacteriuria in non-pregnant women, men and children. She further discussed the features of recurrent UTI/cystitis and the initial treatment and imaging approaches in patients with this condition. Dr. Nahid concluded her presentation by highlighting the importance of non-antibiotic therapies in UTI management such as hydration, analgesics, hormone replacement therapy and interventions for urinary pH alteration.

Q&A session

Q1: Can genetic predisposition be a cause of UTIs and if yes, is it worthwhile to routinely screen for recurrent UTIs in all first-group female relatives of somebody with recurrent UTI?

A: Yes, there is evolving evidence that genetic predisposition could actually link you to UTIs; however, no guidelines currently recommend routine screening to assess genetic predisposition either in patients or their first-degree relatives.

Q2: Are resistance rates rising among fluoroquinolones and are some fluoroquinolones less likely to cause resistance than others?

A: The rates of existing as well as increasing resistance highly depend on the geographical areas. As far as I know, for uropathogens, the resistance mechanisms of all fluoroquinolones are kind of similar.

Q3: For chronic prostatitis, what would be the duration of treatment with fluoroquinolones?

A: Guidelines suggest 4-6 weeks of treatment with fluoroquinolones for patients with chronic bacterial prostatitis.

Q4: Should negative nitrites on a routine urinalysis always rule out UTI?

A: No. As we mentioned, nitrites have a low sensitivity but a high specificity which means that you might have nitrites but if a patient has symptoms and other predisposing factors, a UTI should not be ruled out.

Brought by PASSI PUBLICATIONS (L.L.C.)

In association with BOSTON UNIVERSITY

Educational Support by

SANOFI