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ACUTE PYELONEPHRITIS: CLINICAL FEATURES, DIAGNOSIS, AND PRINCIPLES OF INITIAL MANAGEMENT

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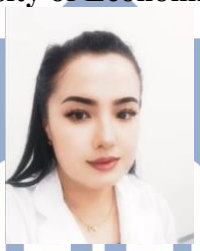

Abstract. Acute pyelonephritis (AP) is an infectious-inflammatory process involving the renal pelvicalyceal system and renal parenchyma and is considered one of the most important clinical manifestations of upper urinary tract infection (upper UTI) in practice. AP is often associated with ascending bacterial invasion from the lower urinary tract (cystitis); etiologically, *Escherichia coli* holds a leading position and has been identified as the principal pathogen in numerous population-based observations. The clinical relevance of the disease is determined by three factors: (1) a high incidence and increased risk of severe course among women, pregnant individuals, older adults, people living with diabetes, and patients with urologic obstruction; (2) complications such as urosepsis and acute deterioration of renal function; and (3) the need to rationalize empiric antibiotic selection amid the growing burden of antimicrobial resistance. The EAU recommendations specifically emphasize infection control and antimicrobial stewardship (rational use) as key principles in the management of AP. This article presents an evidence-based overview of AP clinical signs, laboratory and imaging diagnostic algorithms, criteria for distinguishing “uncomplicated” versus “complicated” cases, indications for urgent hospitalization, and contemporary principles of initial treatment. Within the framework of NICE NG111 and IDSA/EAU guidelines, the analysis addresses empiric therapy strategies, de-escalation based on culture results, the use of imaging investigations (ultrasound/CT) when indicated, and monitoring of treatment effectiveness.

Keywords: acute pyelonephritis, upper urinary tract infection, flank pain, urinalysis, urine culture, empiric antibiotic therapy, urosepsis, obstructive uropathy, imaging diagnostics, antimicrobial resistance.

INTRODUCTION

Acute pyelonephritis (AP) is a frequently encountered infectious syndrome in clinical practice that can nonetheless follow a severe course. Population-based data depict a variable disease burden: for example, in a large cohort observation covering 2009–2018, the overall incidence of

pyelonephritis was reported as 4.2 cases per 10,000 person-years, and it was substantially higher in women than in men (6.6 vs 1.5). Classical epidemiological analyses likewise indicate that rates of both outpatient and inpatient pyelonephritis in women are several times higher than in men, with the outpatient-to-inpatient ratio being particularly large among young women.The pathogenesis of AP is most commonly associated with the ascending route: uropathogenic bacteria first colonize the urinary bladder and then ascend through the ureter, triggering an inflammatory process within the renal parenchyma and the pelvicalyceal system. Etiologically, *E. coli* predominates and is reported to account for 70–80% of AP cases across different populations; the remainder is attributed to other Enterobacteriaceae, enterococci, and occasionally *Pseudomonas* and other organisms. It is emphasized that *E. coli* adhesion factors-such as P fimbriae-enhance attachment to the uroepithelium and facilitate ascent; therefore, the interplay between microbial virulence and the host immune response is critical in the development of AP.From a clinical standpoint, AP is assessed by distinguishing “uncomplicated” and “complicated” forms. The “complicated” group typically includes patients with urologic obstruction (stones, strictures, prostatic hyperplasia), structural abnormalities, catheter or stent use, immunosuppression, significant comorbid conditions (e.g., diabetes), signs of renal insufficiency, features of sepsis, and pregnancy. This stratification is decisive for determining diagnostic strategy (including when imaging is indicated) and for selecting empiric antibiotics (given differences in resistance risk).

Another major driver of clinical urgency is antimicrobial resistance. Among UTI pathogens-particularly *E. coli*-resistance to fluoroquinolones, TMP-SMX, and certain beta-lactams varies by geography and changes over time; consequently, contemporary guidelines require empiric therapy to be aligned with local antibiograms and the patient’s individual risk factors for resistance. The IDSA 2025 recommendations for complicated UTI (including AP) advise limiting empiric use of fluoroquinolones in patients who have received this class within the previous 12 months. NICE NG111 proposes a stepwise (oral/IV) approach matched to clinical severity, with an emphasis on prudent antibiotic use to help curb resistance.

Accordingly, the aim of this article is to provide a systematic account of AP clinical features, to define the minimally necessary diagnostic package (history–examination–laboratory testing) and evidence-based indications for imaging, and to present the principles of initial management (empiric antibiotics, rehydration and symptomatic care, de-escalation, and hospitalization criteria) within the IMRAD format. Note: antibiotics must be prescribed only by a physician based on clinical assessment and local recommendations; this article is intended for scientific and educational purposes.

METHODOLOGY: Study design: an integrative literature review (evidence-based narrative review) combined with the development of a practical clinical algorithm. Data sources were selected from international clinical guidelines, systematic reviews, cohort and population-based studies, and clinically oriented rapid-review materials.Search strategy: Sources published between 2005 and 2025 were searched in PubMed/PMC, the Cochrane Library, major professional society websites (EAU, IDSA), official NICE documents, and sections on acute pyelonephritis within medical “best practice” platforms (e.g., BMJ Best Practice). The main search terms included: “acute pyelonephritis”, “upper urinary tract infection”, “diagnosis”, “urine culture”, “imaging indications”, “computed tomography”, “antimicrobial prescribing”, “complicated UTI”, and “sepsis risk factors”. The following guidelines were treated as key reference documents: EAU Urological Infections Guidelines (2024), the IDSA guideline on complicated UTI (2025), the IDSA/ESCMID guideline on uncomplicated UTI and acute pyelonephritis in women (2011), and NICE NG111 (2018; reviewed in 2019).

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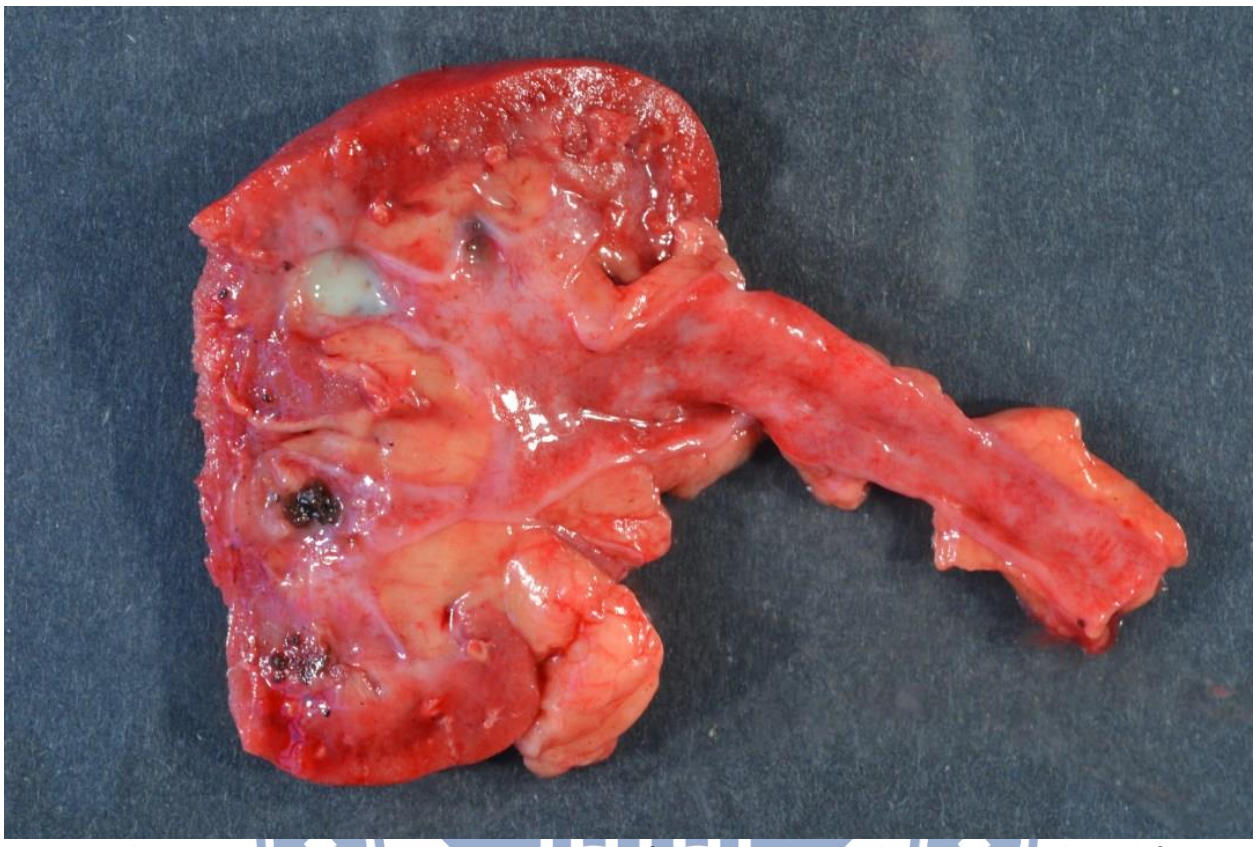
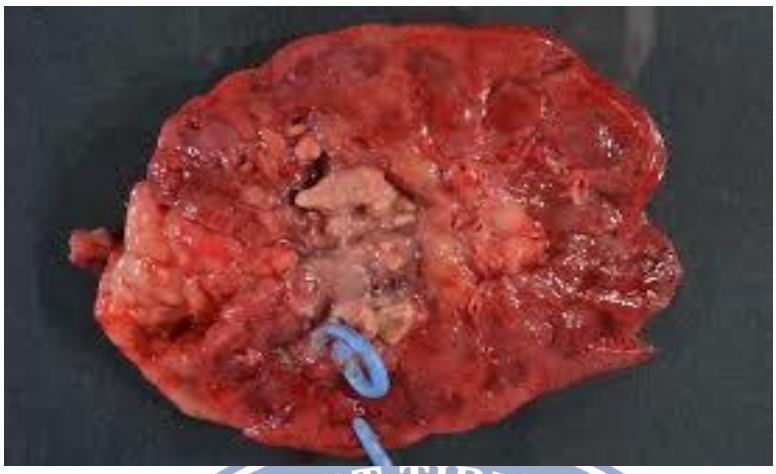


Selection criteria: Sources were included if they (1) clearly described the clinical features of acute pyelonephritis, diagnostic algorithms, or treatment strategies; (2) reported the level of evidence or provided conclusions applicable to clinical practice; and (3) presented data on adult populations and/or specific risk groups (pregnant patients, older adults, obstruction). Exclusion criteria were: small single-center observations with unclear methodology; UTI types not directly related to acute pyelonephritis; and veterinary medicine materials.Data extraction: For each source, information was systematically collected under the following blocks: (a) definition and epidemiology; (b) etiology and risk factors; (c) clinical symptoms and physical examination; (d) laboratory investigations (urinalysis, urine culture, blood tests); (e) indications for imaging diagnostics; (f) treatment (principles of empiric antibiotic choice, IV-to-oral switch, duration, monitoring); (g) complications and hospitalization criteria; and (h) antimicrobial stewardship and management of resistance risk.Analytical approach: Findings were synthesized thematically. Recommendations that aligned across guidelines were categorized as “consensus,” while differences were interpreted as “context-dependent” guidance. Based on this synthesis, a practical “primary care” algorithm for acute pyelonephritis (a stepwise sequence of actions) was proposed.



RESULTS

1. Clinical features and syndromic presentation. Acute pyelonephritis (AP) most often begins abruptly within 24–72 hours and is characterized by a “systemic inflammation + upper UTI” combination: fever, chills/rigors, malaise, nausea/vomiting, flank (loin) pain, costovertebral angle tenderness (Pasternatsky sign), and the possible addition of lower UTI symptoms such as dysuria and urinary frequency. An evidence-based review by the AAFP emphasizes that AP should be suspected particularly when flank pain co-occurs with laboratory evidence of UTI. The severity spectrum is wide: mild cases may be managed on an outpatient basis, whereas severe presentations (hypotension, decreased alertness, dehydration, or signs suggestive of sepsis) require urgent inpatient management. In older adults and patients with immunosuppression, typical dysuria may be absent; therefore, attention to “atypical” manifestations (confusion, generalized weakness) is essential.

2. Laboratory diagnosis: the minimum core package.

A) Urinalysis (UA): pyuria, nitrite positivity, bacteriuria, and occasionally hematuria.

B) Urine culture and antibiogram: evidence synthesis supports obtaining a culture in all AP patients and directing therapy according to the results; the EAU likewise lists urine culture in suspected AP as a strong recommendation.

C) Blood tests: complete blood count (leukocytosis/neutrophilia), CRP/procalcitonin (as supportive markers for severity assessment), creatinine and electrolytes (to evaluate AKI risk and guide treatment decisions). Blood cultures are more selective: they are not always required in “uncomplicated” AP, but they may be clinically useful in severe febrile illness, suspected sepsis, immunosuppression, or when hospitalization is anticipated. An AAFP rapid review also highlights that imaging and some additional tests are not routinely mandatory in uncomplicated cases.

3. Imaging diagnostics: when and why? The synthesis indicates that imaging is not required in clinically “uncomplicated” AP that is responding to therapy; the key goal is to identify situations where complications must be excluded-such as obstruction, stones, renal/perinephric abscess, or emphysematous pyelonephritis. The Cleveland Clinic Journal of Medicine notes that imaging is generally unnecessary in patients without risk factors, but CT (or other imaging) should be considered when fever/leukocytosis persists within 72 hours after antibiotics are started or when risk factors are present. A 2024 review also emphasizes the importance of imaging-especially in complicated AP-and notes that ultrasound and contrast-enhanced ultrasound (CEUS) may be helpful in selected scenarios. Practical conclusion: in primary care, ultrasound is preferred when stone/obstruction is suspected and in pregnancy (safety), while contrast-enhanced CT/MRI has greater diagnostic value in complicated cases and in non-response to treatment.

4. Empiric antibiotic therapy and principles of initial management. Based on NICE NG111 and EAU/IDSA-informed synthesis, the following principles are prioritized: (a) start antibiotics without delay, but obtain a urine culture beforehand whenever feasible; (b) choose oral

versus IV administration according to clinical severity; (c) account for local resistance patterns, prior antibiotic exposure, and risk factors for complicated disease; (d) if clinical response is achieved, switch from IV to oral (step-down) within 48–72 hours and narrow therapy (de-escalation) based on culture results. The IDSA 2025 guidance for complicated UTI/AP advises avoiding empiric fluoroquinolones in patients with exposure to this drug class within the previous 12 months (in the context of resistance and adverse-effect concerns).

Antibiotic classes (general overview): in mild-to-moderate uncomplicated AP, oral regimens may be used if local susceptibility supports them; in severe illness, vomiting/dehydration, sepsis, or complicated-risk settings, parenteral beta-lactams (e.g., third-generation cephalosporins), beta-lactam/beta-lactamase inhibitor combinations, or other broad-spectrum options may be considered. If ESBL risk is present, selection becomes more individualized and typically benefits from infectious diseases/urology input. The EAU guideline highlights antimicrobial stewardship as a key priority in overall UTI management.

5. Symptomatic and supportive care. Initial management is not limited to antibiotics: restoration of fluid balance (correction of dehydration), control of pain and fever with antipyretics/analgesics, antiemetic therapy when nausea is present, and stabilization of comorbid conditions (e.g., glycemic control in diabetes) are required. In severe cases, sepsis protocols, hemodynamic monitoring, and ICU-level care may be considered. A StatPearls overview notes higher mortality risk among older adults, patients with reduced renal function, and those presenting with sepsis.

6. Hospitalization criteria and follow-up. The synthesis suggests inpatient referral is preferred in the following circumstances: suspected sepsis/shock; severe vomiting and inability to take oral medications; pregnancy; acute worsening of renal function; suspected obstruction or stones; immunosuppression; and lack of clinical improvement within 48–72 hours. NICE guidance likewise emphasizes selecting strategy according to severity and complication risk and recommends reassessment if there is no improvement within 24–48 hours.

DISCUSSION: This review suggests that the most effective strategy for managing acute pyelonephritis (AP) is a coherent chain of actions: “high clinical suspicion + minimal laboratory confirmation + targeted (selective) imaging + rational empiric antibiotic therapy + de-escalation.” The main strength of this approach is that it helps avoid unnecessary tests and unnecessary antibiotic exposure while still enabling early identification of complicated cases and timely treatment of complications (abscess, obstructive uropathy, urosepsis).

The first key issue is the practical differentiation between “uncomplicated” and “complicated” AP. Risk factors (obstruction, structural anomalies, diabetes, pregnancy, catheter/stent, immunosuppression) not only increase the likelihood of severe disease, but also shift the likely pathogen spectrum and raise the probability of ESBL-producing and multidrug-resistant strains. Therefore, a standardized “risk screen” should be embedded into the initial assessment: are there signs suggesting a stone, is urinary outflow impaired, what is the history of prior UTIs and antibiotic exposure, and are there relevant comorbidities? Risk-based stratification supports individualized management and reduces the inappropriate application of “one-size-fits-all” regimens described in guidelines.

The second issue is the correct timing and correct patient selection for imaging. A common real-world error is either performing CT routinely even in mild AP, or-conversely-delaying imaging in patients with a high likelihood of obstruction or in those who fail to respond to treatment. The “72-hour response window” concept discussed in CCJM is clinically practical: if there are no risk factors and the patient improves within 72 hours, imaging is usually unnecessary; if there is no response, complications should be actively sought. At the same time, pregnancy requires avoidance of ionizing radiation and prioritization of safer modalities such as ultrasound (and, when appropriate, CEUS), as also discussed in imaging reviews from 2024–2025.

The third issue is resistance-risk management in empiric antibiotic choice. The IDSA 2025 recommendation to restrict empiric fluoroquinolones when there has been fluoroquinolone exposure within the prior 12 months reinforces a patient-tailored approach, since prior exposure can correlate with higher resistance probability in some settings. NICE NG111 emphasizes prudent antibiotic use at the primary-care level, an oral/IV strategy matched to clinical severity, and mandatory reassessment. When these approaches are integrated, a practical model emerges: (1) obtain a culture; (2) start empiric therapy aligned with local antibiogram data and individual risk; (3) reassess clinical response at 48–72 hours; (4) narrow or adjust therapy according to culture results; (5) keep duration at the minimum effective course (avoid unnecessary prolongation).

The fourth issue concerns complications and prognosis. Severe AP can progress to urosepsis; factors such as obstruction, older age, and major comorbidities (e.g., liver cirrhosis) have been associated with worse outcomes in clinical observations. From this perspective, systematic assessment of “red flags” (hypotension, tachypnea, altered mental status, oliguria, severe dehydration, severe flank pain with suspected stone) at the primary-care level supports early escalation in line with sepsis protocols.

Practical algorithm (brief sequence for primary care)

Clinical suspicion: fever/rigors + flank pain or costovertebral angle tenderness + UTI symptoms.

Immediate assessment: hemodynamics, sepsis signs, pregnancy, suspicion of obstruction/stone, comorbid risk factors.

Minimum labs: urinalysis + urine culture (before antibiotics). If needed: CBC, CRP, creatinine, electrolytes.

Empiric management: match route and spectrum to severity and risk; IV strategy if severe or unable to take oral therapy.

Imaging indications: obstruction/stone suspicion, immunosuppression, AKI, non-response at 48–72 hours, atypical course.

Reassessment at 48–72 hours: clinical response + culture result → de-escalation/correction.

Follow-up: prevention-oriented advice to reduce recurrence risk (hydration, hygiene, elimination of underlying urologic causes).

CONCLUSION

Acute pyelonephritis is a clinically significant form of upper urinary tract infection, and early recognition together with rational initial management reduces the likelihood of complications. An evidence-based approach includes: (1) suspecting AP based on a characteristic symptom constellation; (2) etiologic confirmation with urinalysis and especially urine culture; (3) avoiding unnecessary imaging in “uncomplicated” cases while using ultrasound/CT in a timely manner when complicated risk is present or when there is no response within 72 hours; (4) selecting empiric antibiotics according to local resistance patterns and individual risk; and (5) narrowing therapy (de-escalation) based on culture results while adhering to the principle of a minimally sufficient treatment duration. Across EAU, NICE, and IDSA documents, antimicrobial stewardship occupies a central role in AP management; given that excessive antibiotic use amplifies resistance, routine risk stratification and systematic reassessment should be incorporated into everyday practice.

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