HCFI Dr KK Aggarwal Research Fund

Minutes of an International Weekly Meeting on "Acute Pyelonephritis: Diagnosis & Treatment"

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- Pyuria is often taken as *sine qua non* of urinary tract infection (UTI), but this is not true. Also, inappropriate use of antibiotics can cause side effects and emergence of drug resistance (extended-spectrum beta-lactamase/multidrug resistance [ESBL/MDR]).
- Pyuria is not equivalent to UTI unless the clinical picture is compatible.
- UTI is the presence of organisms $>10^5$ mL in urine with or without symptoms. Lower counts $10^2/10^3$/ could also be UTI if the patient has symptoms that are appropriate for the clinical setting.
- The bacterial count has to be supported by urine microscopy, urine test strip (leukocyte esterase/ Griess nitrate test), and clinical features (history).
- The types of UTI include cystitis (mostly uncomplicated), acute pyelonephritis (complicated if risk factors such as diabetes, stone, prostatitis are present), acute bacterial prostatitis is considered complicated as there is no risk of recurrence, catheter-associated UTI (CAUTI), and asymptomatic bacteriuria.
- UTI may present as lower urinary symptoms, upper urinary tract symptoms. Sometimes, there is fever with no localization; this is urosepsis (occult pyelonephritis). Few patients may have vague chronic ill health due to pyelonephritis of subacute nature.
- The purple urinary bag syndrome is due to chronic stasis in the urinary catheter giving the picture of hematuria with associated asymptomatic bacteriuria.
- Upper UTI can be clinically recognized by symptoms such as lumbar pain, shaking chills, loin tenderness, hematuria.
- Lower UTI is characterized by frequency, dysuria, urgency, frank hematuria, suprapubic pain; small void, foul smell, cloudy urine, or asymptomatic (covert)/sepsis syndrome.
- Acute pyelonephritis can also be precipitated by heat stress if the water intake is inadequate.
- The possible symptoms of acute uncomplicated cystitis include dysuria, urinary frequency, urinary urgency, suprapubic pain, absence of vaginal symptoms/upper tract symptoms/systemic symptoms (rigors, shaking chills). May require only urine analysis or urine dipstick to support the diagnosis. Culture may not be required and may be treated empirically.
- Fifty percent of patients will have classical picture of bacterial cystitis with colony count $>10^5$ CFU/mL, while 20% with the same clinical picture may have low colony count (10^2-10^4). This will still be considered as true UTI.
- About 15% of patients may have urethritis, 5% may have vaginitis. In less than 1% patients, the symptoms may be due to noninfectious causes (chemical irritation or estrogen deficiency).
- There are few overlooked causes of UTI such as less fluid intake, spicy diet, neurological problems (neurogenic bladder, normal pressure hydrocephalous), bladder outlet obstruction (benign prostatic hyperplasia [BPH], prostate cancer, urethral stenosis, bladder calculus/cancer), or drugs (caffeine, diuretics).
- In the elderly, children, immunosuppressed, diabetics, the presentation may be atypical in the form of vomiting, loose motions, shock, mental obtundation, and jaundice. One must have high index of suspicion.
- Clinically, pyelonephritis can present as acute pyelonephritis with classical symptoms of loin pain, rigors, fever. But it can have other presentations too such as emphysematous pyelonephritis, papillary necrosis, occult or subacute pyelonephritis, recurrent/ relapsing pyelonephritis, or xanthogranulomatous pyelonephritis/malakoplakia.
- Diagnosis is based on positive urine analysis (≥10 WBC per HPF, leukocyte esterase, nitrites) and positive urine culture; no catheter (≥10,000-1,00,000 CFU/mL of a urinary pathogen, catheter ≥1,000 CFU/mL of a urinary pathogen). Blood cultures must be obtained if pyelonephritis or urosepsis is suspected.

- In symptomatic patients, bacteriuria + pyuria is true UTI. Pyuria is 10 cells/HPF of spun urine (10 mL, 2000 rpm, 5 min).
- If only pyuria with symptoms and less significant bacteriuria, this could still be true UTI (likely to be cystitis).
- If pyuria with insignificant bacteriuria ($<10^2$) + pyuria, this could be chlamydia or nongonococcal urethritis.
- Symptomatic but no bacteriuria/pyuria could be acute urethral syndrome.
- In asymptomatic patients, no bacteriuria + pyuria is sterile pyuria (analgesic nephropathy, tuberculosis, steroid, chronic prostatitis).
- Some factors predispose to the risk of recurrence. These include obstruction (stricture, BPH, stone, neoplasm), diabetes, nonsteroidal anti-inflammatory drug abuse, vesicoureteral reflux, catheterization/instrumentation, renal disease (polycystic kidney disease, medullary sponge kidney, horse shoe kidney, ectopic kidney), hypokalemia, hypocalcemia.
- Any male patient, any female with recurrent UTI, any complicated UTI, history of hematuria/stone/voiding disturbance and any child with pyelonephritis (high incidence of cakut – congenital abnormalities of kidney and urinary tract).
- Investigate the patient radiologically with X-ray KUB. Now contrast CT is done, instead of intravenous pyelogram. Voiding cystourethrogram is done in young patients with recurrent UTIs to exclude possibility of posterior urethral valves or vesicourethral reflux. Ultrasound is the first radiological test.
- Purple urinary bag syndrome can occur due to metabolic byproducts of bacteria such as *Providencia stuartii, Providencia rettgeri, Klebsiella pneumoniae, Proteus mirabilis, Escherichia coli, Morganella morganii*, and *Pseudomonas aeruginosa*. Risk factors include bacteriuria, constipation and female gender. It is a benign condition.
- Asymptomatic bacteriuria is common and it is generally benign. Treat only in pregnant women at 12 to 16 weeks of gestation or in case of an impending urologic procedure (this does not include placement of a urinary catheter) in which mucosal bleeding is expected.
- As per the ICMR-AMRSN (Indian Council of Medical Research-Antimicrobial Resistance Research and Surveillance Network) data 2017, the common organisms causing UTI include *E. coli* (49.2%), *Klebsiella* spp. (17.4%), *Proteus* spp. (1.4%), *Citrobacter* (1.3%), *Enterococcus* spp. (10.9%), *Staphylococcus aureus* (0.9%), and nonfermented Gram-negative bacilli (8.2%).
- Based on resistance pattern, the ICMR recommends that initial empiric therapy for infections caused by Enterobacteriaceae (*E. coli* and *Klebsiella*) (pyelonephritis) should be with an agent active against ESBL producers, e.g., a carbapenem or with a β-lactam/β-lactamase inhibitor for less severely ill patients.
- ICMR has defined standard doses of antimicrobial agents in its 2019 guidelines. It says that drugs should be given in the appropriate dose.
- In a study published in the *Indian Journal of Nephrology*, 89% organisms in acute pyelonephritis were *E. coli* and 09% were *Klebsiella*. In this study, the drug with 100% benefit was ertapenem, while the drug with 0% benefit was ceftriaxone.
- The Centers for Disease Control and Prevention (CDC) has defined three criteria for a CAUTI: Indwelling catheter in place for more than 2 consecutive days in an inpatient location, urine culture with no more than 2 organisms present and 1 organism with bacterial count of $>10^5$ CFU/mL and presence of at least 1 of the following: fever (38^oC), suprapubic tenderness, costovertebral angle pain/tenderness, urinary urgency, frequency, or dysuria.
- If all the three criteria are met, only then it is CAUTI and has to be treated appropriately. In the absence of these, it is considered asymptomatic bacteriuria.
- The 2018 guideline for CAUTI recommends against urine culture in an asymptomatic catheterized patient. Do not try to treat it.
- To prevent UTI, increase fluid intake, regularity in taking drugs, last dose of the day after urination, voiding after sex, careful removal of sanitary pads, avoid constipation, use 16F catheter in adult males and look at predisposing factors.
- Other palliative measures for symptomatic relief are cranberry extract, local estrogens, probiotics, alkalizers/analgesics, anticholinergics, avoid spicy/nonveg diet, and plenty of water.
- New antibiotics are available such as ceftazidime-avibactam, ceftriaxone-sulbactam/disodium edetate (1.5-3 g OD), aminoglycosides (isepamicin 400 OD, arbekacin 200 OD), and biapenem (300 mg BID).

- Patients with cystitis can be treated empirically with 5 days of antibiotics (no culture) – nitrite and leukocyte esterase test.
- Acute pyelonephritis – culture is needed – 7 days treatment in most or 14 days. No radiology tests unless extra risk.
- Do not culture in catheterized patient unless symptoms. Asymptomatic bacteriuria is common, no treatment. Treat CAUTI for 10 days, if needed, based on CDC criteria.
- Suspect acute bacterial prostatitis in males who come with voiding pattern. Do digital rectal examination/transrectal ultrasound and treat for 14 to 28 days.
- Treat recurrent cystitis with vaginal cream or postcoital antibiotics.
- In cases of candida growth in urine, repeat after catheter removal and treat as per clinical sense.
- Sodium-glucose cotransporter 2 can be continued if no additional risk of recurrence.
- Treat infection not colonization/contamination.
- Be aware of antimicrobial resistance patterns.

Participants: Dr Yeh Woei Chong, Singapore, Chair of Council-CMAAO; Dr Akhtar Hussain, South Africa; Dr Qaisar Sajjad, Pakistan; Dr Ashraf Nizami, Pakistan; Dr Benito Atienza, Philippines

Invitees: Dr Monica Vasudev, USA; Dr Mulazim Hussain Bukhari, Pakistan; Dr Poonam Chablani; Dr Poonam Saith; Dr Sanjay Shah; Dr Tan Wan Ghee; Dr Anjali Agarwal; Dr S Sharma, Editor-IJCP Group

Moderator: Mr Saurabh Aggarwal

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