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Original Article

Internal Medicine Section

Clinical Profile and Predictors of Outcomes in Older Inpatients with Pyelonephritis in a Tertiary Care Hospital in Southern India

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ABSTRACT

Background: Pyelonephritis is a serious infection associated with significant morbidity and mortality in the elderly with an estimated annual incidence rate of around 10% from previous studies. Older people are at a higher risk for pyelonephritis due to multiple factors including structural, functional and co-existent conditions. There is very little data on the incidence, clinical features and outcomes among elderly patients with pyelonephritis in India.

Materials and Methods: We performed a retrospective review of case records of 100 consecutive patients over the age of 60 years with pyelonephritis admitted to a tertiary care hospital. **Results:** One fourth of our patients (26%) did not have fever, 49% had delirium and 52% had systemic inflammatory response syndrome (SIRS). Sixty five percent of the patients were diabetic and 60% had infections caused by extended spectrum beta lactamase (ESBL) producing organisms. As in other studies, the commonest organism isolated was *E.coli* (49%). A low serum albumin level was a predictor of mortality ($p<0.001$) and increased length of hospital stay ($p<0.005$). Delirium was also associated with a poor outcome ($p=0.009$) in these patients. Patients with pyelonephritis secondary to ESBL producing organisms had a higher length of stay ($p<0.005$).

Conclusion: Hypoalbuminemia and delirium predicted poor outcomes in our patients. We found a high prevalence of ESBL infections in this study. Further research is required to assess the efficacy of aggressive management of delirium and low albumin in improving health and cost outcomes.

Keywords: Albumin, Delirium, ESBL, Geriatric, India, Mortality, Pyelonephritis

INTRODUCTION

Acute pyelonephritis, an infection of the kidney manifests classically in younger adults with lower urinary tract symptoms associated with fever, chills, flank pain, costovertebral angle tenderness and nausea/vomiting. It is a frequent cause of hospitalization and a major cause of increased morbidity and mortality in older frail patients [1-3]. It is important to note that many older patients with pyelonephritis do not present with classical features such as high fever, dysuria, abdominal or flank pain and hence a wrong diagnosis may be made [4]. The annual incidence of pyelonephritis is estimated to be around 7 per 100 patient years in women aged between 55-75 years and 2.8 to 7.8/1000 men aged more than 75 years [5]. Older people are at greater risk for developing pyelonephritis due to poor immunity, higher colonization rates with Gram negative organisms, multiple co-morbidities, structural changes such as benign prostatic hypertrophy in males, atrophic vaginitis in females and increased post void residual urine in older people [6]. Although acute pyelonephritis is the most common cause of bacteremia/sepsis in older people, it has been poorly researched in older people, especially in developing countries [7].

A holistic approach to treatment with emphasis on control of the underlying abnormalities in the urinary tract is important in the management of pyelonephritis in older patients [8]. We performed this study with an aim to describe the clinical characteristics, laboratory profile and analysis of possible risk factors associated with poor outcomes (i.e. deaths and discharge against medical advice) and higher length of stay (LOS) among older patients with pyelonephritis in India.

MATERIALS AND METHODS

We undertook a retrospective chart audit of 100 consecutive patients with acute pyelonephritis aged 60 years and older admitted to the Geriatric Medicine inpatient unit of Christian Medical College and Hospital, Vellore, Tamilnadu, India. Patients with one or more of the following features were considered to have pyelonephritis - high grade fever (temperature >101°F), lower urinary tract symptoms (dysuria, hesitancy, frequency, urgency), vomiting and renal angle tenderness, delirium or SIRS. After admission, supportive radiological features such as abnormal echogenicity of the renal parenchyma, gas bubbles, particulate matter in the collecting system, renal abscesses, perinephric collections and positive blood or urine cultures in these patients helped to confirm the diagnosis. Patients who had clinical and laboratory features suggestive of other focal infections and patients with cystitis, underlying immunodeficiency states and pyelonephritis secondary to recent urological procedures were excluded from the analysis. All cases were reviewed by at least two consultant geriatricians at different times. The study protocol was approved by the institutional ethics review board.

The details described above were extracted from the electronic discharge records and inpatient case notes. Information on history of past urinary tract infections, past catheterization, diabetes mellitus, need for haemodialysis and length of stay (LOS) were also collected. The diagnosis of SIRS was made using standard criteria [9]. Microbiological evidence included growth of significant colonies of usually implicated organisms or other organisms in the appropriate clinical setting. Most of the patients underwent radiological imaging to look for features and complications of pyelonephritis. Delirium was diagnosed based on collateral history of a recent change in cognition along with a low mini mental status examination (MMSE) score [10]. Laboratory investigations collected included haemoglobin (g%), albumin (g%), creatinine (mg%) and details of organism grown either in urine or blood culture along with the antibiogram.

Patients who died and those discharged against medical advice (DAMA) were grouped as patients with poor outcome. These DAMA patients were generally critically ill. Length of stay was calculated from the time of admission to the ward (time spent in accident and

emergency department was not included) till the time they were discharged.

Descriptive statistics including means and standard deviations were used to summarize the baseline characteristics of these patients. For analysis of factors affecting outcome, we used Fishers-Exact Test to test for an association between poor outcome and the following binary variables: Past urinary tract infections, past catheterization, SIRS, delirium, diabetes mellitus, patients requiring dialysis and ESBL producers. Independent samples t-tests were used to test for a mean difference in haemoglobin and albumin while the non-parametric Mann-Whitney test was used to test for a difference in creatinine between the patients with poor outcome and the other patients. Due to the small patient population, we could not undertake multivariate regression analysis to assess the relation between poor outcome and the aforementioned variables. To assess the relationship between length of stay and binary variables, non-parametric Mann-Whitney test was used while the Pearson's correlation coefficient was used to assess the relationship between length of stay and laboratory variables. Finally, a multiple linear regression model was used to assess the impact of delirium, haemoglobin, albumin, creatinine, ESBL producers and SIRS on length of stay based on earlier studies [7,8] showing a poor outcome and increased length of stay in delirious patients, those with low haemoglobin, albumin levels and elevated creatinine in older patients. We felt that patients with: a) infections due to ESBL producing organisms; b) patients manifesting SIRS would be more ill requiring prolonged courses of antibiotics and therefore we chose these additional variables in our analyses.

RESULTS

The baseline characteristics of these patients are presented in [Table/Fig-1]. The mean age of patients was 71.5 ± 16.3 years and there were 53 men. Seventy four patients presented with high grade fever while 79 had LUTS.

Characteristics	Total Patients (100)	Poor outcome (18) n (%)	Other Patients (82) n (%)
Mean age (yrs)	71.5 ± 16.3	74.2 ±17.6	70.9 ± 15.9
Number of males	53	12 (67%)	41 (50%)
Fever	74	11 (61%)	63 (77%)
Past catheterisation	27	2(11.1%)	25(30.5%)
Past urinary tract infections	27	5 (27.8%)	22 (26.8%)
Diabetes Mellitus	65	10(55.6%)	55(67.1%)
LUTS	79	7(39%)	72 (88%)
Delirium	49	14(78%)	35(43%) #
SIRS	52	12(67%)	40(49%)
Total positive cultures	65	11 (61%)	54 (66%)
Bacteremia	15	6 (33%)	9 (11%)
ESBL infections	39	5(27.8%)	34(41.5%)
Emphysematous pyelonephritis	11	4 (22%)	7 (9%)
Need for dialysis	8	1(5.6%)	7(9%)
		Mean ± SD (95% CI)	Mean ± SD (95% CI)
Haemoglobin		11.4 ± 2.6 (10.1, 12.7)	11.2 ± 2.5 (10.6, 11.7)
Albumin		2.25 ± 0.56 (1.97, 2.53)	3.27 ± 0.67 * (3.12, 3.41)
		Median (95% CI)	Median (95% CI)
Creatinine		1.85 (1.00 to 2.30)	1.40 (1.20 to 1.70)
Length of stay		4 (3 to 6)	8 (7 to 9) *

[Table/Fig-1]: Patient characteristics, Clinical presentations and univariate analysis
*p-value = 0.009 for difference in outcome
#p-value <0.001 for difference in outcome
LUTS- lower urinary tract symptoms
SIRS- systemic inflammatory response syndrome
ESBL- extended spectrum beta lactamase

	N (Median)	25th – 75th percentile	p-value
Past urinary tract infections	27 (7)	4-17	0.827
Past catheterization	27 (7)	5-17	0.364
SIRS	52 (6.5)	5-10	0.088
Delirium	49 (7)	5-11	0.577
Diabetes mellitus	65 (7)	5-10	0.679
ESBL infections	39 (9)	7-14	<0.001 *
Dialysed patients	8 (6.5)	5-11	0.721
Pearson correlation coefficient r (95% CI)			
Haemoglobin	0.076 (-0.122 to 0.268)		0.452
Albumin	0.247 (0.053 to 0.423)		0.013 *
Creatinine	-0.157 (-0.343 to 0.041)		0.119

[Table/Fig-2]: Relationship between length of stay and variables
*p-value <0.005 on multiple linear regression analysis

Sixty five patients had positive microbiological (urine ± blood) cultures. The most common organism isolated was Escherichia coli (49%) followed by *Klebsiella* and *Proteus* species. There was a high prevalence of ESBL production with as many as 39 (60%) organisms being ESBL producers. There were 18 patients with poor outcomes (11 deaths and 7 DAMA). Delirium (p =0.009) and a low albumin (p <0.001) were significantly associated with a poor outcome [Table/Fig-1]. We also found that length of stay was significantly shorter in patients with a poor outcome (p<0.001). Among patients with a poor outcome, patients who died had a mean LOS of 4.1 days while patients who were DAMA had a mean LOS of 3.8 days. Patients with ESBL infections (p< 0.001) and a low albumin (p<0.013) were associated with increased length of stay in our patients [Table/Fig-2] and on multivariate linear regression analysis, we found that after adjusting for other variables, patients with ESBL infections (p<0.001, beta coefficient, 0.35) and those with low albumin (p=0.004, beta coefficient, 0.28) had a higher length of stay.

DISCUSSION

As observed in previous studies, atypical presentation was common among our patients with a substantial number of patients (26%) failing to manifest fever [4,11,12]. Almost half of the patients had features suggestive of delirium and SIRS and the former had a significant impact on the discharge outcome. In a prospective study done by Falcone et al., patients with SIRS due to blood stream infections caused by ESBL organisms had higher mortality and morbidity. In our study, a higher proportion of patients (67%) with poor outcomes had SIRS when compared to patients with good outcomes (49%). However, we found no difference in length of stay between the two groups of patients [13].

Delirium and a low albumin were associated with a poor outcome while low albumin also increased the length of stay. Low albumin has been associated with higher mortality, longer hospital stays and higher readmission rates in adults [14]. People with poor outcomes had a significantly shorter length of stay (median length of stay 4 days vs 8 days, p<0.001). This could be due to poor health seeking behaviour among older patients in our community whereby patients present late in the course of the illness making them more likely to succumb to their illness earlier.

Serum albumin may represent a person's nutritional status and is associated with morbidity and mortality in older patients [15,16]. However, care should be exercised while using a low albumin level as an indicator of poor nutritional status as it may be a mere marker of severe illness. Weight is considered as an important marker of nutrition but we did not assess weight in these patients. Previous studies showed that older patients with delirium had an increased

length of stay as well as significantly higher initial and long-term mortality [17]. In this study, delirium was noted in 14 out of 18 patients with a poor outcome (77%) and it had a significant impact on the discharge outcome (p=0.009). Further research is required to assess whether aggressive management of delirium is effective in improving patient outcomes.

The high prevalence of infections with ESBL producing organisms (60%) among our patients is most likely due to indiscriminate antibiotic use and unregulated availability over the counter in India. Inadequate courses of antibiotics elsewhere may have facilitated resistance necessitating the use of higher antibiotics for longer duration leading to longer LOS noted in our study. In a study done by Ny et al., they found that patients with *Klebsiella* ESBL infections had higher APACHE scores, higher likelihood of being admitted to an intensive care unit, longer inpatient stays and higher readmission rates when compared to patients with non ESBL *Klebsiella* infections [18]. It is pertinent to note that previous studies have shown that asymptomatic bacteriuria is common in older people [19] and it is possible that they are prescribed antibiotics for a presumed urinary tract infection by physicians. Injudicious use of antibiotics also puts patients at risk of opportunistic diseases such as *Clostridium difficile* infections.

LIMITATION

An important limitation of our study was that it was a retrospective review based on inpatient case notes and electronic case records. Therefore, the results reported here are dependent on the quality of record entries. Delirium for example was diagnosed based on clinical assessment and MMSE. It is well known that MMSE has poor specificity for delirium. Under-reporting of conditions is therefore highly likely. This was a cross sectional study and hence cause and effect cannot be confirmed.

CONCLUSION

Pyelonephritis in older patients can have varied presentations. Hypoalbuminemia and delirium predict poor outcomes while hypoalbuminemia and ESBL infections predict longer hospital stays. Our study has demonstrated a high prevalence of ESBL infections in this region and clinicians should be educated on the risk of highly resistant organisms causing urinary tract infections and appropriate antibiotic usage to curb emergence of these organisms.

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