

Causes and management of acute Pyelonephritis

Abstract:

Acute pyelonephritis is a bacterial infection that causes kidney inflammation. Pyelonephritis is a kidney infection that develops as a result of an ascending urinary tract infection that travels from the bladder to the kidneys. Acute pyelonephritis affects over 250,000 people each year, resulting in more than 100,000 hospitalizations. Infection with *Escherichia coli* is the most prevalent cause. Fever, vomiting, abdomen or loin discomfort, and fatigue are all symptoms of acute pyelonephritis, however Fever is the most clinically useful symptom. *Escherichia coli* is the causative agent in more than 80% of instances of acute pyelonephritis. *Staphylococcus saprophyticus*, and enterococci are among the other etiologic factors. While Infections caused by *Klebsiella*, *Enterobacter*, *Clostridium*, or *Candida* are more common in diabetic patients. Acute pyelonephritis can be treated as an outpatient or as an inpatient procedure. Outpatient treatment is available for healthy, young, non-pregnant women with uncomplicated pyelonephritis. The choice of first-line oral antibiotics depends on local antibiotic resistance characteristics, although trimethoprim alone or in combination with sulphamethoxazole, cephalexin, or amoxicillin-clavulanic acid. In this article we will be looking the causes and management of acute pyelonephritis.

Introduction:

Acute pyelonephritis is a bacterial infection that causes kidney inflammation. Pyelonephritis is a kidney infection that develops as a result of an ascending urinary tract infection that travels from the bladder to the kidneys. Fever, flank discomfort, nausea, vomiting, burning when urinating, increased frequency, and urgency are common symptoms. [1] Acute pyelonephritis affects over 250,000 people each year, resulting in more than 100,000 hospitalizations. Infection with *Escherichia coli* is the most prevalent cause. For urinary tract infection, a combination of the leukocyte esterase and nitrite tests (with either test showing positive) has a sensitivity of 75 to 84 percent and a specificity of 82 to 98 percent. In 90% of patients with acute pyelonephritis, urine cultures are positive, and cultures should be collected before antibiotic therapy is started. [2]

Fever, vomiting, abdomen or loin discomfort, and fatigue are all symptoms of acute pyelonephritis, however Fever is the most clinically useful symptom. Fever is extremely sensitive but has very low specificity when compared to the reference standard for pyelonephritis, technetium-99m dimercaptosuccinic acid scanning. The renal parenchyma is impacted in just a few afebrile children, with the exception of extremely young newborns. In contrast, the renal parenchymal is damaged in roughly half of all children with clinical pyelonephritis. [3] There are two types of acute pyelonephritis: simple and complicated. Pregnant women, diabetic patients, kidney transplant recipients, urinary anatomical defects, acute or chronic kidney failure, immunocompromised patients, and those with hospital-acquired bacterial infections are all at risk for complicated pyelonephritis. It's critical to distinguish between severe and uncomplicated pyelonephritis since it affects patient care and outcome.

Medical interest in pyelonephritis dates back to the early days of nephrology, when Richard Bright (1789–1858) published Reports of Medical Cases in 1827, associating dropsy and proteinuria to kidney illness. Bright classified his illness as an inflammatory disorder, or nephritis, a term that goes back to 1567 and refers to "kidney inflammation." This was a significant conceptual shift from the past, when the kidney was thought to be immune to inflammation, a belief Bright still holds, stating, "Inflammation of one or both kidneys, as a purely idiopathic condition, is less commonly encountered than with other phlegmasiae." [4,5] APN is characterised by suppurative inflammation of the renal parenchyma and pelvocalyceal system, which is spread along one or more medullary rays and supports an ascending infection pathway. It appears as hypoenhancing areas with or without renal edoema on contrast enhanced computed tomography (CECT) scans and can be localised or widespread. APN refers to any acute infection including parenchymal abnormalities that has not been confirmed as an abscess radiologically. [4]

Acute pyelonephritis is a bacterial infection of the renal pelvis and kidneys that occurs when a bacterial pathogen ascends the ureters from the bladder to the kidneys. Acute pyelonephritis is expected to cause roughly 250,000 office visits and 200,000 hospital admissions in the United States each year, as well as approximately 11 hospitalizations per 10,000 Canadian women. Acute pyelonephritis is most common in otherwise healthy women between the ages of

15 and 29, followed by newborns and the elderly. Although men, children, and pregnant women can get acute pyelonephritis, they account for a tiny number of occurrences. As a result, the focus of this study is on the diagnosis and management of acute pyelonephritis in women who are not pregnant. [5-9]

In the United States, there are 27.6 instances per 10,000 people, but in South Korea, there are 35.7 cases per 10,000 people. The global prevalence and incidence of the disease remain unclear. The summer months have the highest prevalence of pyelonephritis. Women are five times more likely than males to be admitted to the hospital with acute pyelonephritis. [11]

Etiology and Pathophysiology:

Gram-negative bacteria, the most prevalent of which is *Escherichia coli*, are the principal cause of acute pyelonephritis. *Proteus*, *Klebsiella*, and *Enterobacter* are examples of gram-negative bacteria that cause acute pyelonephritis. The infectious organism will most likely arise from the patient's faecal flora. *Escherichia coli* is the causative agent in more than 80% of instances of acute pyelonephritis. *Staphylococcus saprophyticus*, and enterococci are among the other etiologic factors. The bacterial spectrum linked to various forms of urinary tract infections (UTIs) is diverse. *E. coli* is a less prevalent (60 percent) cause of acute pyelonephritis in the elderly. These patients are more likely to get infections caused by gram-negative bacteria such as *Proteus*, *Klebsiella*, *Serratia*, or *Pseudomonas* due to their greater usage of catheters and equipment. [2,12] Bacteria can enter the kidneys through two routes: hematogenous spread and ascending infection through the urine system. Hematogenous spread is rare, occurring mostly in individuals with ureteral blockages or those who are immunocompromised and weak. The majority of individuals develop acute pyelonephritis as a result of an ascending infection. Several processes are involved in the progression of infection. [1]

Infections caused by *Klebsiella*, *Enterobacter*, *Clostridium*, or *Candida* are more common in diabetic patients. They're also more likely to get emphysematous pyelonephritis and papillary necrosis, which can lead to shock and renal failure. Bacteriuria, which is typically polymicrobial, occurs in more than half of patients who require catheterization for more than five days, and in nearly all patients who have urinary catheters in situ for more than one month. [2,13,14] Bacteria

adhere to urethral mucosal epithelial cells before travelling to the bladder via the urethra, either by instrumentation or urinary tract infections, which are more common in women. Females are more likely than males to have UTIs due to their shorter urethras, hormonal fluctuations, and proximity to the anus. Acute pyelonephritis can be caused by a blockage in the urinary system, such as a kidney stone. A blockage in the urine outflow can result in partial emptying and urinary stagnation, allowing germs to proliferate without being flushed out. Vesicoureteral reflux, a congenital disease in which urine runs backward from the bladder into the kidneys, is a less common cause of acute pyelonephritis.

Immunosuppression encourages the development of subclinical (silent) pyelonephritis, as well as infections caused by nonenteric, aerobic, gram-negative rods and *Candida*. Because of simultaneous immunosuppression and postsurgical vesicoureteric reflux, 30 to 50 percent of patients develop acute pyelonephritis within two months after receiving a kidney transplant. Because males are more likely to develop urinary tract abnormalities, prostatic enlargement producing urethral blockage with partial voiding, or an age-related decline in antibacterial activity in prostatic secretions, acute pyelonephritis is considered complicated in men. [2,15]

Epidemiology:

Acute pyelonephritis is reported at an incidence of 15 to 17 cases per 10,000 females and 3 to 4 cases per 10,000 men in the United States per year. The individuals who are most commonly impacted by acute pyelonephritis are young sexually active women. [1] In the United States, acute pyelonephritis, is projected to cause for more than 250 000 physician visits and approximately 200 000 hospital admissions per year. Women account for the great majority of these infections, and the majority of these women are treated in ambulatory care settings. While several research have looked at characteristics that predispose to acute cystitis, the majority of pyelonephritis investigations have been therapeutic or descriptive studies involving hospitalised patients. [16-22].

Due to fluctuations in anatomy and hormonal fluctuations, groups at the extremes of age, such as the elderly and babies, are also at danger. Pregnant women are also at risk, with 20 percent to 30 percent developing acute pyelonephritis in the second and early third trimesters, respectively. There is no

racial tendency to acute pyelonephritis. [1,23] according to Cohorts Urinary tract infections are more common with greater risk factors. Female anatomy, advancing age, diabetes, obesity, and frequent intercourse are all risk factors (although UTI is not defined as a sexually transmitted infection). Simple UTIs (infected nonpregnant immune competent females) are expected to occur at a rate of 0.7 infections per person per year. At some point in their lives, 50% of girls will get at least one UTI. The occurrence of complicated UTIs is linked to particular risk factors. With indwelling bladder catheters, for example, there is a 10% daily risk of developing bacteriuria, and a 25% chance that bacteriuria may advance to a UTI. [24]

Evaluation and clinical presentation:

The basis of assessing acute pyelonephritis is a thorough history and physical examination, but laboratory and imaging investigations can also be beneficial. For a urinalysis, a urine sample should be acquired. Pyuria is the most prevalent finding in patients with acute pyelonephritis, thus search for it on urinalysis. The presence of nitrites indicates that E.coli is the causal organism. On urinalysis, proteinuria and microscopic hematuria may also be observed. If hematuria is present, other reasons, such as kidney stones, should be examined. [1] Acute pyelonephritis has a wide range of symptoms, ranging from a minor disease to sepsis syndrome. Physicians must depend on evidence of UTI from urine or culture, as well as signs and symptoms of upper UTI, to diagnosis acute pyelonephritis (fever, chills, flank pain, nausea, vomiting, costovertebral angle tenderness). Cystitis-like symptoms, such as dysuria, urine bladder frequency and urgency, and suprapubic discomfort, may also be present. [2]

Research found that 98 percent of young and middle-aged women who presented to an emergency department with fever, pyuria, and other upper UTI symptoms had acute pyelonephritis. Alternative diagnoses were provided to Percentage of patients who did not have a fever. However, up to one-third of older individuals with acute pyelonephritis do not have a fever, and 20% of elderly patients have gastrointestinal or pulmonary symptoms. In patients with indwelling bladder catheters, fever and leukocytosis are of limited utility in detecting acute pyelonephritis, especially when infections are caused by gram-positive cocci or Candida. [2] Urine cultures should be provided to all patients with suspected

acute pyelonephritis for optimal antibiotic therapy. A complete blood cell count (CBC) is performed to check for an increase in white blood cells. To examine kidney function, the whole metabolic panel can be performed to look for abnormalities in creatinine and BUN. [1]

Blood cultures are frequently taken from patients with acute pyelonephritis who are sick enough to require hospitalisation, while they are not always required in individuals with simple acute pyelonephritis. Bacteremia and sepsis are observed in around 15 to 30 percent of individuals with acute pyelonephritis; elderly people and those with complex acute pyelonephritis are more likely to develop bacteremia and sepsis. [5,25-28]

Pelvic inflammatory disease, cholecystitis, appendicitis, lower lobe pneumonia, perforated viscus, and the prodrome of herpes zoster are among the differential diagnoses for acute pyelonephritis. [2] Abdominal/pelvic CT with contrast is the imaging study of choice for acute pyelonephritis. Imaging studies are usually not required for the diagnosis of acute pyelonephritis, but they are recommended for patients who have had a kidney transplant, are in septic shock, have poorly controlled diabetes, have complicated UTIs, are immunocompromised, or have toxicity that lasts longer than 72 hours. [1]

Although ultrasonography can identify pyelonephritis, a negative result does not rule out acute pyelonephritis. Regardless, ultrasonography can be a beneficial study for evaluating for acute pyelonephritis since it can be done at the patient's bedside, exposes the patient to no radiation, and can detect kidney abnormalities, prompting additional testing or therapy. [1] Upper urinary tract involvement (subclinical pyelonephritis) affects up to 30% of women with cystitis-like symptoms, but these infections seldom cause cortical damage. Pregnant women and patients with recurrent UTI, diabetes, immunosuppression, renal tract pathology, or a prior UTI before the age of 12 are more likely to be in this scenario. Acute pyelonephritis can be exceedingly severe and resistant to therapy in the presence of blockage (stone, tumour, bladder neck obstruction, enlarged prostate), and may proceed to renal abscess. [2]

A urine culture and antimicrobial susceptibility testing should be performed on all patients with suspected acute pyelonephritis to guide possible adjustments to the initial antimicrobial regimen (if there is no improvement) and the selection of

step-down oral therapy for patients who were previously treated with intravenous therapy. after vulva washing, a midstream urine sample should be requested. However, when empty urine specimens were collected with or without prior washing, no significant variations in the frequency of contaminated or false culture findings were identified in several trials. Catheterization is not required to obtain a urine sample. according to studies There are no variations in colony counts or organisms between catheterized and midstream voiding samples. [5,29-32]

Management:

Acute pyelonephritis can be treated as an outpatient or as an inpatient procedure. Outpatient treatment is available for healthy, young, non-pregnant women with uncomplicated pyelonephritis. Patients who are extremely young, old, immunocompromised, those with poorly managed diabetes, renal transplant patients, patients with structural abnormalities of the urinary system, pregnant patients, or those who are unable to tolerate oral ingestion frequently require inpatient care. Antibiotics, analgesics, and antipyretics are the mainstays of acute pyelonephritis therapy. Pain and fever associated with acute pyelonephritis are well treated with nonsteroidal anti-inflammatory medications (NSAIDs). [1] Outpatient oral therapy is successful in 90% of selected patients with uncomplicated acute pyelonephritis who can tolerate oral intake, will be compliant with the treatment regimen, will return for early follow-up, and have adequate social support, despite the fact that patients with acute pyelonephritis are traditionally hospitalised and treated with intravenous antibiotics. Hospitalization is recommended for patients with complex acute pyelonephritis who are more unwell or have not responded to outpatient care. Up to 70% of patients can be chosen for outpatient treatment using specified hospitalisation criteria. [2] The choice of first-line oral antibiotics depends on local antibiotic resistance characteristics, although trimethoprim alone or in combination with sulphamethoxazole, cephalexin, or amoxicillin-clavulanic acid are common first-line antibiotics. Amoxicillin alone should not be administered since E. coli is the causal organism in 90% of cases and -lactamase production is present in at least 50%. [3]

In uncomplicated cases *E. coli* can be treated with oral cephalosporins or TMP-SMX for 14 days. Acute pyelonephritis that is complicated requires intravenous (IV) antibiotic therapy until the symptoms resolve. Piperacillin-tazobactam, fluoroquinolones, meropenem, and cefepime are examples of IV antibiotics. Vancomycin can be used to treat people who are allergic to penicillin. Non-admitted individuals should be followed up on in 1 to 2 days to see if their symptoms have resolved. [1] Antibiotics should be taken for how long for children? There is evidence that short-course therapy (3-4 days) is equally effective as standard-course treatment (7-10 days) in children with urinary tract infections other than pyelonephritis. However, none of the three trials that looked at the length of therapy in children with pyelonephritis compared these clinically relevant options. Because children with acute pyelonephritis often recover clinically in 3-4 days, it is sensible to prolong antibiotic treatment for another 7-10 days until more trials investigating treatment duration are conducted. [3,33,34] Resistant organisms and nephrolithiasis are the two most prevalent reasons of initial therapy failure. Many clinicians collect a blood count, urinalysis, and blood and urine cultures in the lack of clinical response, looking for signs of infection or antibiotic resistance; however, there is no evidence to support the routine use of these tests. It is necessary to undertake a rectal or vaginal examination. [2]

Conclusion:

Acute pyelonephritis is a serious bacterial infection that causes kidney inflammation. It's common more among women with some studies indicating that's 5 times more in women than men. Infection with *Escherichia coli* is the most prevalent cause. Fever, vomiting, abdomen or loin discomfort, and fatigue are all symptoms of acute pyelonephritis, however Fever is the most common symptom. Acute pyelonephritis can be treated as an outpatient or as an inpatient procedure. Outpatient treatment is available for healthy, young, non-pregnant women with uncomplicated pyelonephritis. The choice of first-line oral antibiotics depends on local antibiotic resistance, and thus fast and accurate testing is the key to successful treatment.

References:

1. Belyayeva M, Jeong JM. Acute Pyelonephritis. [Updated 2021 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK519537/>
2. Ramakrishnan K, Scheid DC. Diagnosis and management of acute pyelonephritis in adults. *Am Fam Physician*. 2005 Mar 1;71(5):933-42. Erratum in: *Am Fam Physician*. 2005 Dec 1;72(11):2182. PMID: 15768623.
3. Craig JC, Hodson EM. Treatment of acute pyelonephritis in children. *BMJ*. 2004 Jan 24;328(7433):179-80. doi: 10.1136/bmj.328.7433.179. PMID: 14739166; PMCID: PMC318473.
4. Anumudu S, Eknayan G. Pyelonephritis: A Historical Reappraisal. *J Am Soc Nephrol*. 2019 Jun;30(6):914-917. doi: 10.1681/ASN.2019010017. Epub 2019 Apr 26. PMID: 31028101; PMCID: PMC6551776.
5. Diagnosis and Treatment of Acute Pyelonephritis in Women, RICHARD COLGAN, JAMES R. JOHNSON, MD, University of Minnesota, Minneapolis, Minnesota, *Am Fam Physician*. 2011 Sep 1;84(5):519-526.
6. Nicolle LE. Epidemiology of urinary tract infection. *Infect Med*. 2001;18:153–162
7. Foxman B, Klemstine KL, Brown PD. Acute pyelonephritis in US hospitals in 1997: hospitalization and in-hospital mortality. *Ann Epidemiol*. 2003;13(2):144–150.
8. Nicolle LE, Friesen D, Harding GK, Roos LL. Hospitalization for acute pyelonephritis in Manitoba, Canada, during the period from 1989 to 1992; impact of diabetes, pregnancy, and aboriginal origin. *Clin Infect Dis*. 1996;22(6):1051–1056.
9. Czaja CA, Scholes D, Hooton TM, Stamm WE. Population-based epidemiologic analysis of acute pyelonephritis. *Clin Infect Dis*. 2007;45(3):273–280.
10. Bright R: Reports of Medical Cases, London, Longman, Rees, Orme, Brown and Greer, 1827.
11. Neumann I, Moore P. Pyelonephritis (acute) in non-pregnant women. *BMJ Clin Evid*. 2014 Nov 4;2014:0807. PMID: 25373019; PMCID: PMC4220693.

12. Stamm WE, Hooton TM. Management of urinary tract infections in adults. *N Engl J Med*. 1993;329:1328–34.
13. Bass PF 3d, Jarvis JA, Mitchell CK. Urinary tract infections. *Prim Care*. 2003;30:41–61
14. Roberts JA. Management of pyelonephritis and upper urinary tract infections. *Urol Clin North Am*. 1999;26:753–63.
15. Bergeron MG. Treatment of pyelonephritis in adults. *Med Clin North Am*. 1995;79:619–49.
16. Scholes D, Hooton TM, Roberts PL, Gupta K, Stapleton AE, Stamm WE. Risk factors associated with acute pyelonephritis in healthy women. *Ann Intern Med*. 2005 Jan 4;142(1):20-7. doi: 10.7326/0003-4819-142-1-200501040-00008. PMID: 15630106; PMCID: PMC3722605.
17. Hooton TM, Stamm WE. Diagnosis and treatment of uncomplicated urinary tract infection. *Infect Dis Clin North Am*. 1997;11:551–81.
18. Foxman B, Klemstine KL, Brown PD. Acute pyelonephritis in US hospitals in 1997: hospitalization and in-hospital mortality. *Ann Epidemiol*. 2003;13:144–50.
19. Nicolle LE. Management of acute uncomplicated pyelonephritis. In: Bergan T, Zeichhardt H, Mahy BW, editors. *Urinary Tract Infections, Infectiology*. Basel: Karger; 1997. pp. 8–13
20. Nicolle LE, Friesen D, Harding GK, Roos LL. Hospitalization for acute pyelonephritis in Manitoba, Canada, during the period from 1989 to 1992; impact of diabetes, pregnancy, and aboriginal origin. *Clin Infect Dis*. 1996;22:1051–6.
21. Raz R, Gersham M, Flatau E, Stoler Z. Acute pyelonephritis in hospitalized women. *Infectious Diseases in Clinical Practice*. 1999;8:335–40.
22. Talan DA, Stamm WE, Hooton TM, Moran GJ, Burke T, Irvani A, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis pyelonephritis in women: a randomized trial. *JAMA*. 2000;283:1583–90.
23. Czaja CA, Scholes D, Hooton TM, Stamm WE. Population-based epidemiologic analysis of acute pyelonephritis. *Clin Infect Dis*. 2007 Aug 01;45(3):273-80
24. Sabih A, Leslie SW. Complicated Urinary Tract Infections. [Updated 2021 Aug 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing;

2021 Jan-. Available from:
<https://www.ncbi.nlm.nih.gov/books/NBK436013/>

25. Velasco M, Martínez JA, Moreno-Martínez A, et al. Blood cultures for women with uncomplicated acute pyelonephritis: are they necessary? *Clin Infect Dis*. 2003;37(8):1127–1130.
26. Thanassi M. Utility of urine and blood cultures in pyelonephritis. *Acad Emerg Med*. 1997;4(8):797–800.
27. Otto G, Sandberg T, Marklund BI, Ulleryd P, Svanborg C. Virulence factors and pap genotype in *Escherichia coli* isolates from women with acute pyelonephritis, with or without bacteremia. *Clin Infect Dis*. 1993;17(3):448–456.
28. Finkelstein R, Kassis E, Reinhertz G, Gorenstein S, Herman P. Community-acquired urinary tract infection in adults: a hospital viewpoint. *J Hosp Infect*. 1998;38(3):193–202
29. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011;52(5):e103–e120.
30. Bradbury SM. Collection of urine specimens in general practice: to clean or not to clean? *J R Coll Gen Pract*. 1988;38(313):363–365.
31. Immergut MA, Gilbert EC, Frensilli FJ, Goble M. The myth of the clean catch urine specimen. *Urology*. 1981;17(4):339–340.
32. Bray PA, Corry MF. Mid-stream urine collection: is preparatory cleansing essential? *N Z Nurs J*. 1979;72(3):13–14.
33. Bloomfield P, Hodson EM, Craig JC. Antibiotics for acute pyelonephritis in children. *Cochrane Database Syst Rev* 2003;(3): CD003772.
34. Michael M, Hodson EM, Craig JC, Martin S, Moyer VA. Short compared with standard duration of antibiotic treatment for urinary tract infection: a systematic review of randomised controlled trials. *Arch Dis Child* 2002;87: 118-23.
35. Venkatesh L, Hanumegowda RK. Acute Pyelonephritis - Correlation of Clinical Parameter with Radiological Imaging Abnormalities. *J Clin Diagn Res*. 2017 Jun;11(6):TC15-TC18. doi: 10.7860/JCDR/2017/27247.10033. Epub 2017 Jun 1. PMID: 28764263; PMCID: PMC5535453.

UNDER PEER REVIEW