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A STUDY ON RISK FACTORS, MICROBIOLOGICAL SPECTRUM AND OUTCOMES OF PATIENTS WITH ACUTE PYELONEPHRITIS: A TERTIARY CARE CENTRE EXPERIENCE IN SOUTH INDIA.

Nephrology

Bhavani K V* Senior Resident, Department of Nephrology, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India *Corresponding Author

Nagarajan P Head of the Department, Department of Nephrology, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India.

Archana Chiniwalar Assistant Professor, Department of Nephrology, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India.

Noor Mohammed Associate Professor, Department of Nephrology, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India.

Seenivasan M Associate Professor, Department of Nephrology, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India.

Aravinth Kumar R Assistant Professor, Department of Nephrology, Government Mohan Kumaramangalam Medical College Hospital, Salem,Tamil Nadu, India.

Manokaran S Assistant Professor, Department of Nephrology, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tami Nadu, India.

ABSTRACT

Background Acute pyelonephritis is a severe urinary tract infection syndrome.With increasing antibiotic resistance, fatal outcomes are noticed in complicated pyelonephritis. Hence, we conducted a study to know the risk factors,microbiological spectrum,local antibiogram and outcome of patients admitted with acute pyelonephriris **Materials and Methods** A prospective observational single center study in a government tertiary care hospital in South India.Adult patients admitted in our hospital with a diagnosis of Acute pyelonephritis from July 2022 to june 2023 were included in the study **Results** Total of 82 patients were included in the study.44 patients were females and 38 were males. 61% had diabetes mellitus. E.coli was the most common organism cultured followed by Klebsiella. Majority of organisms were resistant to aminopencillins, quinolones, cotrimoxazole and sensitive to carbapenams, aminoglycosides, cefaperazone-sulbactam, piperacillin-tazobactam.85.4% patients recovered and mortality was seen in 14.6% .Older age was associated with poor outcome and was statistically significant. Thrombocytopenia,septic shock and Multi organ dysfunction were associated with poor outcome.19.5% required renal replacement therapy.Patient requiring renal replacement therapy had poor outcome.Patients with uncontrolled hyperglycemia had poor outcome. **Conclusion** Local antibiogram pattern is essential to prevent further resistances in organisms.When patients presents with Older Age,Uncontrolled hyperglycemia,multi organ dysfunction,severe renal dysfunction,thrombocytopenia ,septic shock these local antibiogram will be useful in reducing mortality.

KEYWORDS

Acute pyelonephritis,E.coli, Extended spectrum beta lactamase,Diabetes Mellitus,UTI.

INTRODUCTION

Acute pyelonephritis (APN) is an infection of renal pelvis and parenchyma.It is considered uncomplicated if the infection is caused by a typical pathogen in an immunocompetent person who has normal urinary tract anatomy and renal function (1). Acute pyelonephritis is a severe urinary tract infection syndrome; other UTI syndromes are febrile UTI, acute prostatitis, and urinary-source bacteremia (2). These conditions can precipitate a dysregulated host response that results in sepsis or septic shock(3).Acute pyelonephritis classically present with fever, chills,costovetebral pain or tenderness and lower urinary symptoms in the form of dysuria, frequency, urgency. Host risk factors for pyelonephritis are very similar to those of lower urinary tract infection (UTI), namely recent UTI, female sex, recent sexual intercourse, the use of a diaphragm and spermicides, oestrogen deficiency, increasing age, pregnancy, renal transplantation, impaired voiding, diabetes (95% of those patients with emphysematous pyelonephritis), obesity, stones, congenital urological abnormalities, neuropathy affecting the bladder, and recent catheterization or urological intervention (4).The estimated annual incidence of pyelonephritis is 459,000 to 1,138,000 cases in the United States and 10.5 million to 25.9 million cases globally(5,6). Indian studies addressing incidence and prevalence of Acute Pyelonephritis are lacking to the best of our knowledge.

A wide range of causative organisms can cause APN,mostly Gram-negative bacilli, Escherichia coli (E.coli) being the most prevalent type accounting for 75%–90% of infections (7).These infections are treated with a variety of antibiotics, including fluoro-quinolones, β-lactams, β-lactam plus β-lactamase inhibitor, and carbapenems.(8).However, in recent times, these pathogens have increasingly become resistant to most of these antibiotics due to emergence of organisms producing extended-spectrum β-lactamase(ESBL),which is an enzyme produced by Gram-negative bacilli responsible for the increasing resistances worldwide(9-11).

AIMS AND OBJECTIVES

1. To study on risk factors and microbiological spectrum.
2. To study the outcomes in acute pyelonephritis.
3. To study antibiogram and prepare a local antibiotics protocol.

MATERIALS AND METHODS

A Prospective observational single centre study in Government Mohan Kumaramangalam Medical College Hospital Salem,Tamil Nadu India;a tertiary care hospital in South India. Patients demographic details, clinical details at the time of admission,laboratory and radiological data were collected.Details of treatment given and in-hospital outcome were recorded.

Inclusion Criteria

Patients admitted with Acute pyelonephritis in our hospital with age>18 years.

Exclusion Criteria

- Patients <18 years of age.
- Kidney transplant recipients
- Pregnant patients

DEFINITIONS

Diagnostic criteria for acute pyelonephritis (APN) was defined as by Infectious Disease Society of America/CDC criteria[1,12] (i.e., at least one of the symptoms of fever >38°C, urgency, frequency, dysuria, or suprapubic tenderness, costovertebral tenderness).

Along with one of the following: 1. A positive dipstick for leukocyte esterase or nitrate or >10 white blood cells on a high-power

microscopy field and quantitative urine culture with bacterial growth of >10 ^{5}CFU/mL or 10 ^{3}–10^{4} CFU/mL in symptomatic patient 2. Organisms cultured from blood/urine 3. Imaging test evidence of infection [e.g., ultrasound, CT scan, magnetic resonance imaging (MRI), or radiolabel scan (gallium, technetium)].

Complicated Pyelonephritis was defined as Pyelonephritis occurring in male patient, patients with functional or anatomical abnormalities of the urinary tract, immunosuppressed patients, patients with a single kidney, permanent bladder catheter, nephrostomy, or double-J catheter, or those patients who had experienced urinary tract manipulation in the previous 2 weeks.
Multiple organ dysfunction syndrome (MODS): dysfunction of more than one organ, requiring intervention to maintain homeostasis.

Septic shock was defined as sepsis with a systolic blood pressure <90 mmHg or 40 mmHg less than the patient's baseline blood pressure for at least 1 h, despite adequate fluid resuscitation

Emphysematous pyelonephritis (EPN) was defined as based on the presence of gas in the renal parenchyma, collecting system, or perinephric tissue

Renal abscess: clinical manifestations of renal and perinephric abscess were similar to those of APN. Imaging studies were done to localize abscess.

Renal dysfunction: patients with Serum Creatinine >1.2 mg/dl

Statistical Method
The collected data were analysed with IBM SPSS Statistics for Windows, Version 29.0. (Armonk, NY: IBM Corp).To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the Independent sample t-test was used. To find the significance in qualitative categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In all the above statistical tools the probability value .05 is considered as significant level.

RESULTS
Total of 82 patients were included in the study.53% were females and 47% were males.Mean age of the study population was 53.8 (SD 12.2).Majority of people were from age group 51-60 years.

Out of the 82 patients ,82.9 %(n=68)patients presented with fever,89%(n=73) had flank pain, 54.9%(n=45)had dysuria,17.1% had increased frequency and urgency of micturation,40.2% presented with classical triad of pyelonephritis,43.9% had nausea,vomiting,14.6% had previous history of urinary tract infection.

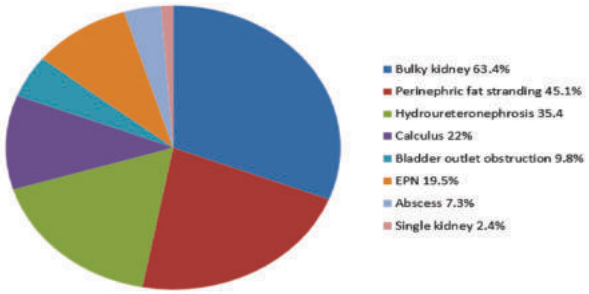
Majority of patients had diabetes mellitus as risk factor.Out of the 82 patients with pyelonephritis 61% had diabetes mellitus, calculus was present in 22%, previous history of urological intervention like DJ stent was present in 9.8%,benign prostatic hypertrophy was present in 6.1%, bladder pathology was present in 3.7%,single functioning kidney was present in 2.4%,neurogenic bladder 2.4%. immunocompromised state was present in 1.2%,stricture urethra was present in 1.2%, Of the 82 patients 9.8% had underlying chronic kidney disease.

Patients who were seriously ill were 15.9% who presented as multi organ dysfunction,13.4% required ionotropic support, 4.9% required ventilatory support.

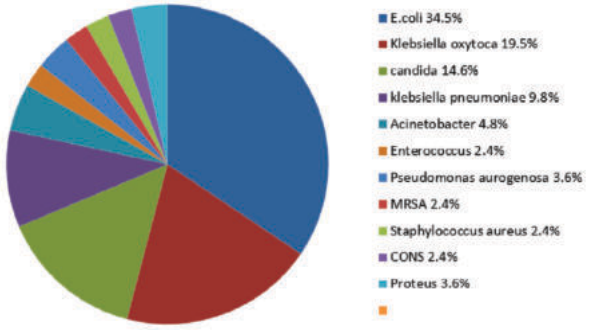
Leucocytosis was present in 79.3%, 54.9% had hemoglobin below 10g/dl, thrombocytopenia was present in 78%,57.3% had RBS above 200mg/dl. Urine analysis of patients with acute pyelonephritis showed pyuria in 93.9% and hematuria in 42.6%.

Out of 82 patients 84.1% had s.creatinine more than 1.2 mg/dl,mean s.creatinine was 2.9mg/dl.

Radiological feature
Emphysemayous Pyelonephritis(EPN)was present in 19.4%,length of hospital stay was more in Emphysematous pyelonephritis patients compared to non EPN patients.Mortality in EPN patients were 25% were as non EPN it was 12.1%.93.8% of patients who presented with EPN presented had renal dysfunction and 18.8% required renal replacement therapy.



Out of the 82 patients 50.1% of the patients had organisms cultured in urine,18.2% had blood culture positivity. The most common organism isolated in urine culture was E.coli 34.5% followed by Klebsiella oxytoca in 19.5%, Klebsiella pneumoniae 9.8%,candida in 14.6%,Pseudomonas aurogenosa in 3.6%, Acinetobacter 4.8%,Proteus in 3.6%,staphylococcus aureus 2.4%,methicillin resistant staphylococcus 2.4%,coagulase negative staphylococcus 2.4%, Enterococcus in 2.4%.



Organism cultured
E.coli was sensitive to aminopencillin in 21.4% of E.coli positive cultures; similarly quinolones were also sensitive in 21.4%, cephalosporins in 28.5%, cotrimoxazole in 21.4%,nitrofurantoin in 64.2%,aminoglycosides in 92.8%, piperacillin tazobactam and cefaperazone sulbactam in 78.5% of E.coli cultures.

Antibiogram of E.coli cultured in our hospital

Antibiotic	Sensitivity Percentage
Aminopencillin	21.4%
Quinolones	21.4%
Cephalosporin	28.5%
Co-Trimoxazole	21.4%
Nitrofurantoin	64.2%
Aminoglycosides	92.8%
Piperacillin-Tazobactam	78.5%
Cefaperazone-Sulbactam	78.5%
Carbapenams	85.7%

Klebsiella was not sensitive to aminopencillin and was sensitive to quinolones, cephalosporins , nitrofurantoin and cotrimoxazole in only in 16.6% in urine culture positive for Klebsiella.

Kelbsiella species were sensitive to aminoglycosides and cefaperazone – sulbactam in 83.3% cases of Klebsiella and piperacillin tazobactam 75% of cases.

ESBLs as defined were resistant to cephalosporin and quinolones but showed good sensitivity to carbapenems,Cefaperazone-sulbactam, Piperacillin- Tazobactam.Extended spectrum beta lactamase organisms were present in 24.4%;out of which 55% were females and 45% were males.25% of patients with ESBL organism required renal replacement therapy compared to 17.7% of patients infected with Non-ESBL organism. Length of hospital stay was more in ESBL infected patients than non ESBL infected patients (p=0.026).

Surgical Management
In our study 37.8% required surgical intervention for obstruction, emphysematous pyelonephritis or abscess.DJ stenting was required in 25.7%,4.9% required Percutaneous Drainage, 3.7% required

Percutaneous Nephrostomy.

Outcome

Parameter		Outcome		p-value
		Recovered	Mortality	
Age	Mean age	52.1years	63.75years	0.002
Sex	Male	45.7%	50%	0.783
	Female	54.3%	50%	
Wbc count	<11000	18.6%	33.3%	0.260
	>11000	81.4%	66.7%	
Platlet count	>100000	85.7%	33.3%	0.0005
	<100000	14.3%	66.7%	
Hemoglobin	>10g/dl	44.3%	50%	0.713
	<10g/dl	55.7%	50%	
CKD	yes	8.6%	83.3%	0.332
	no	91.4%	16.7%	
S.creatinine	<1.2mg/dl	18.6%	0	0.198
	>1.2mg/dl	81.4%	100%	
Renal dysfunction requiring dialysis	yes	12.9%	58.3%	0.0005
	no	87.1%	41.7%	
RBS	<200mg/dl	48.6%	8.3%	0.01
	>200mg/dl	51.4%	91.7%	
Shock requiring Ionotropic support	yes	2.9%	75.0%	0.0005
	no	97.1%	25%	
MODS	yes	5.7%	75%	0.0005
	no	94.3%	25%	
ESBL	yes	25.7%	16.7%	0.721
	no	74.3%	83.3%	

In hospital outcome, 85.4% patients recovered and poor outcome in the form of mortality was present in 14.6%. In patients with poor outcome mean age was 63years, as compared to good outcome where mean age was 52years. Older age was associated with poor outcome at statistically significant level.Thrombocytopenia and septic shock were associated with poor outcome with high statistical significance(p<0.0005) .Multi organ dysfunction was also associated with poor outcome(p-0.0005) and out of the 13 patients who had multi organ dysfunction, 7 patients required renal replacement therapy for worsening renal failure.Out of the 82 patients, 19.5% required some form of renal replacement therapy.Patient who had severe renal dysfunction requiring renal replacement therapy and had poor outcome (p-0.0005); also patient majority of patients with underlying ckd required renal replacement therapy.Similarly hyperglycemia was associated with poor outcome at statistical significance of p-0.01.

DISCUSSION

Acute Pyelonephritis is a serious infection and if it is not diagnosed, early or treated adequately can be fatal (13.) There has been a steady increase in the frequency of this disease in recent times. Mean age of patients with pyelonephritis in our study was 53.8 (SD 12.2) and majority were from sixth decade as in other studies.Majority of patients were females unlike in other indian studies(14,15);but which is similar to western studies where females outnumbered males(16). Classical triad of fever with rigors, flank pain and dysuria was seen in 33% patients in our study which was almost similar 35% to a study by Dhamotharan et al (17).

Among hospitalized patients with acute pyelonephritis, Diabetes Mellitus has been shown to be the most common predisposing risk factor(18) Age, longer duration of diabetes, and poor glycemic control were significantly associated with UTI among subjects with diabetes(19).Most common risk factor for APN in the current study was diabetes as in other Indian studies(14,15) It was present in 61% of all patients.To diagnose EPN in diabetics presenting with features of pyelonephritis early imaging studies are required, especially if blood sugars are poorly controlled. Even in Non-EPN is diabetics may be associated with renal failure and a high mortality rate(20). In our study, out of 50 diabetics, 92% had renal dysfunction,26% had emphysematous pyelonephritis, and 24% were ESBL producers.In this study 11 out of 12 patients who expired had hyperglycemia.

It is better to perform CT scan than ultrasound in suspected cases of acute pyelonephritis(16). The reported sensitivity of plain X-ray of kidney, ureter, and bladder, ultra-sound,and CT scan for picking up EPN is 65%, 69%,and 100%, respectively(21). The most specific test for diagnosis of APN is an isolation of organism via cultures which also provides antibiotic sensitivity pattern of antibiotics.(22).

However, in our study, 50.1% of the patients had organisms cultured in urine which is similar to other Indian studies. A large number of culture negativity was attributed to prior antibiotic usage either at outside hospitals before referral or to the late collection of samples.Most common organism in this study as in other studies was Escherichia coli[14,15,20] but unlike in other studies second most common organism was Klebsiella oxytoca and not Klebsiella pneumonia .

ESBLs are plasmid-encoded b-lactamases that confer significant resistance to a wide range of b-lactam antibiotics, including all extended-spectrum cephalosporins, except carbapenem and cephamycin;also, ESBL-encoding plasmids frequently carry resistance genes for additional antibiotic classes, such as quinolones, aminoglycosides and trimethoprim sulfamethoxazole[23]. In our study, E. coli and Klebsiella showed high-grade resistance to all commonly used antibiotics such as co-trimoxazole, quinolones, nitrofurantoin,aminopencillin and cephalosporin and were mostly sensitive to aminoglycosides,Cefoperazone-Sulbactam, Piperacillin-Tazobactam and carbapenem . ESBL producers have good sensitivity to carbapenems, cefoperazone-sulbactam,piperacillin-tazobactam and aminoglycosides. This is consistent with other studies.The increasing antibiotic resistance makes it difficult to choose empirical therapy.Clinicians should be keen on sending culture samples before starting antibiotics.In 60% of ESBL organism infected patients diabetes was present ,but in our study we couldn't establish statistically significant association.Length of hospital stay was more in case of ESBL infected patients as compared to non ESBL infected at statistically significant level.

Older Age, Uncontrolled hyperglycemia,multi organ dysfunction, severe renal dysfunction requiring renal replacement therapy, thrombocytopenia, septic shock, was associated with poor outcome.

Limitations

Though this study has significance in our population in choosing antibiotics according to local antibiogram as this study reveals the prevalence of antibiotic resistance and importance in predicting emperical therapy in South Indian population and also in identifying at risk individuals for poor outcome in the form of mortality it has certain limitations.It is a single center study and sample size is small.In addition, it was a prospective study with only In hospital outcome.

CONCLUSION

Local antibiogram pattern is essential to prevent further resistances in organisms.When patients presents with Older Age,Uncontrolled hyperglycemia,multi organ dysfunction,severe renal dysfunction requiring renal replacement therapy,thrombocytopenia ,septic shock these local antibiogram will be useful in reducing mortality till culture reports are available.

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