

## Management of patients with clinically suspected pyelonephritis in a resource poor setting

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### Abstract

**Background:** This study aimed to determine the aetiology, antimicrobial susceptibility pattern and the clinical response to antibiotics in pyelonephritis.

**Methods:** Bacterial culture and ABST, clinical response and onset of renal failure were analyzed in 240 clinically suspected pyelonephritis patients admitted to Medical Units at Base Hospital, Tangalle.

**Results:** Of the 240 patients 61% had culture positive UTI mainly due to *E. Coli* (94%). Pathogens were 100% sensitive to meropenem, imipenem and amikacin while it showed 96%, 93%, 85%, 81%, 60%, 36%, 13% sensitivity for nitrofurantoin netilmicin, gentamicin, co amoxiclav, ceftriaxone, ciprofloxacin and ampicillin. The average duration of fever in days after administration of IV antibiotic was gentamicin 1.66, co amoxiclav 1.98, ceftriaxone 2.14, and ciprofloxacin 2.34.

**Conclusion:** Gentamicin was the most clinically effective antibiotic from the antibiotics used for the treatment of pyelonephritis in the selected patient population.

**Key words:** pyelonephritis, gentamicin, uropathogens, Sri Lanka

### Introduction

Pyelonephritis affects all age groups and is associated with serious complications, if not properly treated.<sup>1</sup> Due to significant local differences in urinary pathogens, the emergence of new pathogens, and variation of antibiotic susceptibility pattern in different

geographic locations, periodic evaluation of epidemiology of pathogens is recommended, in order to revise treatment regimes.<sup>2,3</sup> Initial diagnosis of pyelonephritis is mainly clinical and it takes three days for laboratory culture and antibiotic sensitivity test results. The extensive use of antimicrobial agents have invariably resulted in development of antibiotic resistance, and increased cost to the patient as well as to the government. Hence evaluation of clinical response to treatment together with its adverse effects, and current management modalities (treatment of pyelonephritis etc.) is important. Studies to increase knowledge on aetiological agents, their resistant patterns to antibiotics are very important to guide clinicians in empirical treatment.<sup>4</sup> Therefore in this study the aetiology, antimicrobial susceptibility pattern and the clinical response of pyelonephritis was examined without interfering with routine treatment regimes in the hospital.

### Methods

This was a non randomized descriptive study and ethical approval was granted from the ethical review committee, Faculty of Medicine, University of Ruhuna. For two years, all patients (240) admitted with (clinically suspected) acute pyelonephritis to the Medical Units at Base Hospital, Tangalle were included.

Pyelonephritis was diagnosed clinically in the presence of dysuria, fever and loin tenderness. Loin tenderness was considered as the essential clinical sign to differentiate pyelonephritis from cystitis. Patients were initially treated with a single intravenous antibiotic empirically. Antibiotics used were gentamicin as single daily dose of 4 mg/kg, ciprofloxacin twice daily, co amoxiclav three times daily and ceftriaxone twice daily, cephalexin twice daily for three to five days. A mid stream urine sample was taken before treatment and sent for culture and antibiotic susceptibility testing (ABST). Clinical response was assessed in the terms of time taken for disappearance of fever. Information on patient was collected using a standard questionnaire.

Blood urea and creatinine was done on day one and day three for all the patients. If initial results suggested altered renal functions those tests were

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done daily and such patients treated with ceftriaxone. In those patients who showed a rise in serum creatinine level after treatment, the initial antibiotic was changed to ceftriaxone. All patients were discharged when fever settled with oral antibiotics for 7 to 10 days and was followed up in clinic.

Data was analyzed using SPSS. Chi Square test was used to describe the associated factors. All inferential statistics were tested at  $p < 0.05$

## Results

Of the 240 patients 72% were females and mean age was 50.42. Eighteen percent (18%) had diabetes and 45% had past history of urinary tract infection (UTI). Twenty two (22%) of them were already on antibiotics at the time of admission.

### Results of urine cultures and its ABST sensitivity

Sixty one per cent (146/240) of the patients had culture positive UTI. Main causative agent of pyelonephritis was *E. coli* (94%) followed by *Klebsiella* species 2%. Urine culture showed 100% sensitivity to meropenem, imipenem and amikacin while it showed 96%, 93%, 85%, 81%, 60%, 36%, 13% sensitivity for nitrofurantoin, netilmicin, gentamicin, co-amoxiclav, ceftriaxone, ciprofloxacin and ampicillin respectively.

### Clinical response

The patients who were treated with antibiotics before admission and those patients who had to change their antibiotic treatment or those who were treated with more than one antibiotic within first five days due to various reasons were excluded in the analysis of the clinical response. We analyzed only four commonly used antibiotics as none of the other antibiotics were used in more than 25 patients. Average duration of fever in days after administration of IV (intravenous) antibiotic and percentage of patients whose fever responded within first 24 hours are shown in table 1. Majority (77%) of patients who were treated with gentamicin improved with fever coming down after the administration of the first dose.

The incidence of serum creatinine rising more than 50% of baseline at 3<sup>rd</sup> day were low and as follows: gentamicin 7.14% (4/56), co amoxiclav 4% (2/50), ceftriaxone 3.3% (1/30), and ciprofloxacin 7.36% (2/26). Those patients who had elevated serum creatinine (>50%) were treated with ceftriaxone and with good hydration the renal function became normal. Out of the treated patients, 186 were followed at two weeks and one month at clinic level, and 67 repeat urine cultures were done. Out of them all urine culture reports were found to be sterile. None of those pyelonephritis patients in the study developed renal failure.

**Table 1. The average duration of fever in days after administration of single IV antibiotic**

Antibiotic	Frequ- ency	Average duration of fever in days	% of patients whose fever responded within 24 hrs
Gentamicin	56	1.66	77
Co amoxiclav	50	1.98	56
Ceftriaxone	30	2.14	49
Ciprofloxacin	26	2.34	23

## Discussion

In this study gentamicin was used as single daily dose of 4 mg/kg and found to be the most effective drug in treatment of pyelonephritis among the selected four antibiotics, when considering both in vitro antibiotic sensitivity pattern as well as clinical response of the patient. In the case of clinical response assessment using disappearance of fever as a parameter the best results was obtained from gentamicin (average duration of fever 1.66 days) followed by co-amoxiclav. Majority (77%) of gentamicin treated patients responded after a single daily dose of the drug and this may be due to higher antibiotic sensitivity and better tissue penetration ability of the drug.<sup>5</sup> It exhibits concentration-dependent bactericidal activity, meaning that a higher serum concentration for shorter period amplify its efficacy.<sup>5</sup> This is an important fact and should be further investigated to evaluate the efficacy of single daily dose of gentamicin followed by oral co-amoxiclav as an outpatient.

Co-amoxiclav was the second best antibiotic found in the study which showed both in-vitro and in-vivo response. As this drug is available as oral as well as IV it is another good option in treatment of pyelonephritis. It is safer than gentamicin and may be the best drug for outpatient treatment.

Ciprofloxacin which is a widely used antibiotic to treat UTI had showed very low sensitivity rate (35%) and only 13% of uropathogens were sensitive to ampicillin. However 6 isolates who gave in-vitro resistance had responded to the drug in vivo and fever disappeared within three days despite the in vitro resistance. This finding shows the validity of clinical assessment and also inadequacy of in-vitro tests. Overall ciprofloxacin had shown the slowest clinical response when compared to the other antibiotics. According to our results ciprofloxacin and ampicillin are not effective antibiotics for empirical use in pyelonephritis. In-vitro antibiotic sensitivity showed 100% sensitivity to expensive broad spectrum antibiotics meropenem, imipenem and netilmicin. In

the present study none of the patients were treated with these costly antibiotics. These drugs may be useful in treatment of critically ill patients when indicated.

Onset of renal impairment (more than 50% creatinine rise) was analyzed after commencing of each antibiotic by doing serial serum creatinine levels and was low and transient. Those who developed temporary rise in serum creatinine became ultimately normal after changing the antibiotic to ceftriaxone, good hydration and with the clinical improvement of the patient. This renal impairment also may probably be due to the process of infection rather than the effect of the antibiotic. None of the studied patients developed persistent renal impairment during the course of treatment.

Because of the well documented nephrotoxicity<sup>6,7</sup> and the unavailability of facilities to perform serum gentamicin levels in the study settings, it was given only to carefully selected patients. We avoided gentamicin when there was any suspicion of renal impairment, in patients with hypotension, in those with multiple co-morbidities and in elderly patients. Serum creatinine levels were monitored at day one, day three and at clinic level after discharging the patient. We maintained very good hydration during the treatment, more than 90% of patients received gentamicin for less than three days as they were discharged with oral antibiotics when fever settled. This may be the reason for low incidence of renal impairment with gentamicin and none of those patients developed persistent renal impairment.

On the other hand because of its broad spectrum bactericidal activity<sup>8</sup> gentamicin is still widely used for many infections all over the country and is one of the cheapest available antibiotics. Because of lack of facilities to check serum gentamicin levels and its well documented nephrotoxicity and auto toxicity<sup>8,9</sup> it is very important to select patients carefully, monitor renal functions and maintain good hydration throughout the treatment. However facilities for monitoring serum gentamicin levels in government hospitals are a dire need if gentamicin is to be used as empiric treatment as it is a cheap and effective drug.

## Conclusion

Gentamicin was found to be the most clinically effective and cost effective antibiotic to treat pyelone-

phritis in the study setting. We recommend providing monitoring facilities of gentamicin levels in government hospitals in Sri Lanka as a priority so that use of gentamicin would become safer.

## Competing Interests

The authors declare that they have no competing interests.

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