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ORIGINAL RESEARCH

Prevalence of multidrug resistance (MDR) non- fermenting gram negative bacilli (NFGNB) in urinary tract infection in tertiary care hospital

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ABSTRACT

Background:NFGNB are innately resistant to many antibiotics and have been documented to produce extended spectrum β-lactamases and metallo-β-lactamases. MDR is common and increasing among Non-fermenters. There are few studies from India that provide identification and antimicrobial susceptibility pattern of NFGNB. Therefore, we conducted this study to isolate and identify NFGNB, determine the antimicrobial susceptibility profile of isolates and estimate prevalence of multidrug resistance in NFGNB from urinary samples.

Material and methods: A total of 8362urine samples were collected from all clinical areas of Sri Guru Ram Das CharitableHospital. These samples were inoculated on Blood and MacConkey agar and incubated at 37C for 24 hours. NFGNB were identified by various conventional methods of identification and also by VITEK -2 system.NFGNB were subjected to Antimicrobial Susceptibility testing (AST) by Kirby- Bauer diffusion method and also by VITEK-2 system.The results were interpreted as per Clinical and Laboratory standards institute (CLSI) guidelines.

Results:Out of a total 8362 samples, 2002 (23.9%) were culture positive. Among culture positive samples, fermenters were 1637/2002 (81.7%), non-fermenters 201/2002 (10.0%), gram positive cocci 109/2002 (5.4%) and Candida 55/2002 (2.7%). A total of 134/201(66.6%) of NFGNB isolated were MDR (resistant to at least one of the antibiotics in three or more than three classes of antibiotics) in our study.

Conclusion:Treatment of infections caused by these MDR non-fermenting gram- negative bacilli is challenging due to intrinsic and acquired resistance to commonly used antibiotics. So, early and accurate identification of pathogen and appropriate antibiotic therapy is mandatory

INTRODUCTION

NFGNB are innately resistant to many antibiotics and have been documented to produce extended spectrum β-lactamases and metallo-β-lactamases. MDR is common and increasing among non-fermenters.[1]Development of resistance in **NFGNB** to commonly used antibiotics is multifactorial. Factors involved are efflux pump mechanisms, penicillin binding proteins, mutations in genes encoding porins, chromosomes beta lactamases.[2]

Pseudomonas aeruginosa is the predominant NFGNB. This is due to its easy recognition in the laboratory as it produces pyocyanin, a blue green pigment.[3] Resistance mechanism of *Pseudomonas aeruginosa*, the most frequent cause of infection among NFGNB mostly affecting immunocompromised patients of *P. aeruginosa* may be divided into intrinsic and

acquired resistance mechanisms leading to occurrence of resistant strains against important antibiotics such as β-Lactams, Quinolones, Aminoglycosides & Colistin.[4]

Acinetobacterbaumannii that was susceptible to most of antibiotics in 1970s, has become a major cause of hospital acquired infections worldwide because of its remarkable propensity to rapidly acquire resistance determinants to various antibiotics, making it resistant to almost all available antibiotics through acquisition of plasmids, transposons carrying clusters of genes encoding resistance to many antibiotic families.[5]Resistance to newer drugs including fluoroquinolones, third- generation Cephalosporins and Carbapenems emerged in the 1980s due to a wide variety of genetic mechanisms including DNA substitutions, transposition, recombination and plasmid acquisition.

Carbapenemase activity in *Acinetobacterbaumannii* is mainly due to Carbapenem hydrolyzing class D lactamases specific for this species. These enzymes belong to 3 unrelated groups of Clavulanic acid resistant β-lactamases that can be either plasmid or chromosomally encoded whereas in *Pseudomonas aeruginosa* the dominant mechanism of Carbapenem resistance is loss of Carbapenem specific porin OprD2.[6]

There are few studies from India that provide identification and antimicrobial susceptibility pattern of NFGNB especially *Burkholderiacepacia complex (BCC).* This bacterium causes opportunistic infections in patients suffering from cystic fibrosis, immunocompromised individuals and chronic granulomatous diseases. Acquired resistance is due to various mechanisms such as changes in lipopolysaccharide structure and presence of several multidrug efflux pumps, inducible chromosomes β- Lactamases and altered penicillin-binding proteins.[7]

Stenotrophomonasmaltophilia another NFGNB associated with plants, animals and aquatic environments causes urinary tract infections, respiratory infections and endocarditis. It shows low susceptibility to antibiotics and has been associated with intrinsic resistance factors common to all *Stenotrophomonasmaltophilia* strains such as low permeability, the presence of multidrug resistance efflux pumps, antibiotic modifying genes and quinolones resistance gene Smqnr[8].

NFGNB present a therapeutic challenge to clinicians, due to their increasing resistance to several classes of antibiotics, ultimately leading to MDR, XDR or even pan drug-resistant isolates, leading to prolonged therapy, sequelae and excess mortality in the affected patient population.[9] Antimicrobial resistance is affecting developed and underdeveloped countries and occurrence of multidrug resistance has been increasing in community and health services. This problem is aggravated by lack of innovation for creation of new antibiotics with the risk of returning to pre-antibiotic period.[10]

Therefore, the present study was conducted to isolate and identify **NFGNB**, determine the antimicrobial susceptibility profile of isolates and estimate prevalence of multidrug resistance in **NFGNB**from urinary samples of both inpatients and outpatients attending SGRD charitable hospital, Amritsar.

MATERIALS AND METHOD

This study was carried out in Microbiology department in SGRD charitable Hospital. A total of 8362 Mid-stream urinary samples (MSU) were collected using aseptic and antiseptic precautions from patients attending SGRD hospital and processed in lab for culture and sensitivity from March2020 to June 2021.

These samples were inoculated on Blood and MacConkey agar and incubated at 37ºC for 24 hours.Urine samples showing organisms and pus cells on microscopy and yielding a pure culture of $\geq 10^5$ CFU/ml were denoted as significant bacteriuria.

Isolates which gave Alkaline/Alkaline (K/K) reactions in Triple sugar iron were provisionally considered as NFGNB.The latter were identified by various conventional tests like gram stain

for morphology, hanging drop for motility, Oxidase test, Catalase test, Indole test, Oxidation-fermentative test for glucose, lactose, maltose, mannitol and xylose, gelatinliquefication and lysine and ornithine decarboxylation tests.

NFGNB were subjected to Antimicrobial Susceptibility testing (AST) by Kirby- Bauer diffusion method on Muller-Hilton media using commercially available antimicrobial disc such as Gentamicin (10µg), Amikacin (30µg), Ceftazidime (30µg), Piperacillin / Tazobactam (100µg/10µg), Imipenem (10µg), Meropenem (10µg), Ciprofloxacin (5µg), Cotrimoxazole (25µg), Colistin (10µg), Polymyxin (300µg) and Tigecyclin.Identification and AST was done in parallel by automated Vitek-2 system.

Organism showing resistance to three or more than three classes of antibiotics were considered as Multidrug resistant organism.The results were interpreted as per Clinical and Laboratory standards institute (CLSI) guidelines.

Institutional Ethical committee approval was obtained and Informed consent was also obtained from all the patients who participated in this study.

RESULTS

A total of 8362, urinary samples were received for culture and sensitivity during this period, out of which 2002 (23.9%) were culture positive. Among culture positive samples, fermenters were 1637/2002 (81.7%), non-fermenters 201/2002 (10.0%), gram positive cocci 109/2002 (5.4%) and Candida 552002 (2.7%). As many as 116/201(57.71) **NFGNB** were obtained from females while 85/201 (42.29%) from males.

Table 1: Age Wise Distribution of NFGNB

Age group	No. of cases	%age
<10	10	4.98
11=20	11	5.47
21-30	25	12.44
31-40	22	10.95
41-50	44	21.89
51-60	46	22.89
>60	43	21.39
Total	201	100.00

Majority of patients 46/201 (22.89%) belonged to age group 51-60 years followed by 44/201(21.89%) 41-50 years and 43/201(21.39%) more than 60 years of age as shown in Table 1.

Table 2: Prevalence of NFGNB Isolates by Conventional Methods

Acinetobacterbaumannii	**61**	**30.3**
Acinetobacterlwoffii	8	4.0
Burkholderiacepacia	7	3.5
Pseudomonas aeruginosa	119	59.2
Pseudomonas putida	6	2.9
Total	201	100.0

Among NFGNB isolates, *Pseudomonas aeruginosa* was the most common 119/201 (59.2%), followed by *Acinetobacterbaumannii* 61/201 (30.3%), *Acinetobacterlwoffii* 8/201 (4%), *Burkholderiacepacia* 7/201 (3.5%) and *Pseudomonas putida*6/201 (2.9%) as shown in Table 2

Table 3: Prevalence of NFGNB isolates by vitek-ii system

Organism identified VITEK-II	No. of cases	%age
Acinetobacterbaumannii	59	29.4
Acinetobacterlwoffii	7	3.5
Burkholderiacepacia	6	3.0
NOT IDENTIFIED	8	4.0
Pseudomonas aeruginosa	115	57.2
Pseudomonas putida	6	2.98
Total	201	100.0

Among NFGNB isolates identified by Automated Vitek-II system, *Pseudomonas aeruginosa* were 115/201 (57.2%) followed by *Acinetobactorbaumanni* 59/201 (29.4%), *Acinetobacterlwoffii* 7/201 (3.5%), *Burkholderiacepacia* 6/201 (3%) and *Pseudomonas putida* 6/201 (2.9%). It was observed that Automatic Vitek 2 could not identified 4 *Pseudomonas aeruginosa,2Acinetobactor baumanni,*1*Acinetobacterlwoffii*and 1*Burkholderiacepacia*as shown in Table 3.

Table 4: Antibiotic susceptibility profile of non-fermentative gram negative bacilli by conventional methods

Conventional method	Resistant		Sensitive		Total	
	No.	%age	No.	%age	No.	%age
Gentamicin	104	51.74	97	48.26	201	100.00
Amikacin	92	45.77	109	54.23	201	100.00
Ceftazidine	98	48.76	103	51.24	201	100.00
Piperacillintazobactam	52	25.87	149	74.13	201	100.00
Imipenem	41	20.40	160	79.60	201	100.00
Meropenen	43	21.39	158	78.61	201	100.00
Ciprofloxacin	131	65.17	70	34.83	201	100.00
Cotrimoxazole	103	51.24	98	48.76	201	100.00
Colistin	25	12.44	176	87.56	201	100.00
Polymyxin	35	17.41	166	82.59	201	100.00
Tigecycline	20	9.95	181	90.05	201	100.00

Table 5: Sensitivity pattern of nfgnb to gentamicin by conventional methods and automated VITEK-II

Organisms	Gentamicin Conventional methods						Gentamicin Automated VITEK-II					
	Resistant		Sensitive		Total		Resistant		Sensitive		Total	
	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age
Acinetobacterbaumannii	36	59.02	25	40.98	61	30.35	36	61.02	23	38.98	59	30.57
Acinetobacterlwoffii	1	12.50	7	87.50	8	3.98	1	14.29	6	85.71	7	3.63
Burkholderiacepacia	7	100.00	0	0.00	7	3.48	6	100.00	0	0.00	6	3.11
Pseudomonas aeruginosa	56	47.06	63	52.94	119	59.20	54	46.96	61	53.04	115	59.59

Pseudomonas putida	4	66.67	2	33.33	6	2.99	4	66.67	2	33.33	6	3.11
TOTAL	104	51.74	97	48.26	201	100.00	101	52.33	92	47.67	193	100.00

Table 6: Sensitivity Pattern of NFGNB ToAmikacin By Conventional Methods And Automated VITEK-II

Organisms	**Amikacin conventional methods**						**Amikacin Automated VITEK-II**					
	Resistant		**Sensitive**		**Total**		**Resistant**		**Sensitive**		**Total**	
	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age
Acinetobacterbaumannii	28	45.90	33	54.10	61	30.35	28	47.46	31	52.54	59	30.57
Acinetobacterlwoffii	4	50.00	4	50.00	8	3.98	4	57.14	3	42.86	7	3.63
Burkholderiacepacia	7	100.00	0	0.00	7	3.48	6	100.00	0	0.00	6	3.11
Pseudomonas aeruginosa	49	41.18	70	58.82	119	59.20	1	0.87	68	59.13	69	35.75
Pseudomonas putida	4	66.67	2	33.33	6	2.99	47	783.33	2	33.33	49	25.39
TOTAL	92	45.77	109	54.23	201	100.00	89	46.11	104	53.89	193	100.00

Table 7: Sensitivity pattern of NFGNB to ceftazidime by conventional methods and automated VITEK-II

Organisms	**Ceftazidime Conventional methods**						**Ceftazidime Automated VITEK-II**					
	Resistant		**Sensitive**		**Total**		**Resistant**		**Sensitive**		**Total**	
	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age
Acinetobacterbaumannii	40	65.57	21	34.43	61	30.35	39	66.10	20	33.90	59	30.57
Acinetobacterbaumannii	2	25.00	6	75.00	8	3.98	1	14.29	6	85.71	7	3.63
Burkholderiacepacia	5	71.43	2	28.57	7	3.48	5	83.33	1	16.67	6	3.11
Pseudomonas aeruginosa	48	40.34	71	59.66	119	59.20	45	39.13	70	60.87	115	59.59
Pseudomonas putida	3	50.00	3	50.00	6	2.99	3	50.00	3	50.00	6	3.11
TOTAL	98	48.76	103	51.24	201	100.00	93	48.19	100	51.81	193	100.00

Table 8: Sensitivity pattern of NFGNB to piperacillintazobactum by conventional methods and automated VITEK-II

Organisms	Piperacillintazobactum conventional methods						Piperacillintazobactum automated VITEK-II					
	Resistant		Sensitive		Total		Resistant		Sensitive		Total	
	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age
Acinetobacter baumannii	22	36.07	39	63.93	61	30.35	21	35.59	38	64.41	59	30.57
Acinetobacterlwoffii	0	0.00	8	100.00	8	3.98	0	0.00	7	100.00	7	3.63
Burkholderiacepacia	5	71.43	2	28.57	7	3.48	4	66.67	2	33.33	6	3.11
Pseudomonas aueroginosa	23	19.33	96	80.67	119	59.20	22	19.13	93	80.87	115	59.59
Pseudomonas putida	2	33.33	4	66.67	6	2.99	2	33.33	4	66.67	6	3.11
TOTAL	52	25.87	149	74.13	201	100.00	49	25.39	144	74.61	193	100.00

Table 9: Sensitivity pattern of NFGNB to imipenem by conventional methods and automated VITEK-II system

Organisms	IMIPENEM CONVENTIONAL METHODS						IMIPENEM AUTOMATED VITEK-II					
	Resistant		Sensitive		Total		Resistant		Sensitive		Total	
	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age
Acinetobacter baumannii	14	22.95	47	77.05	61	30.35	14	23.73	45	76.27	59	30.57
Acinetobacterlwoffii	0	0.00	8	100.00	8	3.98	0	0.00	7	100.00	7	3.63
Burkholderiacepacia	1	14.29	6	85.71	7	3.48	0	0.00	6	100.00	6	3.11
Pseudomonas aeruginosa	22	18.49	97	81.51	119	59.20	22	19.13	93	80.87	115	59.59
Pseudomonas putida	4	66.67	2	33.33	6	2.99	4	66.67	2	33.33	6	3.11
TOTAL	41	20.40	160	79.60	201	100.00	40	20.73	153	79.27	193	100.00

Table 10: Sensitivity pattern of nfgnb to meropenen by conventional methods and automated VITEK-II

Organisms	Meropenen Conventionals methods						Meropenen Automated VITEK-II					
	Resistant		Sensitive		Total		Resistant		Sensitive		Total	
	N	%a	N	%ag	N	%ag	N	%a	N	%ag	N	%ag

	o.	ge	o.	e	o.	e	o.	ge	o.	e	o.	e
Acinetobacterbaumannii	15	24.59	46	75.41	61	30.35	15	25.42	44	74.58	59	30.57
Acinetobacterlwoffii	0	0.00	8	100.00	8	3.98	0	0.00	7	100.00	7	3.63
Burkholderiacepacia	1	14.29	6	85.71	7	3.48	1	16.67	5	83.33	6	3.11
Pseudomonas aeruginosa	24	20.17	95	79.83	119	59.20	24	20.87	91	79.13	115	59.59
Pseudomonas putida	3	50.00	3	50.00	6	2.99	3	50.00	3	50.00	6	3.11
TOTAL	43	21.39	158	78.61	201	100.00	43	22.28	150	77.72	193	100.00

Table 11: Sensitivity pattern of nfgnb to ciprofloxacin by conventional methods and automated VITEK-II

Organisms	**Ciprofloxacin Conventional methods**						**Ciprofloxacin Automated VITEK-II**					
	Resistant		**Sensitive**		**Total**		**Resistant**		**Sensitive**		**Total**	
	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age
Acinetobacterbaumannii	41	67.21	20	32.79	61	30.35	40	67.80	19	32.20	59	30.57
Acinetobacterlwoffii	4	50.00	4	50.00	8	3.98	3	42.86	4	57.14	7	3.63
Burkholderiacepacia	6	85.71	1	14.29	7	3.48	5	83.33	1	16.67	6	3.11
Pseudomonas aeruginosa	77	64.71	42	35.29	119	59.20	74	64.35	41	35.65	115	59.59
Pseudomonas putida	3	50.00	3	50.00	6	2.99	3	50.00	3	50.00	6	3.11
TOTAL	131	65.17	70	34.83	201	100.00	125	64.77	68	35.23	193	100.00

Table 12: Sensitivity pattern of nfgnb to colistin by conventional methods and automated VITEK-II

Organisms	**Colistin Conventional methods**						**Colistin Automated VITEK-II**					
	Resistant		**Sensitive**		**Total**		**Resistant**		**Sensitive**		**Total**	
	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age
Acinetobacterbaumannii	6	9.84	55	90.16	61	30.35	6	10.17	53	89.83	59	30.57
Acinetobacterl	0	0.00	8	100.	8	3.98	0	0.00	7	100.	7	3.63

woffii				00						00		
Burkholderiacepacia	7	100.00	0	0.00	7	3.48	6	100.00	0	0.00	6	3.11
Pseudomonas aeruginosa	10	8.40	109	91.60	119	59.20	10	8.70	105	91.30	115	59.59
Pseudomonas putida	2	33.33	4	66.67	6	2.99	2	33.33	4	66.67	6	3.11
TOTAL	25	12.44	176	87.56	201	100.00	24	12.44	169	87.56	193	100.00

Table 13: Sensitivity pattern of nfgnb to polymyxin by conventional methods

Organisms	**Polymyxin Conventional methods**					
	Resistant		**Sensitive**		**Total**	
	No.	%age	No.	%age	No.	%age
Acinetobacterbaumannii	11	18.03	50	81.97	61	30.35
Acinetobacterlwoffii	1	12.50	7	87.50	8	3.98
Burkholderiacepacia	7	100.00	0	0.00	7	3.48
Pseudomonas aeruginosa	13	10.92	106	89.08	119	59.20
Pseudomonas putida	3	50.00	3	50.00	6	2.99
TOTAL	35	17.41	166	82.59	201	100.00

Table 14: Sensitivity pattern of NFGNB to tigecyclin by conventional methods and automated VITEK-II

Organisms	**Tigecyclin Conventional methods**						**Tigecyclin Automated VITEK-II**					
	Resistant		**Sensitive**		**Total**		**Resistant**		**Sensitive**		**Total**	
	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age	No.	%age
Acinetobacterbaumannii	4	6.56	57	93.44	61	30.35	4	6.78	55	93.22	59	30.57
Acinetobacterlwoffii	1	12.50	7	87.50	8	3.98	1	14.29	6	85.71	7	3.63
Burkholderiacepacia	2	28.57	5	71.43	7	3.48	1	16.67	5	83.33	6	3.11
pseudomonas aeruginosa	11	9.24	108	90.76	119	59.20	11	9.57	104	90.43	115	59.59
Pseudomonas putida	2	33.33	4	66.67	6	2.99	2	33.33	4	66.67	6	3.11
TOTAL	20	9.95	181	90.05	201	100.00	19	9.84	174	90.16	193	100.00

Table 15: Multi drug resistace among NFGNB

MDR	**Conventional methods**			**Automated Vitek-II**		
	No.	**Total**	**%age**	**No.**	**Total**	**%age**
Acinetobactor species	61	69	88.40	61	66	92.42

Burkholderia species	6	7	85.71	6	6	100.00
Pseudomonas species	67	125	53.60	65	121	53.72
Total	134	201	66.66	132	193	68.39

DISCUSSION

In the current study, among a total of 8360 urine samples, 23.9% showed significant bacteriuria.Our finding of 10.1%**NFGNB** isolates is similar to the observation of Shobnaet al.[10] who found 9.44% but is lower than study of Brewal et al.[13] who reported 33.3% NFGNB.In our study, **NFGNB** were isolated more from females 57.7% than males 42.29%. These findings were similar to studies done by Berwalet al.[13]in which females were 59.25% and males 40.74%; Majumder et al.[14] in which females were 65.37% and males 34.63%.

Further, majority of patients 22.89% belonged to age group 51-60 years followed by 21.89% in age group of 41-50 years and 21.39% above 60 years. These observations correlated with the studies conducted by Brewal et al.[13] where maximum number of **NFGNB**20.37% were isolated from UTI patients within age range of 51-60 years.[10] Our finding however is different from study conducted by Akram et al.[15] who found majority of patients were more than 60 years of age.

Our finding of *Pseudomonas aeruginosa*as the most common isolate 59.2% among **NFGNB** is similar to study conducted by Gajdacs et al.[16] in which *Pseudomonas species* (outpatient:78.7%; inpatients:85.1%) were most prevalent NFGNB isolated in urine samples and Meharwal et al.[17] who also found *Pseudomonas species*45.4% were commonest **NFGNB** isolates. These differences in the prevalence of various bacterial isolates in different health care setting are likely and well expected as they depend on many local variables.

All *Pseudomonas* species were 89.60%sensitive to Tigecycline in our study which is similar to results reported by Brewalet al.[13], who found 88.89% sensitivity to Tigecycline. However, higher sensitivity 100% to Tigecycline by *Pseudomonas species* found by Maduakoret al.[18] in his study. In our study, *Pseudomonas* species showed high sensitivityof 90.40%to Colistin which is concordant with Brewalet al.[13], who reported 100% sensitivity to Colistin. *Pseudomonas* species also showed 87.20% sensitivity toPolymyxin which is lesser than the observations made by Rainaet al.[12] who reported 95% sensitivity and 100% sensitivity by Yadav et al.[19] in their studies. Sensitivity to Imipenem by *Pseudomonas* species 80% is similar to 80.25% sensitivity found by Berwalet al.[13] but lower than 95% sensitivity found by Raina[12] and 100% sensitivity to Imipenem found by Maduakor et al[18]. in their studies. In our study,sensitivity 78.4% to Meropenem by all *Pseudomonas species* is almost similar to sensitivity of 75% and 80%found by Maduakor et al.[18] However, higher sensitivity of 91.4% to Meropenem by *Pseudomonas* was reported by Brewal et al.[13]

Sensitivity to Tigecycline92.7% by *Acinetobacter species* in our study is quite similar to 95% sensitivity reported by Brewal et al.[13]but much more than that of sensitivity by*Acinetobacter species* to Tigecycline80% found in study of Tewari et al.[20]In our study, *Acinetobacter species* strain percentage sensitivity for Colistin was 91.30% which was almost similar to 100% sensitivity found by both Brewal et al.[13] and Krishnan et al.[21] in their studies.*Acinetobacter species* showed 82.60% sensitivity to Polymyxin in our study which matches with 87.5% sensitivity found by Raina et al.[12] Our observation of sensitivity to imipenem shown by *Acinetobacter species* is 81% similar to 77.27% shown in study done by Berwal et al.[13] in 2020 but higher sensitivity of 100% found by Raina and Najotra[12] in their study. Sensitivity of 75.41% to Meropenem is shown by all *Acinetobacter species* in our study but higher sensitivity of 90.91% found by Brewal et al.[13]However a lower sensitivity of 47.6% by *Acinetobacter species* seen by Yadav et al.[19] Resistance among *Acinetobacter* species 36.07% to PiperacillinTazobactam found in our study is similar to 40% resistance seen by Malhotra et al.[22]

Resistance to Imipenem shown by *Pseudomonas aeruginosa* alone in our study was 18.51% quite similar to 14.28% resistance found in study done by Bhalavi et al.[11]Resistance of 19.33% is shown by *Pseudomonas aeruginosa*to PiperacillinTazobactam in our study lower than 25% and 37% resistance shown by Pseudomonas aeruginosa alone in studies done by Regha[23] and Majumder et al.[14] respectively.However, Bhalaviet al.[11] found 71.4% resistance to PiperacillinTazobactam by *Pseudomonas aeruginosa*which is much higher than our study.

In present study, *Pseudomonas aeruginosa*46.06% resistant to Gentamicin similar to results reported by Ragha et al.[23] and Majumder et al.[14] who found *Pseudomonas aeruginosa*was 53.1% and 50.3% resistant to Gentamicin respectively in their studies. However, Hoqueet al.[24] found much higher resistance of 82% in his study.Resistance shown by *Pseudomonas aeruginosa*to ceftazidime in our study was 40.34% similar to study done by Regha[23] which found 34% resistance to ceftazidime by *Pseudomonasaeruginosa*. Higher resistance of 100% and 92% by *Pseudomonas aeruginosa*to ceftazidime than our results were observed by Balvani et al.[11] and Hoque et al.[24] respectively in their studies. Resistance shown by *Pseudomonas aeruginosa*41.18% to Amikacin is almost similar to 43.34% resistance to Amikacin by Pseudomonas aeruginosa found by Majumdaret al.[14]

MDR NFGNB by definition are resistant to at least one of antibiotics in three or more than three classes of antibiotics was investigated throughout our study. We found 66.66% MDR NFGNB similar to 64.7% MDR NFGNB strains found in study done by Grewal etal.[25] but lesser than 78.1% MDR non fermenters in study done by Yadav et al.[19]

Multidrug resistance shown by most frequent isolates of our study are *Acinetobacterbaumannii* 96.7%, *Burkhloderiacepacia* is 85.71%, *Pseudomonas aeruginosa* 54.6%, *Pseudomonas putida* 33.33% and *AcinetobacterLwoffii* 25%.Among these MDR noted in all *Acinetobacter* species 88.40% in our study is similar 80% and 91% MDR *Acinetobacter species* found by Tiwariet al.[20] and Yadav et al.[19] respectively in their studies. Out of total 7 *Burkholderiacepacia* isolates, 85.71% are MDR similar to 78.8% MDR isolates found by Yadavet al.[19] in his study.

As many as 54.60%*Pseudomonas aeruginosa strains* in our study showed multi drug resistance which is similar to 45.79% and 50% MDR *Pseudomonasaeruginosa*reportedby Shobna et al.[26] and Awasthi et al.[27] respectively. We noted that all *Pseudomonas species* showed resistance of 64% to Ciprofloxacin and 60% to Ceftazidime quite similar to resistance of 66.6% shown to both Ceftazidime and Ciprofloxacin in study done by Agarwalet al.[28]

Our all Acinetobacter species showed highest resistance to Cotrimoxazole 76.81% followed by Ciprofloxacin 65.21% and Ceftazidime 60.89% similar to resistance of 80%, 60% and 80% to Cotrimaxazole, Ciprofloxacin and Ceftazidime respectively in studies done by Malhotra et al.[22] Quite similar resistance of 68.62%to Cotrimoxazole and 74.5% to Ciprofloxacin by Acinetobacter was found in study done by Majumder et al.[14]*Burkholderiacepacia* also showed high resistance to Ciprofloxacin 85.71% and similar resistance 71.43% to both Ceftazidime and Piperacillin/Tazobactam in our study but higher resistance of 88% to Ceftazidime was reported by Yadav et al.[19] in his study.

In our study, alarming finding is that **NFGNB** were resistant to commonly used drugs like Ceftazidime, Ciprofloxacin and Cotrimoxazole limiting the available treatment options. The possible explanation to this high level of multidrug resistant **NFGNB** found in our study may be due to the indiscriminate use of antibiotics and lack of effective implementation of the policy that regulates the use of antibiotics. Early accurate Microbiological diagnosis can go a long way in a positive clinical outcome and decreasing morbidity, mortality and complications of UTI besides cost cutting and reduction of hospital stay.

CONCLUSION

NFGNB are now emerging as important uropathogens with many of them exhibiting MDR. High rate of multidrug resistance was noted in our study may be associated with different variables such as easy availability of drugs, incomplete duration of treatment, self - medication practices, lack of strict laws of drugs that punishes for misuse etc. all contributing to emergence of drug resistance. Therefore, strict compliance of Antibiotic Policy and regular monitoring of the emerging multidrug resistant pathogens has to be carried out for minimizing treatment failure and decreasing morbidity, mortality, hospital stay and economic burden on patients.

Further, treatment of infections caused by these MDR non-fermenting gram-negative bacilli is challenging due to intrinsic and acquired resistance to commonly used antibiotics. So, early and accurate identification of pathogen and appropriate antibiotic therapy is mandatory.

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