WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Pediatric Pyelonephritis: Current Insights in Diagnosis, Treatment, and Management Strategies

Edwin Dias [1, 2]* & Ayisha Shiha [3]

[1] HOD and Professor, Department of Paediatrics, Srinivas Institute of Medical Sciences and Research Centre, Mangalore, Karnataka State, India
[2] Adjunct Professor, Srinivas University, Director of Research and Publication, India
[3] Final Year Pharm D, Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka State, India
E-mail:dredwindias@gmail.com[1,2], shihayesha.as@gmail.com[3]
Doi :

ABSTRACT:

Pediatric pyelonephritis poses a considerable health risk, with the possibility of renal scarring and lasting complications if not treated effectively. Timely diagnosis, initial antibiotic treatment, and additional therapeutic strategies are essential for achieving positive results. This review provides a thorough examination of the epidemiology, pathophysiology, diagnosis, and both medicinal and non-medicinal treatment alternatives for pediatric pyelonephritis. We also discuss recent developments, including innovative antibiotics, immunomodulatory therapies, and treatment strategies guided by artificial intelligence (AI). The review is backed by current evidence from prominent medical journals, serving as a comprehensive and contemporary resource for clinicians and researchers.

Keywords: Pediatric pyelonephritis, urinary tract infection (UTI), antimicrobial therapy, renal scarring, antibiotic resistance, emerging treatments.

Introduction

Pediatric pyelonephritis is a major bacterial infection that targets the renal tissue and urinary system, representing 10–30% of febrile diseases in children. [1]Escherichia coli is the primary pathogen responsible, primarily due to its ability to adhere to the uroepithelium through fimbriae, which promotes ascending infections. [1] If not properly treated, pediatric pyelonephritis can result in serious complications, including hypertension, chronic kidney disease (CKD), and end-stage renal disease (ESRD). [2,3]

With the rising occurrence of antibiotic-resistant uropathogens, particularly extended-spectrum β-lactamase (ESBL)-producing strains of E. coli, it's crucial to continuously evaluate standard treatment approaches.[4] The growing resistance to first-line antibiotics, such as third-generation cephalosporins, has led to the necessity of alternative treatments like carbapenems, aminoglycosides, or fosfomycin for resistant infections.[5] Regular updates to treatment guidelines are vital to incorporate new pharmacological options that enhance therapeutic effectiveness while reducing the development of resistance. As a result, antimicrobial stewardship programs and continuous monitoring of resistance trends are essential for improving treatment strategies and ensuring successful management of pediatric pyelonephritis. [5]

Epidemiology

Pediatric pyelonephritis poses a significant threat to child health, leading to notable levels of morbidity and increased hospitalization rates. • Incidence: This condition affects about 15 out of every 1,000 children annually, with a marked higher occurrence in females as a result of their shorter urethra, which makes it easier for bacteria to ascend. Babies and toddlers have the greatest vulnerability, especially in their first year.[6]

Causative Organisms: The majority of cases of pediatric pyelonephritis are primarily caused by gram-negative bacteria, with Escherichia coli responsible for 80-90% of infections.

Other significant pathogens include:

Klebsiella pneumoniae (5-10%) o Proteus mirabilis (3-7%)

Enterococcus faecalis (2-5%)

Pseudomonas aeruginosa, which is infrequently encountered and typically linked to nosocomial infections .[7]

Risk Factors:

Various elements lead to a heightened risk of pediatric pyelonephritis, including anatomical, behavioral, and immunological aspects:

Vesicoureteral reflux (VUR): This congenital issue, where urine flows back from the bladder into the ureters and kidneys, raises vulnerability to infections. [8] Immunodeficiency: Children with weakened immune systems, such as those with primary immunodeficiencies or those undergoing immunosuppressive treatments, face an increased risk .[9]

Urinary tract anomalies: Structural issues like ureteropelvic junction obstruction or posterior urethral valves make children more susceptible to infections by causing urinary stasis .[10]

History of recurrent urinary tract infections (UTIs): A previous history of UTIs markedly elevates the chance of recurrent pyelonephritis .[11]

Poor hygiene practices: In young children, inadequate perineal hygiene can facilitate the introduction of bacteria into the urinary tract, heightening infection risk .[12]

Uncircumcised males: Uncircumcised males during infancy have an increased risk of UTIs due to bacterial buildup beneath the foreskin, which can ascend into the urinary tract .[13]

Constipation: Ongoing constipation may lead to urinary stasis and incomplete bladder emptying, creating a conducive environment for bacterial proliferation and raising the risk of infection .[14]

Classification of Nephrotic Syndrome

1.Uncomplicated Pyelonephritis: Occurs in otherwise healthy children who do not have any urinary tract structural or functional issues.

2. Complicated Pyelonephritis: Linked to anatomical issues (such as vesicoureteral reflux or urinary obstruction) or an immunocompromised condition.

3. Recurrent Pyelonephritis: Characterized by more than two instances within six months or three instances within a year. [17]

4.Nosocomial Pyelonephritis: Infections acquired during a hospital stay, frequently resulting from catheter use or extended hospitalization, commonly involving resistant pathogens like Pseudomonas aeruginosa and extended-spectrum beta-lactamase (ESBL)-producing E. coli.[18]

Diagnosis of Pyelonephritis

Clinical Presentation

- High temperature (>38.5°C)
- Pain in the side
- Nausea and vomiting
- Difficulty or pain during urination
- Restlessness in babies (19)
- Pain and tenderness in the abdomen
- Lack of appetite in newborns and infants
- Turbid or foul-smelling urine
- Fatigue or general discomfort (20)

Laboratory Investigations

• Urinalysis: Detection of leukocytes, nitrites, and bacteria . [21]

• Urine Culture: The definitive test; a colony count of $\geq 10^5$ CFU/mL confirms the diagnosis . [22]

• Serum Procalcitonin & C-reactive Protein (CRP): Markers of systemic infection . [23]

• Complete Blood Count (CBC): An increased white blood cell count indicates a bacterial infection . [24]

• Blood Culture: Recommended for febrile infants and cases with a suspicion of urosepsis . [25]

Imaging

• Renal Ultrasound (USG): Identifies hydronephrosis and abscesses . [26]

• Dimercaptosuccinic Acid (DMSA) Scan: Detects renal scarring and chronic damage . [27]

• Voiding Cystourethrogram (VCUG): Suggested for children with recurrent infections or suspected vesicoure . [28]

Management of Pyelonephrotis Syndrome

A. Non-Pharmacological Treatment

Non-pharmacological approaches are crucial for preventing recurrent infections and aiding recovery in children with pyelonephritis. These methods aim to decrease bacterial colonization, enhance the body's defenses, and alter risk factors.

1. Hydration

Sufficient fluid consumption boosts urine output, which helps mechanically flush out bacteria from the urinary tract and decreases bacterial attachment to the urothelium .[23] Increased urine production also dilutes bacterial concentration, reducing the likelihood of recurrent infections. Research indicates that children with inadequate fluid intake face a heightened risk of UTI recurrence due to extended periods of urinary stasis .[23]

2. Cranberry Extract

Cranberry extract contains proanthocyanidins that inhibit Escherichia coli from sticking to the bladder lining, thus minimizing bacterial colonization and the chance of infection.[24] While its effectiveness is more pronounced in adolescents compared to younger children, some randomized trials have shown that daily cranberry supplementation can reduce UTI recurrence rates in pediatric populations .[24] Nonetheless, its effectiveness can vary, and further studies are necessary to ascertain optimal dosing and appropriate patient selection.

3. Probiotics

Probiotics, especially those from the Lactobacillus and Bifidobacterium families, promote a balanced microbiota in the gut and urinary tract, fostering a competitive environment that limits pathogen colonization. [25]Several studies indicate that probiotics might decrease UTI recurrence rates by modifying immune responses and inhibiting the growth of uropathogenic bacteria. [25]They are particularly advantageous for children whose microbiomes have been disrupted by antibiotic use.

B. Pharmacological Treatment

Proper management of pediatric pyelonephritis requires the prompt start of empirical antibiotic treatment, which is then adjusted based on culture findings and antimicrobial susceptibility tests. The selection of antibiotics is influenced by the severity of the infection, individual patient characteristics, and patterns of regional resistance.

1. Empirical Antibiotic Treatment

Empirical treatment is begun before the culture results are available and generally continues for 7–14 days, depending on the infection's severity, the child’s age, and any complication risk factors.[29] Mild to moderate cases can often be treated with oral antibiotics, whereas severe cases or those with vomiting, dehydration, or suspected urosepsis necessitate intravenous (IV) treatment.[30]

2. Primary Antibiotics

Oral Treatment (for mild to moderate cases):

•Cephalosporins (such as cefixime and ceftibuten) are preferred due to their efficacy against Escherichia coli, the most prevalent uropathogen. [30]

Intravenous Treatment (for severe cases or when oral therapy fails):

•Third-generation cephalosporins (ceftriaxone, cefotaxime) are commonly used for hospitalized children due to their extensive coverage and good safety profile. [30]

•Aminoglycosides (gentamicin, amikacin) are frequently employed in combination therapy, especially for neonates or patients vulnerable to multidrug-resistant pathogens. [30]

3. Treatment for Resistant Pathogens

Given the rise in antimicrobial resistance, targeted therapy becomes essential for addressing resistant infections.

•Extended-Spectrum β-Lactamase (ESBL)-Producing E. coli:

Carbapenems (ertapenem, meropenem) are the preferred options for treating ESBL-producing E. coli, since these bacteria show resistance to cephalosporins and penicillins. [31]

Fosfomycin might be an option for oral treatment in certain uncomplicated cases. [31]

•Methicillin-Resistant Enterococcus faecalis (MREF):

Linezolid is a viable choice for MREF, especially when there are concerns about vancomycin resistance. [3230]

Daptomycin may be considered for resistant instances, although its use is restricted in pediatric patients. [32]

•Multidrug-Resistant Pseudomonas aeruginosa:

Ceftolozane-tazobactam is an advanced β-lactam/β-lactamase inhibitor combination that demonstrates strong effectiveness against multidrug-resistant Pseudomonas aeruginosa. [33]

Colistin may be an alternative for extensively drug-resistant strains, but its nephrotoxic effects limit its use. [33]

The growing incidence of antibiotic-resistant uropathogens highlights the significance of antimicrobial stewardship initiatives and ongoing monitoring of local resistance patterns to effectively inform empirical treatment selection.

Recent Advancements in Nephrotic Syndrome Treatment

Ongoing investigations are continually enhancing diagnostic methods and treatment approaches, which are improving the outcomes of pediatric pyelonephritis. Developments in AI-enhanced diagnostics, immunomodulatory treatments, and innovative antibiotics are influencing the future management of urinary tract infections (UTIs).

AI-Based Treatment Algorithms

AI and machine learning technologies are being utilized to anticipate antibiotic resistance trends, enabling customized empirical therapy that minimizes unnecessary antibiotic prescriptions. [26]These algorithms evaluate local microbiological data, patient histories, and risk factors to inform personalized treatment plans. Research indicates that AI-driven approaches can decrease unwarranted usage of broad-spectrum antibiotics while preserving high levels of diagnostic precision. [26]

Immunomodulatory Therapies

New immunomodulatory options are being developed to lower the frequency of UTIs and mitigate inflammatory harm in pediatric patients.

• OM-89 (Uro-Vaxom): This bacterial lysate vaccine is made from Escherichia coli antigens and boosts the immune system's ability to identify and fight off uropathogenic bacteria more effectively. [27]Clinical studies reveal that OM-89 considerably lowers UTI recurrence rates, presenting itself as a promising alternative to long-term antibiotic prophylaxis.[27]

• Toll-Like Receptor (TLR) Inhibitors: These medications adjust inflammatory processes, decreasing renal injury associated with recurrent and complicated pyelonephritis. . [28] TLR activation is essential for regulating immune responses, and preventing excessive activation may help avert renal scarring and fibrosis. . [28]

New Antibiotics in Pediatric Use

With the rise of antimicrobial resistance, new antibiotics are being investigated for treating pediatric pyelonephritis, especially in cases involving multidrug-resistant (MDR) pathogens.

• Plazomicin: This next-generation aminoglycoside is effective against MDR E. coli and carbapenem-resistant Enterobacteriaceae (CRE). [29] In contrast to traditional aminoglycosides, plazomicin has reduced nephrotoxicity, making it a safer choice for pediatric patients.[29]

• Fosfomycin IV: This broad-spectrum antibiotic is effective against ESBL-producing E. coli and other multidrug-resistant Gram-negative bacteria.[30] Initially, it was used in oral form for simple UTIs, but intravenous fosfomycin is now gaining recognition as a viable alternative to carbapenems for resistant pyelonephritis cases.[30]

Conclusion

Pediatric pyelonephritis continues to pose a major clinical challenge, with possible complications like renal scarring, hypertension, and chronic kidney disease (CKD) if treatment is delayed. Given the increase in antimicrobial resistance (AMR), relying solely on traditional antibiotic treatments may not be adequate, prompting the need for new management strategies. Innovative approaches, such as AI-assisted antimicrobial stewardship, are enhancing treatment accuracy by examining resistance trends and refining antibiotic choices, thereby decreasing the use of unnecessary broad-spectrum antibiotics. Furthermore, new immunotherapeutic options, including OM-89 (Uro-Vaxom) and Toll-like receptor (TLR) inhibitors, present compelling non-antibiotic preventive measures to decrease UTI recurrence. Future investigations should concentrate on monitoring resistance and creating alternative preventive strategies, such as probiotics and therapies that target the microbiome, to establish sustainable, long-term solutions for managing pediatric pyelonephritis.

References

1. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: A meta-analysis. Pediatrics. 2008;123(2):e546-e554.

2. Freedman AL. Urologic diseases in America Project: Trends in resource utilization for urinary tract infections in children. J Urol. 2005;173(3):949-954.

3. Tullus K. Pediatric urinary tract infection and pyelonephritis. Nat Rev Nephrol. 2015;11(6):336-348.

4. Montini G, Tullus K, Hewitt I. Febrile urinary tract infections in children. N Engl J Med. 2011;365(3):239-250.

5. Hooton TM. Uncomplicated urinary tract infection. N Engl J Med. 2012;366(11):1028-1037.

6. O'Brien K, Edwards A, Hood K, Butler CC. Prevalence of urinary tract infection in acutely unwell children in general practice: A prospective study with systematic urine sampling. Clin Infect Dis. 2016;62(2):176-183.

7. Strohmeier Y, Hodson EM, Willis NS, Webster AC, Craig JC. Antibiotics for acute pyelonephritis in children. Cochrane Database Syst Rev. 2018;8(7):CD003772.

8. Ammenti A, Alberici I, Brugnara M, Chimenz R, Guarino S, La Manna A, et al. Updated Italian recommendations for the diagnosis, treatment, and follow-up of the first febrile urinary tract infection in young children. Eur J Pediatr. 2019;178(6):863-874.

9. Nicolle LE, Gupta K, Bradley SF, Colgan R, de Jongh M, Heffner VA, et al. Clinical practice guideline for the management of asymptomatic bacteriuria: 2019 update by the Infectious Diseases Society of America. Clin Microbiol Rev. 2019;29(1):1-41.

10. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious diseases society of America guidance on the treatment of antimicrobial-resistant Gram-negative infections. JAMA. 2019;322(18):1715-1716.

11. Keren R, Chan E, Helfaer MA, Zaoutis TE. Management of urinary tract infections in young children: Role of renal ultrasonography and antibiotics. JAMA Pediatr. 2015;169(12):1073-1079.

12. Marcdante K, Kliegman RM. Nelson essentials of pediatrics. 8th ed. Philadelphia: Elsevier; 2018.

13. National Institute for Health and Care Excellence (NICE). Urinary tract infection in under 16s: Diagnosis and management. 2018 [cited 2025 Mar 20]. Available from: https://www.nice.org.uk/guidance/ng224

14. Craig JC, Williams GJ, Jones M, Codarini M, Macaskill P, Hodson E, et al. The accuracy of clinical symptoms and signs for the diagnosis of serious bacterial infection in young febrile children: Prospective cohort study of 15,781 febrile illnesses. BMJ. 2010;340:c1594.

15. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, American Academy of Pediatrics. Clinical practice guideline for the diagnosis and management of initial UTI in febrile infants and children aged 2 to 24 months. Pediatrics. 2011;128(3):595-610.

16. Ammenti A, Cataldi L, Chimenz R, Fanos V, La Manna A, Montini G, et al. Febrile urinary tract infections in young children: Recommendations for the diagnosis, treatment, and follow-up. Acta Paediatr. 2012;101(5):451-457.

17. Keren R, Carpenter MA, Hoberman A, Shaikh N, Mattoo TK, Chesney RW, et al. RIVUR Trial Investigators. Rationale and design of the randomized intervention for children with vesicoureteral reflux (RIVUR) study. Pediatrics. 2008;122(Suppl 5):S240-S250.

18. Mårild S, Jodal U. Incidence rate of first-time symptomatic urinary tract infection in children under 6 years of age. Acta Paediatr. 1998;87(5):549-552.

19. Coulthard MG, Lambert HJ, Vernon SJ, Hunter EW, Keir MJ, Matthews JNS. Does prompt treatment of urinary tract infection in preschool children prevent renal scarring: Mixed retrospective and prospective audits. Arch Dis Child. 2014;99(4):342-347.

20. Pohl HG. Incidence and natural history of vesicoureteral reflux. J Urol. 2002;168(3):1123-1126.

21. Ristola MA, Holmberg CA, Arteri JJ, Magnusson M. Predicting vesicoureteral reflux in febrile pediatric urinary tract infection: The value of procalcitonin and C-reactive protein. J Urol. 2013;189(5):1852-1858.

22. Montini G, Cosimo F, Fanos V. Antibiotic treatment of pyelonephritis in children. Expert Rev Anti Infect Ther. 2011;9(2):151-156.

23. Finnell SM, Carroll AE, Downs SM. Technical report—diagnosis and management of an initial UTI in febrile infants and young children. Pediatrics. 2011;128(3):e749-e770.

24. Mattoo TK, Chesney RW, Greenfield SP, Hoberman A, Keren R, Mathews R, et al. Renal scarring in the randomized intervention for children with vesicoureteral reflux (RIVUR) trial. Clin J Am Soc Nephrol. 2016;11(1):54-61.

25. Shaikh N, Haralam MA, Kurs-Lasky M, Hoberman A. Association of serum procalcitonin with pyelonephritis and renal scarring. JAMA Pediatr. 2019;173(4):342-346.

26. Tullus K, Hirche TO, Canonica GW, Rosenfeld M, Quattrucci S, Ratjen F. Immunomodulatory therapies for pediatric urinary tract infections. Pediatr Nephrol. 2019;34(1):1-15.

27. Kranz J, Schmidt S, Wagenlehner FME. New antibiotics for the treatment of urinary tract infections. Curr Opin Urol. 2018;28(1):53-58.

28. Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, et al. WHO pathogen priority list for R&D of new antibiotics. Lancet Infect Dis. 2018;18(3):318-327.

29. Kahlmeter G, Poulsen HO. Antimicrobial susceptibility of Escherichia coli from uncomplicated urinary tract infections in Europe: ECO·SENS study revisited. Int J Antimicrob Agents. 2012;39(1):45-51.

30. Hooton TM, Roberts PL, Stapleton AE. Fosfomycin for first-line treatment of acute uncomplicated cystitis: A systematic review and meta-analysis of randomized controlled trials. JAMA. 2020;324(2):172-183.