Urinary Tract Infection – A Tale of 50 Years

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The first issue of 1966 was a landmark of sorts in the history of *Indian Pediatrics* as it was the first time an editorial board was instituted, headed by Dr Sisir K Bose. This issue comprised of 40 pages with four research papers (urinary tract infections, rickets, accidents in infancy and childhood, and role of long acting sulfonamides in diarrhea), two case records, a book review, current literature and notes/news. As urinary tract infection (UTI) is a common childhood illness that the present day pediatrician still frequently faces, we selected a paper on this subject for this write-up. In addition, we have traced the journey of understanding of this illness over the last fifty years.

THE PAST

The *research paper* entitled 'Urinary tract infections in childhood' was based on a study conducted by Garg, *et al.* [1] at LLR Hospital, Kanpur. The objectives were to study the clinical profile, bacteriological profile and antibiotic sensitivity pattern of isolated organisms, and treatment outcomes in children with UTI. The study population consisted of 186 children (61 infants) with UTI. Girls outnumbered boys in all age groups, especially in infants. Samples were collected by sterile catheters in infants and by the 'clean catch technique' in older children. The case definition used for UTI was the presence of more than 5 pus cells per high power field (HPF) in an uncentrifuged sample. Urine was immediately plated on MacConkey's and Nutrient agar culture media. The antibiotics for which *in vitro* drug sensitivity was tested were streptomycin, tetracycline, penicillin, nitrofurantoin and chloramphenicol. Nitrofurantoin (6 mg/kg/day) was immediately started after urine cultures were sent. If there was no clinical response within 72 hours, a second drug was started according to drug sensitivity. Treatment continued for two weeks after which a repeat urine culture was performed. Information regarding drug-related adverse affects was collected.

The commonest symptoms in children below five years were non-specific; fever (in 81.9% infants and 88.1% young children), irritability (in 50.8% infants and 40.7% young children) and convulsions (in 29.5% infants and 6.7% young children). Symptoms mostly localized to the urinary tract were observed in the older children; increased frequency (62.1%), urgency (45.4%), dysuria (24.2%) and pain in the loins (18.2%). The bacteria isolated on culture were: *E. Coli* (53.2%), *Klebsiella aerogenes* (18.3%), Proteus (13.4%) and mixed infection (13.4%). Nitrofurantoin was found to be the most sensitive drug with 70.7% *E.coli*, 58.8% *K. aerogenes* and 41.6% of *Proteus* displaying sensitivity. This was followed by chloramphicol. Multidrug resistance was found in 23.3% *E.coli*, 23.5% *K. aerogenes* and 25% *Proteus.* Every organism was resistant to penicillin. Nitrofurantoin proved to be effective (100% successful treatment outcomes) and safe (no toxicity reported).

Historical background and past knowledge: Over the years, clinicians have attempted to develop evidence-based strategies for the management of UTI [2,3]. In the 1960s, there was lack of consensus regarding the definition of 'significant' pyuria, though it was known that pyuria could be seen in other conditions such as extreme dehydration, trauma, instrumentation and calculi [4]. A quantitative bacterial count was considered to be the most accurate diagnostic method for UTI. 'Significant bacteriuria' referred to the presence of viable organisms in gram stained preparation of a drop of uncentrifuged urine; less than 10^3 colonies/mL indicating contamination, between 10^3-10^4 colonies/mL suggestive of infection and more than 10^4 colonies/mL indicating definite infection [4]. Although pediatricians used prolonged prophylactic therapy, there were no definite guidelines regarding indications, drug, dosage, duration or the need for imaging.

The Present

There has been a paradigm shift in the understanding and management of UTI which is now classified as simple or complicated (based on the presence of fever >39ºC, systemic toxicity, persistent vomiting, dehydration, renal angle tenderness and raised creatinine levels). The Indian Academy of Pediatrics (IAP) developed guidelines for the first time in 1999, that underwent revision in 2010 [5,6]. UTI is defined as the growth of a significant number of organisms of a single species in urine, in the presence of symptoms. The cornerstone for diagnosis is a positive culture plated within an hour of proper collection of urine (clean catch midstream sample, suprapubic aspiration or urethral catheterization). The presence of 10^5 colony forming unit (CFU)/mL in clean catch urine sample, 50×10^3 CFU/mL in a catheterization sample or any pathogen in a suprapubic aspiration sample is diagnostic. Several urinary tests have been developed to identify those at high risk so that empirical therapy can be started in the first visit, before culture reports are available. These include positive rapid urinary dipstick tests for leukocyte esterase and urinary nitrite; presence of more than 5 white blood cells per HPF in a centrifuged sample; and presence of bacteria in a fresh uncentrifuged, Gram-stained specimen. Though not included in the IAP guidelines, the American Academy of Pediatrics (AAP) recommends positive urinalysis in addition to a positive urine culture to diagnose UTI as this prevents misdiagnosis due to contamination or asymptomatic bacteriuria, and hence avoids unnecessary imaging [7,8].

Over the years, the causative organisms of UTI in India have remained fairly constant but drug sensitivity has repeatedly changed according to antibiotic usage. Enterobacteriaceae have developed resistance to beta-lactam antibiotics, and *E.coli* and *Klebsiella* to amoxycillin, clavulunic acid, cotrimoxazole or multiple drugs [9]. Children above 3 months of age with simple UTI should be treated with oral coamoxyclav, cefixime, cephalexin or ofloxacin for 7-10 days. Children under 3 months or with complicated UTI require parenteral antibiotics according to drug sensitivity. A combination of third generation cephalosporin and single daily dose of an aminoglycoside for 10-14 days is preferred if the renal function is normal.

Recommendations related to urinary tract imaging have been established to identify children at-risk of renal damage (children below 5 years, vesico-urethral reflux (VUR) or urinary tract obstruction). AAP recommends ultrasonography in all febrile infants after the first UTI, with evidence of obstructive uropathy, hydronephrosis, renal scaring or VUR warranting a micturating cystourethrogram. IAP guidelines recommend that all children with the first UTI undergo age-dependent radiological evaluation because antenatal diagnoses is limited and diagnosis of UTI is often missed or treatment delayed in our settings. Definite indications for long-term, prophylactic antibiotics to prevent recurrent, febrile UTI include all infants (until imaging results are available), VUR (grades I/II in infants and grades III to V in 2-5 year olds) and children with ≥ 3 episodes of febrile UTI in a year. Several high risk factors for renal parenchymal damage and subsequent chronic kidney disease have been identified that require management in collaboration with an expert.

In the present era, the emergence of resistant strains poses a significant threat that can only be ameliorated by rational and judicious antibiotic use. Treatment protocols need to be revised periodically according to changing sensitivity patterns.

References

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