



## Therapeutic Challenge in Urinary Tract Infection - Drug Resistant Non Fermenter Gram Negative Bacilli

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### Abstract

**Background:** Non fermenting gram-negative bacilli are now emerging as one of the most important multidrug resistant uropathogens posing serious therapeutic challenges. This study was undertaken to know the burden in our setup.

**Materials and Methods:** This is a retrospective study carried out on the 1416 urine samples received in the microbiology laboratory from patients suffering from urinary tract infection. The samples were processed as per standard techniques and antibiotic susceptibility was performed and results were compiled.

**Results:** Out of the 1416 urine samples 282 showed significant growth. 33(11%) yielded the growth of non-fermenters. *Acinetobacter* spp 25(75%) and *Pseudomonas aeruginosa* was 8(25%). Highest susceptibility in *Acinetobacter* was seen to Nitrofurantoin (60%) least to ceftazidime(12%) while in *Pseudomonas aeruginosa* highest was to Imipenem (75%) and least to Nitrofurantoin(12%). Both non fermenters showed susceptibility to Aminoglycosides in the range of 43% *Pseudomonas* showed susceptibility of 62% to gentamicin. Quinolones susceptibility in both the species are 25%. Majority on non-fermenters were multi drug resistant (MDR).

**Conclusion:** This study revealed that the non-fermenters are emerging as important cause of urinary tract infections (UTI's). In this study, *Acinetobacter* spp was found to be the most common non-fermenter isolated. Non fermenters showed good susceptibility towards Carbapenems and Aminoglycosides. Since majority of non-fermenters were MDR, antibiotic susceptibility testing (AST) is necessary for adequate and effective management of urinary tract infections in hospitalised patients.

**Keywords:** Antibiotic susceptibility testing; Drug resistance; Non-fermenting gram-negative bacteria; Resistant; Sensitive

### Introduction

The term non-fermenters refer to the group of gram-negative (NFGNB), aerobic, non-spore-forming bacilli that do not either use carbohydrates as a source of their energy or degrade them through metabolic pathways other than that of fermentation [1]. Apart from being present as saprophytes in the surrounding environment, some of them are also

found as commensals in the human gastrointestinal tract [2].

Hospital environment provides a niche for them to survive and flourish [3]. In addition to being commonly found on the skin of healthcare workers and various instruments, they also account for 12%–16% of all bacterial isolates from the clinical

microbiology laboratory [4]. Widespread patient-to-patient transmission is known to occur either through contaminated surfaces or through the hands of the health care providers themselves, especially in patients who are immunocompromised [3].

It has been documented that in hospital and long-term care facilities non-fermenters are more often the etiologic agents of urinary tract infection (UTI) in inpatients [6]. Risk factors for the infections caused by the non-fermenting gram-negative bacteria (NFGNB) are immunosuppressive diseases conditions (especially cancer, organ transplantation and AIDS), neutropenic scenarios, diabetes, trauma as well as foreign bodies which include commonly indwelling catheters, ventilators as well as implants, non-regulated use of broad-spectrum antibiotics and Foley’s catheterisation [3].

NFGNB include the organisms to the likes of Pseudomonas species and Acinetobacter species apart from others like Alkaligenes species, Stenotrophomonas maltophilia and Burkholderia cepacia complex (BCC) of which P. aeruginosa and A. baumannii are presently the most commonly isolated non-fermenters [6]. The incidence of multidrug resistance among NFGNB is becoming very common and is alarmingly rising posing serious challenges in clinical management of infections. Furthermore, carbapenem resistance occurring among Pseudomonas and Acinetobacter leaves a dent in the therapeutic armamentarium against them [8].

Due to their increased isolation from urine samples with significant bacteriuria which indicates and establishes their pathogenic role in causing UTI, NFGNB has now been given a status of more than just a contaminant [7-9]. In the light of this the present study was conducted to underscore the importance of NFGNB in causing UTI.

**Materials And Methods**

**Tables And Figures**

**Table 1: Age distribution of patients in whom NFGNB were isolated.**

Age groups	Acinetobacter (n=25) (n,%)	Pseudomonas (n=8) (n,%)	Total (n=33) (n,%)

The present study was a retrospective study. Urine culture and sensitivity data either from outpatient or inpatient was collected from the records. Urine samples received in the microbiology laboratory were cultured on chrome agar (HiCrome UTI Selective Agar, Himedia). As per the protocol monomicrobial growth of  $\geq 10^5$  CFU/ml and irrespective of the colony count in case of catheterized sample was processed by phenotypic methods for identification. Isolates were tested for antimicrobial susceptibility test. Antibiotic sensitivity was done by adopting Kirby-Bauer disc diffusion method. commercially available discs Imipenem, Piperacillin-tazobactam, Amikacin, Ciprofloxacin, Ceftazidime, Gentamicin, Nitrofurantoin and Norfloxacin were used. Susceptibility results were interpreted as per Clinical and Laboratory Standards Institute (CLSI) guidelines.

Collected data was analyzed by MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA). A descriptive analysis of qualitative variables was performed through frequency tables.

**Results**

Of the total 1416 urine samples, 282 showed significant bacteriuria. Non fermenters were isolated in 33(11%) Out of total urine samples received prevalence of non-fermenters was 2.3%.

All isolates of non-fermenters were obtained from inpatients. Among the NFGNB cases, 26(79%) were from mid-stream urine samples and 7 (21%) were from samples obtained from indwelling catheter (Foley’s catheter). Maximum number of isolates of non-fermenters were from age group 51 – 60 yrs (Table 1). Ratio of males (51.5%) to that of females (48.5%) was 1.06 (Table 2). Three (9%) out of 33 isolates of non – fermenters were from pregnant women.

Acinetobacter species 25 (75%) was the predominant non fermenter isolated followed by Pseudomonas aeruginosa 8 (25%).

≤10 yrs.	5 (20%)	1 (12.5%)	6 (18.2%)
11-20 yrs.	1 (4%)	0 (0%)	1 (3%)
21-30 yrs.	2 (8%)	0 (0%)	2 (6.1%)
31-40 yrs.	1 (4%)	2 (25%)	3 (9.1%)
41-50 yrs.	5 (20%)	1 (12.5%)	6 (18.2%)
51-60 yrs.	2 (8%)	1 (12.5%)	3 (9.1%)
61-70 yrs.	4 (16%)	1 (12.5%)	5 (15.2%)
71-80 yrs.	4 (16%)	1 (12.5%)	5 (15.2%)
81-90 yrs.	1 (4%)	1 (12.5%)	2 (6.1%)

\*NFGNB: Non fermenting gram-negative bacteria

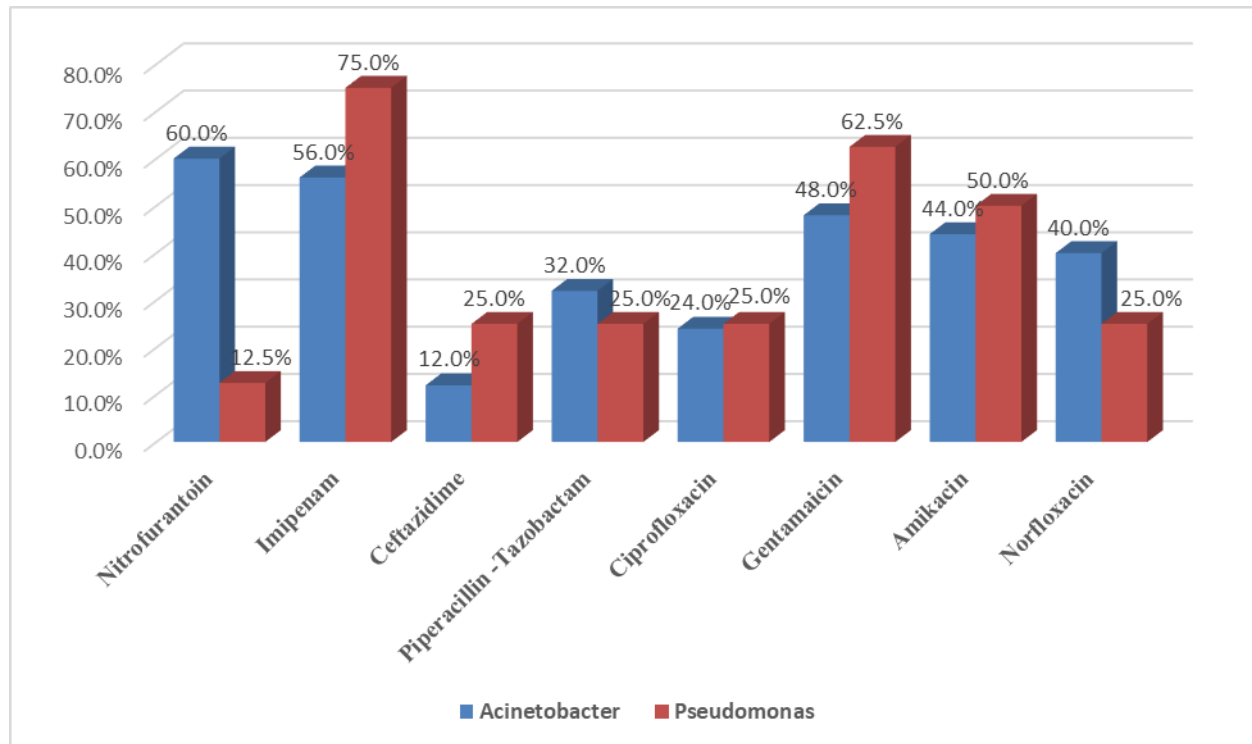
**Table 2: Gender distribution of patients in whom NFGNB were isolated.**

Gender	Acinetobacter (n=25) (n,%)	Pseudomonas (n=8) (n,%)	Total (n=33) (n,%)
Male	12 (48%)	5 (62.5%)	17 (51.5%)
Female	13 (52%)	3 (37.5%)	16 (48.5%)

\*NFGNB: Non fermenting gram-negative bacteria

**Table 3: Antibiotic susceptibility pattern of Non fermenting gram-negative bacilli (NFGNB)**

Antibiotics	Acinetobacter (n=25) Sensitivity %	Pseudomonas (n=8) Sensitivity %
Nitrofurantoin	60.0%	12.5%
Imipenam	56.0%	75.0%
Ceftazidime	12.0%	25.0%
Piperacillin Tazobactam	32.0%	25.0%
Ciprofloxacin	24.0%	25.0%
Gentamaicin	48.0%	62.5%
Amikacin	44.0%	50.0%
Norfloxacin	40.0%	25.0%

**Figure 1: Antibiotic susceptibility pattern of non-fermenting gram-negative bacteria.**

## Discussion

The importance of isolation and identification of non-fermenting gram-negative bacteria (NFGNB) has increased significantly over the last decade because numerous numbers of reports have emerged associating them with either hospital outbreaks of infections or healthcare-associated infections [10].

In our study out of 1416 samples significant bacteriuria was detected in 282 (20%). In which 33 (11%) yielded Non-fermenting gram-negative bacteria isolates. In a similar study done by Berwal et al [3] at Manipal, Karnataka, India, it was found that NFGNB were found in 120 (9.44%) cases out of 1271 midstream urine isolates with significant bacteriuria.

Out of the 33 patient's males were 51.5% and females were 48.5% (Table.2). NFGNB were isolated in highest numbers 7 (21%) in the age group of 51 – 60 yrs (Table.1) which was similar to a study done by Teena Julmaria et al[11] in Punjab, India.

Acinetobacter species was isolated from 25(75%) samples were as Pseudomonas aeruginosa was isolated from 8(25%). Studies done by Parajuli et al., (2017) and Sah et al., (2014) also identified Acinetobacter species to be the predominant NFGNB in hospitalized patients. But the studies conducted by

Malini et al., (2009) and Seema et al., (2017) revealed Pseudomonas aeruginosa as the most common NFGNB in hospitalized patients.

Acinetobacter species was most sensitive to Nitrofurantoin (60%) followed by Imipenem (56%) (Table 3). Pseudomonas aeruginosa was most sensitive to Imipenem (75%) followed by Gentamicin (62.5%). It is similar to a study done by Berwal A[3] et al., were sensitivity of Pseudomonas species to Imipenem was 80% and to Gentamicin was 58%. Acinetobacter species and Pseudomonas aeruginosa showed most resistance towards Ceftazidime and Nitrofurantoin respectively. Among the various drugs, towards Imipenem both Acinetobacter (56%) as well as Pseudomonas aeruginosa (75%) showed good sensitivity (Figure 1).

As the non-fermenters are hospital acquired multidrug resistant organisms' drugs commonly used for community acquired UTI such as quinolones showed less sensitivity towards them. Both the non-fermenters were sensitive to aminoglycosides (Gentamicin and Amikacin). On the other hand, Nitrofurantoin showed activity against 60% of the Acinetobacter isolates.

Multidrug resistance (MDR) was observed in Acinetobacter 14(56%) and Pseudomonas species

5(62%). Similarly, 4(16%) samples of *Acinetobacter* and 1(12%) of *Pseudomonas* species isolated were found to be resistant to all the tested antibiotics. (pan drug resistance - PDR)..

### Conclusion

UTIs are a considerable economic burden for healthcare institutions and national economies; additionally, they also have a substantial economic impact, as they result in lost working days. The results of this study reveal that non fermenting gram-negative bacteria causing UTI is most susceptible to Carbapenem group of antibiotics. MDR & PDR are common among NFGNB. There is scope for further studies to detect the various enzymes produced by these multi and pan drug resistant non-fermenters, such as Extended spectrum beta lactamases (ESBL's) and Carbapenamases which render the antibiotics inactive.

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