



Original Research Article

Multidrug Resistant Gram Negative Bacilli in Clinical Isolates in a Tertiary Care Hospital

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ABSTRACT

Introduction: Antibiotic resistance is emerging as major health related issue in last few years. All over world there have been growing epidemics of infections due to gram negative bacteria resistant to many classes of antibiotics. New terminologies like multidrug resistant (MDR) and pandrug resistant (PDR) bacteria have been established.

Aims: 1) To find out incidence of Multidrug resistant gram negative bacilli in clinical isolates. 2) To find out sensitivity profile for antibiotic groups. 3) To find out incidence of Pan drug resistant gram negative bacilli.

Materials and Methods: Clinical specimens received in Microbiology department over a period of 6 months were included in the study. Bacterial identification was done by standard methodology. Isolated organisms sensitivity testing for antibiotic groups like aminoglycosides, fluoroquinolones, cephalosporins, penicillins, phenicols, tetracyclines, folate inhibitors was done by Kirby - Baur Disk diffusion method.

Results: Of 772 gram negative isolates, 62.2 % were MDR gram negative bacilli and 26.1 % were PDR gram negative bacilli

Conclusion: There was alarming drug resistance level. There should be judicious use of antibiotics and Antibiotic Stewardship Program may help the worsening condition of drug resistance.

Key Words: Gram Negative Bacilli, Multidrug Resistant (MDR), Pandrug Resistant.(PDR)

INTRODUCTION

Antibiotic resistance is emerging as major health related issue in latest few years. In fact world health day 2011 theme was “Antimicrobial Resistance: no action today, no cure tomorrow.” All over world, epidemics due to resistant gram negative bacilli are increasing rapidly. ⁽¹⁾ Studies related to prevalence and epidemiology of antimicrobial resistant bacteria have become

important focus. ^(2,3) New terminology like multidrug resistant (MDR), extensive drug resistant (XDR) and pandrug resistant (PDR) bacteria have been established. ^(4,5) Superbugs and NDM 1 have caused more worrisome in the present therapeutic scenario. ⁽⁶⁾ MDR GNB (Multidrug resistant gram negative bacilli) is defined as organism which is resistant to at least one antibiotic from minimum three antimicrobial groups.

(4,5) PDR bacteria (pandrug resistant) are defined as organism which is resistant to all available antibiotics. (4,5) Though gram positive organisms like MRSA and vancomycin-resistant *enterococcus* has got much attention, simultaneous development of multidrug resistant gram negative bacilli has caused alarming situation. (6) The present study therefore was undertaken to find out of MDRGNB and possible PDR bacteria in a tertiary care hospital in Western Maharashtra, India from clinical isolates.

MATERIALS AND METHODS

Clinical specimen received in department of microbiology, over a period of six months were included in the study. For this, Institutional Ethical Committee clearance was taken first. Specimens were pus, endotracheal secretions, sputum, urine, stool, catheter tips, blood, and body fluids. Bacterial identification was done by standard methodology. (7) Repeat isolates from same patients, were excluded from study. Isolated organisms were tested for various antibiotic groups like aminoglycosides, fluoroquinolones, cephalosporin, penicillins, phenicols, tetracyclines, folate inhibitors by Kirby-Baur Disk diffusion method. (8) Interpretation of test was done as per CLSI guidelines. (9) Quality control of disk diffusion test was

done by standard ATCC strains like *E.coli* 25922, and *Ps. aeruginosa* 27853. (9)

Any strain isolated which is resistant to at least one antibiotic from minimum three antimicrobial groups, was considered as MDRGNB. (4,5) Of these bacilli, those which were resistant to all antibiotics in present study were considered as possible PDR gram negative bacilli. (4,5) Such gram negative bacilli from various clinical specimens were included for comparison and data analyzing. For this GraphPad InStat software demo version was used.

OBSERVATIONS AND RESULTS

Table 1: Gram Negative organisms isolated from Various Clinical Specimens.

Clinical Specimens	Total (No)	G N B No. (%)
Pus	260	312 (40.5)
Urine	292	148 (19.2)
ETT	82	119 (15.5)
Body Fluids	241	25 (3.3)
Blood	205	25 (3.3)
Stool	61	18 (2.4)
Sputum	174	90 (11.7)
Other	64	35 (4.6)
Total	1379	772

Total 772 gram negative bacilli were isolated from 1379 specimens over a period of six months. Maximum (40.5 %) isolates were from pus specimens.

Table 2: Distribution of Organisms Isolated from Clinical Specimens

Specimen	<i>Acinetobacter</i> species	<i>Klebsiella</i> species	<i>E.coli</i>	<i>Ps. aeruginosa</i>	<i>Citrobacter</i> species	<i>Proteus</i> species	Total
Pus	32	84	57	103	19	17	312
Urine	3	29	78	27	11	0	148
ETT	31	30	15	40	3	0	119
Fluids	3	10	7	3	1	1	25
Blood	3	11	3	4	4	0	25
Stool	0	3	15	0	0	0	18
Sputum	10	38	9	29	4	0	90
Other	5	10	8	10	2	0	35
Total (%)	87 (11.3)	215 (27.9)	192 (24.9)	216 (28)	44 (5.7)	18 (2.4)	772

Of the total isolates, *Ps. aeruginosa* (28 %) followed by *Klebsiella* species (27.9 %) were among the maximum isolates, while *Proteus* species (2.4%) was the least isolated organism.

Table 3: Antibiotic Sensitivity profile of Organisms

Organism (No.)	Sensitivity to Antibiotic Groups				
	Cephalosporins	Quinolones	Aminoglycosides	Penicillins	Other*
<i>Acinetobacter</i> species. (87)	3	6	15	6	0
<i>Klebsiella</i> species. (215)	22	21	41	7	30
<i>E.coli</i> (192)	26	14	48	10	42
<i>Ps. aeruginosa</i> (216)	29	24	32	37	11
<i>Citrobacter</i> species. (44)	5	4	6	2	4
<i>Proteus</i> species. (18)	6	5	5	3	0
Total (772) (%)	91 (11.7)	74 (9.6)	147 (19.1)	65 (8.5)	87 (11.3)

Other* antibiotics included were phenicols, folate inhibitors, tetracycline.

Total 147 (19.1 %) of the isolates were sensitive to aminoglycosides while least (8.5 %) of the organisms were susceptible to penicillin group.

26.1 % of the total strains were PDR gram negative bacilli, *Acinetobacter* species 39 % were maximum followed by *Klebsiella* species 31.6 %

Table 4: Proportion of Multidrug Resistant Gram negative bacilli

Organism	Total Isolates	MDRGNB (%)	Non MDRGNB (%)
<i>Acinetobacter</i> species.	87	63 (72.4)	24 (27.6)
<i>Klebsiella</i> species.	215	158 (75.3)	57 (24.7)
<i>E.coli</i>	192	107 (55.7)	85 (44.3)
<i>Ps. aeruginosa</i>	216	118 (54.6)	98 (45.6)
<i>Citrobacter</i> species.	44	28 (63.6)	16 (36.4)
<i>Proteus</i> species.	18	6 (33.3)	12 (66.7)
Total	772	480 (62.2)	292 (37.8)

Of the 772 total isolates, 480 (62.2 %) were MDRGNB which was significant. (P < 0.0001 using χ^2 test.)

Table No 5: Multidrug Resistant and Pan drug resistant Gram negative bacilli

Organism	Total Isolates	MDRGNB (%)	PAN (%)
<i>Acinetobacter</i> species.	87	63 (72.4)	39 (44.8)
<i>Klebsiella</i> species.	215	158 (75.3)	68 (31.6)
<i>E.coli</i>	192	107 (55.7)	20 (10.4)
<i>Ps. aeruginosa</i>	216	118 (54.6)	62 (28.7)
<i>Citrobacter</i> species.	44	28 (63.6)	12 (27.2)
<i>Proteus</i> species.	18	6 (33.3)	0
Total (%)	772	480 (62.2)	201 (26.1)

DISCUSSION

Emergence of multiple drug resistant bacteria has caused much of problems especially in relation to public health. ⁽⁴⁾ In fact the condition is worsening with less or no new availability of antimicrobials. ⁽⁴⁾ Various surveys has indicated that there is significant rise in antibiotic resistance in gram negative bacilli isolated from infections in hospitalized patients. ^(10,11) This study therefore was undertaken to know the present scenario of multidrug resistant bacilli in this area.

Of the 772 isolates included in the study, 312 (40.5 %) were from pus specimens. This is justifiable as most pus specimens are polymicrobial in nature. ⁽¹²⁾ Also it was obvious that *Ps.aeruginosa*, *Klebsiella* species outnumber the other bacteria among the total isolates. ⁽¹²⁾

For treatment of gram negative bacilli, of late the antimicrobial groups most commonly used are cephalosporins, aminoglycosides, fluoroquinolones, β lactam and antipseudomonal penicillin group. ⁽¹³⁾ In present study, aminoglycosides showed maximum sensitivity but that too only 19.1 %.This was because urine isolates (total 148) were second most contributory

specimen (Table 2) among total isolates. These isolates were susceptible to aminoglycosides especially amikacin and gentamicin. All other antimicrobial groups showed further less sensitivity. In surveys carried out in European countries in 2007 more proportions of *Ps. aeruginosa* and *Klebsiella species* were susceptible. (14) Less susceptibility to cephalosporins might be due to ESBL producing strains while overuse of quinolone and penicillin group may be responsible for resistance against these groups. (13)

What was alarming was 62.2 % of the total isolates, were MDRGNB in the present study. Various national and international surveys rarely report data on MDR or PDR due to lack of uniformity of definitions for these terms. (14) In a study carried out in long term care centre by O'Fallon E and others more than 80% of MDRGNB were resistant to commonly prescribed antimicrobials. (15) Natural response of organisms to selective pressure of antimicrobials is in the form of development of antimicrobial resistance. (16) The present study being carried out in a tertiary care hospital, most patients have already exposure to antibiotics, as many are referred patients. Factors responsible for irrational use of antimicrobials are, easy availability of antimicrobials at chemist, injudicious use in private clinics, hospitals and by traditional practitioners practicing allopath. Also there is uncontrolled use of antibiotics in agriculture and animal husbandry. (16) Prescription of irrational antibiotic combination because of patient and time pressure, diagnostic and treatment uncertainty and poor patient compliance also contribute to development of multidrug resistance. (16)

Of the total isolates, 201 (26.1%) of the strains were resistant to all tested antimicrobials and were considered as possible pan drug resistant bacilli.

Proportion (%) of PDR gram negative bacilli in present study was more compared to other study as carbapenems, colistin, and polymixin were not tested. (13,14) In fact studies have suggested use of combination of polymixin with other antibiotics. (13,17) What must be stressed is, available antibiotics should be used properly, which is nothing but implementing Antibiotic Stewardship Program. Or else it is not too far, that the title "Bad Bugs, No Drugs: No ESKAPE!" comes in reality. (18)

CONCLUSION

Considering the threatening drug resistance level in the present scenario, the antibiotics should be used judiciously. Right antimicrobial, to right patient with right dose, at right time, using right route with least harm to present and future patients should be used. This Antimicrobial Stewardship Program, should not only be followed at every hospital or state but also at national level.

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