A retrospective study of antimicrobial resistance pattern of Pseudomonas aeruginosa isolates from urine samples over last three years (2013-2015)

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ABSTRACT

Background: Problem of antibiotic resistance is compounding day by day because of overuse and misuse of antibiotics. There is no systematic national surveillance of antibiotic resistance and insufficient data is available to quantify the problem in our country. This study aims at studying the changing pattern of antimicrobial resistance of Pseudomonas aeruginosa isolates from patients of urinary tract infections over last three years.

Methods: A retrospective, record based study carried out based on the records of C/S (Culture sensitivity) reports of indoor patients, during past three years (2013 - 2015). The types of organisms causing urinary tract infections were noted and the drugs still effective for the Pseudomonas aeruginosa were noted.

Results: Pseudomonas aeruginosa is inherently resistant to many antimicrobial agents. Analysis of the results year wise indicated that the lowest percentage of resistance manifested against imipenem was 14%, 24.48% and 20.99% for the years 2013-2015. Resistance for fluoroquinolones decreased over the three consecutive years from 84.67% (2013) to 78.27% (2015). Over the successive years, the resistance to ceftriaxone tends to increase from 80% (2013) to 92.59% (2015). C/S reports showed on an average 69% were resistant to aminoglycosides. Multi drug resistant pseudomonas percentage resistant to fluoroquinolones, third generation cephalosporines and aminoglycosides were 78% (2013), 78.33% and 80.33% (2015) over the consecutive years.

Conclusions: The antimicrobial resistance patterns are constantly evolving and vary from region to region it has become a necessity to do constant antimicrobial sensitivity surveillance. This will help clinicians to provide safe and effective empirical therapies.

Keywords: Antidiabetic agents, Prescriptions, Changing pattern

INTRODUCTION

Urinary tract infection (UTI) is a common nosocomial infection and an important source of morbidity in the community as well. Pseudomonas aeruginosa being a very resistant organism is resistant to high concentration of salts and dyes, weak antiseptics and commonly used antibiotics. Pseudomonas aeruginosa (P. aeruginosa) is also an opportunistic human pathogen. Many epidemiological outcome studies have concluded that infections caused by drug-resistant P. aeruginosa are associated with significant increases in morbidity, mortality, need for surgical intervention, increased length of hospital stay, chronicity and overall cost of treating the infection. P. aeruginosa presents a big therapeutic challenge for treatment of various infections and selection of the appropriate antibiotic as empirical therapy is essential to optimize the clinical outcome. The extensive and inappropriate use of antimicrobial agents has invariably resulted in the development of antibiotic resistance which, in recent years, has become a major problem worldwide. Resistance pattern of microorganisms vary from country to country, state to state, large hospital to small hospital and hospital to community. Hence, there is a need to conduct area-specific monitoring studies to profile different pathogens responsible for specific infections and their resistance...
patterns, so as to generate data that would help clinicians to choose the correct empirical treatment.

The estimation of local etiology and susceptibility profile could support the most effective empirical treatment.\textsuperscript{11} Multiple antibiotic resistance in bacterial populations is a pervasive and growing clinical problem, which is recognized as a threat to public health. In our country, the problem of antibiotic resistance is compounding because of overuse and misuse of antibiotics. There is no systematic national surveillance of antibiotic resistance and insufficient data is available to quantify the problem. The aim of this study was to evaluate the in vitro resistance pattern to commonly used antimicrobial agents. This study will further help in formulating most optimal empirical treatment regimen for UTI cases, while awaiting culture sensitivity reports with minimal therapeutic failure.

**METHODS**

A retrospective, record based study was carried out in department of pharmacology in collaboration with microbiology department of a teaching tertiary care hospital. The study was carried out based on the records of C/S (culture sensitivity) reports of indoor patients, during past three years from January to December of years 2013 to 2015 admitted in wards of Rajindra Hospital and Govt. Medical College Patiala, a tertiary care 1100 bedded hospital. Permission was taken from ethical committee and in-charge of microbiology laboratory prior to the study. All the C/S reports of urine samples, maintained in the record registers of microbiology laboratory received from various wards during the period 2013 to 2015 were included and analysed. Reports of Isolates from repeat culture of previously recruited patients and isolates identified as commensals or contaminant were excluded from the study. Number of reports/years for three years of urine samples which were already registered was noted. Only reports with positive *Pseudomonas aeruginosa* c/s report were considered for this study. Positive reports for *Pseudomonas aeruginosa* out of total no. of urine samples positive for the years 2013, 2014 and 2015 were 196 (947), 151 (1058) and 86 (1102) respectively. Sample size for the present study was 333 for the three years. The data was collected year wise starting from the year 2013. The provisional diagnosis was noted.

Antibiotic sensitivity pattern of *Pseudomonas aeruginosa* isolates was determined on Muller Hilton agar plates by Kirby-Bauer disc diffusion method. Isolates were declared as sensitive or resistant on the basis of zone of inhibition following the criteria of clinical laboratory standards institute (CLSI).\textsuperscript{12} The antibiotics tested were broad-spectrum penicillin, third generation cephalosporin, quinolones, aminoglycosides, and carbapenems and nitrofurantoin. Type of organisms most common in urine sample were noted and drugs still effective for the particular organism were noted. Whole of the data was collected and compiled in the year wise manner and compared year wise to see the trend in the resistance pattern. An isolate was considered as MDR if found resistant to three or more antimicrobials belonging to different classes/groups of antimicrobials.\textsuperscript{12} C/S reports for other common uropathogens will also be further analysed.

**Statistical analysis**

Descriptive statistics was used for analysis. Proportions were used to study the resistance pattern of *Pseudomonas aeruginosa* and variables were expressed as percentages. Licensed SPSS version 20 was used for statistical analysis. All the data was expressed as Tables and bar Figure.

**RESULTS**

Over a 3 year period of 2013-2015, a total of 2,464 positive urine isolates including 333 *Pseudomonas aeruginosa* were analysed. As an average of 14 % of the total isolates was *Pseudomonas aeruginosa* while E. coli was the most frequent isolate throughout the three years (average of 67.66% of the total isolates). Analysis of the results year wise indicated that the lowest percentage of resistance manifested against imipenem was 14%, 24.48% and 20.99% for the years 2013-2015 (Table 1).

**Table 1: Antibiotic resistance patterns of *P. aeruginosa* against different group of antibiotics.**

| Antimicrobial agents          | Resistant 2013 | Resistant 2014 | Resistant 2015 |
|-------------------------------|---------------|---------------|---------------|
| Piperacillin                  | 43.33         | 58.62         | 79.01         |
| Aminoglycosides               | 68.9          | 69.78         | 69.54         |
| Fluoroquinolones              | 84.67         | 79.31         | 78.27         |
| Ceftriaxone                   | 80            | 85.52         | 92.59         |
| Cefoperazone-sulbactam        | 53.33         | 65.52         | 51.85         |
| Imipenem                      | 14            | 24.48         | 20.99         |
| Nitrofurantoin                | 73.33         | 70.69         | 83.95         |
| Ceftazidime+tazobactum        | 83.33         | 77.59         | 100           |
| Polymyxin B                   | 100           | 70.69         | 29.63         |

Resistance for fluoroquinolones decreased over the three consecutive years from 84.67% (2013) to 78.27% (2015). Over the successive years, the resistance to ceftriaxone, tends to increase from 80% (2013) to 92.59% (2015). C/S reports showed on an average 69% were resistant to aminoglycosides (Figure 1).

**MDR (multi-drug resistant) *P. aeruginosa***

Those strains which are found to be resistant to three or more than three groups of antimicrobials were taken as multi drug resistant strains. MDR pseudomonas percentage resistant to fluoroquinolones, third generation cephalosporines and aminoglycosides were 78% (2013), 78.33% and 80.33% (2015) over the consecutive years.
Piperacillin and aminoglycosides are consistently showing high resistance percentage over the successive three years. Third generation cephalosporines like ceftiraxone is showing very obvious increasing trend of resistance over the three years ranging from 80% (2013) to 92% (2015). In a study done in Gujarat ceftiraxone resistance is found to be 75% which is quite similar to our study.\textsuperscript{18} This may be due to the increasing clinical use of third generation cephalosporins following the resistant strains to fluoroquinolones.

Lowest resistance is seen to imipenem in our study between 14% (2013) and 20% (2015). This is quite similar to the study done in Merrut, Uttar Pradesh.\textsuperscript{21} High level resistance to nitrofurantoin is seen in our study which is very similar to other studies.\textsuperscript{19,21}

In the present study another finding which raises an alarm is about MDR, urinary isolates of P. aeruginosa show 78% (2013), 78.33% and 80.33% (2015) resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides collectively. The rising trend of MDR is seen over the successive years.

In a study of antibiotic susceptibility done in Merrut, Uttar Pradesh fluoroquinolone resistance is 15%.\textsuperscript{21} These results are quite different from our study thereby stressing upon the regional differences and importance of surveillance of antimicrobial resistance and suggestion of empirical therapy accordingly.

In this retrospective study, there is no consideration of patient’s demographic data like age, gender etc., and clinical symptoms, complicated versus uncomplicated UTI, which are surely the limitations of this study. On the other hand the large sample size of UTI patients and comparison of three years data are strengths of the study.

CONCLUSION

Easy over the counter availability of antimicrobial agents and ability of P. aeruginosa to resist antimicrobial agents by their inherent or acquired antimicrobial mechanisms has led to high level of drug resistance. Our study showed that 80% P. aeruginosa of isolates from urine samples were MDR. Because of this a bacterium resistant to one antibiotic is often much more likely to be resistant to second choice of antibiotics, thereby increasing the chances of failure of therapy in UTI. The antimicrobial resistant patterns are constantly evolving and vary from region to region it is a necessity for constant antimicrobial sensitivity surveillance. This will help clinicians to provide safe and effective empirical therapies with minimal therapeutic failures.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee
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Cite this article as: Sharma N, Gupta AK, Walia G, Bakhshi R. A retrospective study of antimicrobial resistance pattern of Pseudomonas aeruginosa isolates from urine samples over last three years (2013-2015). Int J Basic Clin Pharmacol 2016;5:1551-4.