

CLINICAL AND LABORATORY EVALUATION OF URINARY TRACT INFECTIONS IN ELDERLY POPULATION

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ABSTRACT

Introduction: Urinary tract infection (UTI) is one of the most common infections in the geriatric population. The management of geriatric urinary tract infections is difficult due to the various factors. This study evaluated the clinical and laboratory characteristics of 101 patients who were monitored for upper UTI (acute pyelonephritis) in a tertiary care hospital.

Materials and methods: One hundred and one patients over the age of 65 years, who were monitored for acute pyelonephritis (APN) at a tertiary care hospital between January 2008 and December 2012, were included in the study. The medical charts of the patients monitored with the diagnosis of APN were retrospectively examined and the anamnesis and physical examination findings, laboratory parameters, and empirical and targeted treatments and outcomes of the patients were evaluated.

Findings: The most common symptoms in the patients were functional debilitation (32%), mental confusion (27%), and emesis (26%) while the most frequent physical examination findings were fever (57%), costovertebral angle tenderness (CVAT) positivity (42%), and tachycardia (27%). The most frequently isolated microorganism from the urine cultures was *E. coli* (66%).

Conclusion: In conclusion, APN is an infectious disease that is common in the elderly population and can result in death. It should be remembered that the typical symptoms and signs of infection may not be present in elderly patients with APN and that these patients may present with atypical findings such as mental confusion and functional debilitation. The increase in antibiotic resistance in *E. coli* strains limits the treatment options and once more reminds us, the clinicians, of the importance of rational antibiotic use.

Key words: Acute pyelonephritis, elderly population, antibiotic resistance.

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Introduction

The elderly population is gradually increasing throughout the world and the proportion of elderly in the general population is expected to increase up to approximately 20% by the year 2050⁽¹⁾. Despite the advances in the diagnosis, treatment, and prevention methods, infection is one of the most important reasons for hospitalizations and deaths in the elderly^(2,3). The diagnosis and treatment of infections are difficult in geriatric population. Classical symptoms of infection, such as fever and local signs of infection, may not be detected in geriatric patients; therefore elderly patients with infection generally present with atypical symptoms such as confusion, impaired general condition, functional disability, and with a poor medical history⁽¹⁾.

Urinary tract infection (UTI) is one of the most common infections in the geriatric population and mortality rates of up to 5% are reported in cases with bacteremia^(4,5). The incidence of UTI increases with age in both women and men^(6,7). In addition, the majority of these infections are complicated due to the functional and structural alterations that develop with older age⁽⁸⁾. Moreover, one third of the patients with UTI present with atypical symptoms and this situation makes the management of UTI in the elderly more difficult⁽⁵⁾.

This study evaluated the clinical and laboratory characteristics of 101 patients who were monitored for upper UTI (acute pyelonephritis) in a tertiary care hospital.

Materials and methods

One hundred and one patients over the age of 65 years, who were monitored for acute pyelonephritis at the Infectious Diseases Ward of the SDU School of Medicine Hospital between January 2008 and December 2012, were included in the study. The study has only included patients with urinary tract infection and the patients with concomitant infections (e.g lung, soft tissue, heart, and other infections) have been excluded from the study. The medical charts of the patients monitored with the diagnosis of APN were retrospectively examined and the anamnesis, physical examination findings, laboratory parameters, and empirical and targeted treatments and outcomes of the patients were recorded on separate forms and transferred to SPSS software.

Only patients with community-acquired infections were included in the study. The diagnosis of APN was based on the presence of clinical findings (at least two of these findings: body temperature $>37.9^{\circ}\text{C}$, unexplained impaired general condition, confusion, flank pain, the presence of CVAT, and new-onset incontinence) and pyuria (≥ 10 WBC/mL in the urinary microscopic examination) or bacterial growth ($\geq 10^5$ coloni-forming units/mL bacteria in urine culture). Non-specific laboratory tests (CRP and WBC count) were also used to support the diagnosis. Patients with the same bacteria growing in both the blood culture and urine culture were considered to have bacteraemia in APN. Patients diagnosed with asymptomatic bacteriuria (ASB) or cystitis were excluded from the study.

Statistical evaluation

The statistical evaluation was performed using the chi-square and Fisher's chi-square tests using the SPSS analysis software.

Results

A total of 101 patients over the age of 65 years were enrolled in the study including 45 females and 56 males. The mean age of the patients was 75.1 ± 12.4 years. The most common symptoms in the patients were functional debilitation (32%), mental confusion (27%), and emesis (26%) while the most frequent physical examination findings were fever (57%), costovertebral angle tenderness (CVAT) positivity (42%), and tachycardia (27%). Sixty-six percent of the patients had leukocytosis

and 87% elevated C-reactive protein (CRP) levels. Ninety percent of the patients had growth in urine culture, while 23 patients had growth with the same bacterium in the blood culture. It was found that all patients who did not have growth in the urine culture but were diagnosed with APN based on other clinical and laboratory findings had recently received antibiotic treatment. The most common predisposing factors and underlying diseases were previous urinary tract surgery (35%), diabetes mellitus (31%), and indwelling urinary catheter use (22%). Various clinical and laboratory characteristics of the cases are presented in Table 1.

Symptoms	% (n=101)
Functional debilitation	32
Confusion	27
Emesis	26
Dysuria	25
Pollakiuria	23
Urgency	22
Chills	22
Vomiting	20
Flank pain	17
Physical examination findings	
Fever	57
CVAT positivity	42
Tachycardia (Pulse > 100)	27
Suprapubic tenderness	12
Hypotension (Systolic blood pressure < 90)	10
Predisposing conditions	
Urinary tract surgery	35
Diabetes mellitus	31
Prostatic hypertrophy	23
Urinary catheter	22
Cerebrovascular diseases	17
Urolithiasis	13
Laboratory Findings	
Elevation of CRP (CRP > 6 mg/L)	87
Leukocytosis (WBC > 11000/ μL)	66
Pyuria (Urine WBC $\geq 10/\text{mL}$)	100

Table 1: Various clinical and laboratory characteristics of the cases.

When various characteristics of the patients with or without bacteremia were compared, it was observed that fever, hypotension, and leucocytosis was statistically significantly more frequent in the bacteremia patients compared to patients without bacteremia ($p < 0.05$).

Microorganisms	n (%)
Escherichia coli	60 (66)
Klebsiella pneumoniae	8 (8,8)
Enterococcus faecalis	5 (5,5)
Staphylococcus aureus	3 (3,3)
Pseudomonas aeruginosa	5 (5,5)
Enterobacter aerogenes	3 (3,3)
Proteus vulgaris	3 (3,3)
Candida albicans	2 (2,2)
Providencia sp.	1 (1,1)

Table 2: Causative microorganisms.

Antibiotic	Sensitivity %
Ampicilline	26
Levofloxacin	42
Cefazolin	43
Ciprofloxacin	44
Cefuroxim	47
Trimetoprim-sulfametaxazole	49
Cefixim	52
Ceftriaxone	52
Ampicilline-sulbactam	60
Gentamicin	64
Ceftazidime	65
Cefoperazone-sulbactam	83
Piperacilline-tazobactam	84
Ertapenem	90
Meropenem	98
Imipenem	100

Table 3: Antibiotic susceptibility of gram-negative microorganisms.

The most frequently isolated microorganism from the urine cultures was *E. coli* (66%), followed by other gram-negative bacteria and gram-positive bacteria such as enterococci. It was found that 52% of *E. coli* produced extended-spectrum beta-lactamase (ESBL). The causative microorganisms and antibiotic sensitivity rates are presented in Table 2 and Table 3.

Mortality occurred in the four patients who also had bacteremia, while other patients were discharged with full recovery in terms of urinary tract infection.

Discussion

UTI can be divided into two clinical pictures as (i) cystitis, where the infection is generally insignificant and limited to the bladder and can easily be treated and (ii) APN, where the infection is more severe and serious, spread to the kidneys and is even associated with mortality rates up to 5% especially in cases with bacteremia. Any underlying predisposing condition causes UTI to become complicated⁽⁹⁾. Particularly, APN is the second most frequent cause of hospitalization in the elderly population⁽³⁾. Patients with APN constituted 33% of the geriatric patients with infection who were monitored in our ward during the same period.

UTI is particularly common in women and occurs more frequently in females during all periods of life except newborns⁽¹⁰⁾. Both ASB and symptomatic UTIs increase with age in both genders^(6,7). These infections are also common in men due to the predisposing factors in the elderly such as benign prostatic hypertrophy, urinary tract surgery, indwelling urinary catheter use and diabetes mellitus. Hence, male patients constituted 54% of the cases included in this study, which evaluated only the patients with pyelonephritis.

The majority of the UTI cases among the elderly are complicated due to the functional and structural alterations of the genitourinary system that develop with older age⁽⁸⁾. The conditions predisposing UTI such as indwelling catheter use, history of urinary tract surgery, cerebrovascular disease, diabetes mellitus, and prostatic hypertrophy were found in 22%, 35%, 17%, 31%, and 23% of the cases, respectively. All of these factors are independent risk factors associated with the development of UTI and complicate these infections.

APN is a serious renal infection that may be life-threatening^(10,11). The diagnosis can be made

based on the symptoms and physical examination and laboratory findings. Patients with APN typically present with complaints such as fever, nausea, vomiting, and chills. The physical examination revealed CVAH positivity. Cystitis symptoms and signs including dysuria, pollakiuria, urgency, and suprapubic tenderness may sometimes be seen in patients with APN (11). However, these classical findings are not necessarily present in elderly patients. In some studies, it was reported that urinary symptoms may be absent even in bacteremia UTIs in elderly patients^(12, 13). Symptoms such as impaired general condition, cognitive and functional debilitation and mental confusion may be the only signs of UTI^(13, 14). Even fever, a finding commonly used in the APN's diagnosis and differentiation from cystitis, may not be present in 20-30% of elderly patients with APN^(11, 15). Again, the frequency of findings such as dysuria and pollakiuria, which may be seen during the course of APN, is decreased in the elderly⁽¹⁵⁾. The current study also found that fever was present only in 57% of the cases, and findings such as mental confusion and functional debilitation were common and sometimes the only symptoms of UTI. Complaints such as dysuria, pollakiuria, and urgency were found in approximately 25% of the cases, while only 42% of the cases had CVAT. These results are an important reminder that the classical signs of infections may not always be present and patients may present with atypical findings in the geriatric population.

Poor history taking is also one of the factors complicating diagnosis^(15, 16). In this study, 27% of the cases had mental confusion and it was impossible to obtain reliable information from these patients. Moreover, ongoing urinary symptoms in the elderly such as incontinence, nocturia, and urgency also make the diagnosis more difficult^(5, 13). ASB frequency is as high as 6-16%, particularly in patients over the age of 65, and this causes diagnostic confusion in this patient group who has ongoing urinary symptoms^(16, 17).

As also seen in the cases included in this study was the diagnosis of UTIs that have some difficulties. Laboratory studies can partly eliminate these difficulties. Particularly the detection of pyuria in the direct microscopy of urine and a growth of 105 cfu/ml in the urine culture support the diagnosis, but these alone are not enough for a definitive diagnosis. In this study, pyuria was found in the urine examinations of all cases and 90% of the cases had growth in culture. Urine culture should be conduct-

ed in all cases that are suspected to have APN and the treatment should be rearranged according to the sensitivity pattern of the grown bacterium. In particular, in light of the increases in antibiotic resistance in recent years, this step is highly important in terms of diagnosis as well as treatment^(18, 19). Some patients may have negative urine culture results. Previous antibiotic therapy is the the most important underlying reason for this is situation, and 10% of the patients had a negative urine culture in our study⁽⁵⁾. Studies reported that 21-42% of patients with APN have positive blood cultures^(11, 20, 21). Growth was seen in 23% of the cases in this study and this rate is similar to the literature. In one study, five risk factors were described for bacteremia in patients with APN. These include nursing home residency, Foley catheter, band formation on peripheral smear, chills, and neutrophilia⁽²²⁾. In the current study, it was observed that the frequency of hypotension, fever, and leukocytosis was statistically significantly higher in patients with bacteremia. We think that attention should be paid to the presence of bacteremia, especially in this patient group. Leukocytosis is found in 70% of both younger and older patients with APN⁽¹⁵⁾. In this study this percentage was 66%. Again, CRP levels are known to be elevated in patients with APN^(10, 13). In this study, 87% of the cases had CRP elevation. We believe that both parameters are useful to support the diagnosis of APN.

The most frequent causative agent of APN in the elderly is *Escherichia coli*^(4, 11, 23-26). The causative agent may also be other gram-negative bacteria such as *Klebsiella*, *Proteus*, *Enterobacter*, *Citrobacter*, *Pseudomonas aeruginosa*, and *Acinetobacter* or gram-positive bacteria such as *Staphylococci* and *Enterococci*. It is reported that the *Candida* species may also cause this condition, especially in diabetic patients⁽¹¹⁾. The causative agents in this study are similar to those in the other studies. The most common causative agent is *E. coli* with a rate of 66% and 23% of the cases had gram-negative and gram-positive bacteria and *Candida* species as the causative agents.

It was reported in the recent years that antibiotic resistance is increasing in bacteria that are causative agents for UTI. Resistance against trimethoprim-sulfamethoxazole (SXT) and quinolones is increasing, particularly in *E. coli* strains, which are causative agents for UTI⁽²⁶⁻²⁸⁾. This also limits the empirical use of these antibiotics in UTIs. In this study, the rate of resistance

against SXT and ciprofloxacin in *E. coli* was 51% and 56%, respectively. The level of sensitivity is high to carbapenems and relatively high to piperacillin-tazobactam and cefoperazone-sulbactam and it is notable that high rates of resistance exist against other antibiotics. Local sensitivity patterns should be considered in the empirical treatment of UTIs. These results show that SXT, third generation cephalosporins, or quinolones are not appropriate options for the empirical treatment of APN in our region. In geriatric patients treated for APN, a carbapenem antibiotic such as ertapenem, meropenem, or imipenem or piperacillin-tazobactam and cefoperazone-sulbactam appear to be appropriate choices for empirical treatment. The spectrum may be narrowed by de-escalation based on the culture results.

ESBL production is one of the most important resistance mechanisms in enteric gram-negative bacteria. ESBL production significantly limits the antibiotic options in serious infections⁽²⁹⁾. The rates of resistance of bacteria producing ESBL against other antibiotics such as aminoglycosides and quinolones are increasing and thus carbapenems appear to be the most appropriate option for the treatment of APN caused by these microorganisms. ESBL production was found in 52% of *E. coli* strains in this study. This rate demonstrates that ESBL production is high in the geriatric population. This could be caused by the frequent hospitalizations and more frequent antibiotic use in this patient population.

Mortality rates of up to 5% are reported in APN cases in the elderly⁽⁵⁾. Also in this study, mortality occurred due to bacteremia and urosepsis caused by APN. Other patients were discharged with full recovery in terms of APN.

In conclusion, APN is an infectious disease that is common in the elderly population and can result in death⁽³⁾. It should be remembered that the typical symptoms and signs of infection may not be present in elderly patients with APN and that these patients may present with atypical findings such as mental confusion and functional debilitation. Pyuria, leucocytosis, and elevated CRP levels may be used to support the diagnosis of these infections. Urine culture should always be collected for both diagnosis and treatment management and regional sensitivity patterns should be considered in the selection of empirical treatment. The increase in the antibiotic resistance in *E. coli* strains limits the treatment options and once more reminds us, the

clinicians, of the importance of rational antibiotic use.

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