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Antimicrobial Resistance Pattern of Bacterial Isolates in a Tertiary Care Hospital Of North-East India

Antara Roy[1], Supriya Laifangbam[2], Kh Vyas[3]

1. *Post Graduate Student, Department of Microbiology, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal.*
2. *Professor and HOD, Department of Microbiology, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal.*
3. *Associate Professor, Department of Surgery, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal*

**Corresponding Author: Dr. Supriya Laifangbam, Professor and HOD, Department of Microbiology Jawaharlal Nehru Institute of Medical Science (JNIMS), Imphal*

Abstract:
Background: *Antimicrobial resistance (AMR) refers to a phenomenon in which there is development of resistance to antimicrobial agents by a micro-organism to which they were previously sensitive. It is one of the most serious problem to global public health. Isolation of alarming rates of Multi-Drug Resistance Gram-negative bacilli among the in-patients were observed at the Bacteriology Section of Microbiology Department which prompted this study in collaboration with Department of Surgery.*
Aims and Objectives: *To assess the antimicrobial resistance profile of bacterial isolates from clinical samples of patients admitted in a tertiary care hospital of North-East India.*
Materials and Methods: *This is a hospital-based cross sectional study conducted in the Department of Microbiology during the period from November 2018 to October 2019. The clinical specimens from indoor patient departments (IPD) were included in the study. The bacterial strains were isolated from those clinical samples and antibiotic susceptibility testing were done by conventional method, Kirby Bauer disc diffusion method and VITEK 2 automated system. Data were recorded as numbers and proportions.*
Results: *Of the total 3256 samples, 810 (25%) were positive for bacterial growth. Female patients constituted more 493 (60.8%) than males 317 (39%). Majority of the bacteria were isolated from urine culture at 68 (25.43%) followed by sputum 151 (18.64%), pus 123 (15.18%) and blood 112 (13.82%). In this study, most of the identified isolates were Gram-negative at 496 (61.23%) while the remaining at 314 (38.76%) were Gram-positives. The most frequently identified isolates were Escherichia coli at 206 (25.43%) followed by Staphylococcus aureus 199 (24.56%), Klebsiella pneumoniae 153 (18.88%) and Pseudomonas aeruginosa 78 (19.02%). In this study, commonest GNB-MDR was E.coli and GNB-XDR was P. aeruginosa. Among Gram positive bacteria 30% Staphylococcus aureus were found to be methicillin resistant Staphylococcus aureus (MRSA). The resistance rate of Enterococcus species for vancomycin (VRE) was found to be 2%.*
Conclusions: *Unless and until resistant organisms are detected and their incidence is known, the strategies for their control cannot be adopted properly in healthcare setups. For detection of change in AMR resistance patterns irregular Ward-ICU based surveillance need to be replaced with laboratory-based ward-liaison surveillance by the infection control doctors and nurses working in close coordination.*
Key Words: *Antimicrobial resistance, IPD, Surveillance.*

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I. Introduction

Antimicrobial resistance (AMR) refers to a phenomenon in which there is development of resistance to antimicrobial agents by a micro-organism to which they were previously sensitive.[1] It is one of the most serious problem to global public health.[2] AMR is causing increase in mortality and morbidity from infectious disease.[1] Moreover, the percentages of organisms exhibiting AMR, especially resistance to multiple antibiotics are continuingly increasing.[3] A high percentage of hospital acquired infections and medical complications are widely common around the globe due to increasing AMR pathogens, yet the issue received little concern by health care sectors.[4]

The clinical isolates such as *Pseudomonas aeruginosa*, Methicillin Resistant *Staphylococcus aureus* (MRSA), Vancomycin Resistant *Enterococci* (VRE), and members of Family Enterobacteriaceae, for example, *Klebsiella pneumonia, Escherichia coli, and Proteus* sp. rapidly develop antibiotic resistance and spread in the

hospital environment.[5] As per standardized international terminology created by European Centre for Disease Control (ECDC) and Centre for Disease Control & Prevention (CDC), Atlanta, the multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan drug-resistant (PDR) bacteria have been well defined. Multidrug resistance (MDR) was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories. Extensively drug resistance (XDR) was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e., bacterial isolates remain susceptible to only one or two antimicrobial categories). Pan drug resistance (PDR) was defined as non-susceptibility to all agents in all antimicrobial categories.[6]

Previously, clinicians have been treating infection successfully by relying on their experience in prescribing antibiotics.[7,8] However this situation has now become an exception to the rule since resistance has been observed to essentially all of the antimicrobial agents which made clinicians more dependent on data from in vitro antimicrobial susceptibility testing and highlights the importance of the diagnostic laboratory in clinical practice.[9] The problem of the antimicrobial resistance is not only the development of the resistance but also the spread of the resistant strains, especially by inadequate sanitary condition and uncontrolled sale of antibiotics over the counters without prescription.[10] Data on AMR among local pathogens help define the best possible treatment for individual patients.[11,12] The proportion of resistant bacteria can vary from one area to another.[13] There is paucity of information regarding antimicrobial resistance pattern of pathogenic bacteria in Manipur. Therefore, the present study highlights the screening of the antimicrobial resistance profile of bacterial isolates from clinical samples of patients admitted in a tertiary care hospital of North-East India

II. Material and Methods

This is a hospital-based cross sectional study conducted in the Department of Microbiology in collaboration with the department of Surgery during the period from November 2018 to December 2019. The bacterial strains were isolated from different clinical samples and were identified by conventional methods and VITEK 2 automated system.[14] The clinical specimens from indoor patient departments (IPD) were only included in the study. Antibiotic susceptibility testing of bacterial strains was done by Kirby Bauer disc diffusion method.[15] For antibiotics like vancomycin, in case of *S.aureus* and Colistin for the Gram Negative bacteria, Minimum Inhibitory Concentration (MIC) was performed by VITEK 2 automated system as per Clinical Laboratory Standard Institute (CLSI) guidelines.[16] Antibiotics used for Gram positive cocci (GPC) were ciprofloxacin, levofloxacin, vancomycin, teicoplanin, ceftriaxone and linezolid , and those for Gram negative bacilli (GNB) were ceftazidime, ceftriaxone, cefoperazone-tazobactum, ciprofloxacin, levofloxacin, azithromycin, gentamicin, piperacillin-tazobactum, meropenem, and colistin respectively. Linezolid and colistin were used as supplementary drugs. For routine Quality Control of antibiotic susceptibility test, S. aureus ATCC 25923, E. coli ATCC 25922, and Pseudomonas aeruginosa ATCC 27853 were used. Resistant strains were detected as per criteria described by CDC.[17] Data collection was done from laboratory report registry in the Bacteriology Section of Department of Microbiology. Data was reported in numbers and proportions

III. Result

Of the total 3256 samples, 810 (25%) were positive for bacterial growth. Female patients constituted more 493 (60.8%) than males 317 (39%). Most of the patients were in the age group of > 60years at 174 shown in **Table 1**. Majority of the bacteria were isolated from urine culture at 373 (46%) followed by sputum 151 (18.64%), pus 123 (15.18%) and blood 112 (13.82%). In this study, most of the identified isolates were Gram-negative at 496 (61.23%) while the remaining at 314 (38.76%) were Gram-positives shown in **Fig 1**. The overall distribution of the isolates from each kind of clinical samples is summarized in **Table 2**. Out of 652 bacterial isolates, resistant strains were isolated highest from Surgery ward 209/503 (41%), followed by Pulmonary Medicine ward 15/45 (33%), Medicine ward 181/622 (29%), Paediatrics ward 76/326 (23%), Post-Natal ward 85/401 (21%), Orthopaedics ward 16/62 (25%), Otorhinolaryngology ward 9/40 (22%), Dermatology ward 4/36 (11%) Endocrine ward 9/43 (20%), Hematology ward 11/74 (14.86%), Gynaecology ward 16/134 (12%), Antenatal ward 24/480 (5%), Neurosurgery ward 1/21 (4.76%) shown in **Fig 2.**In total 158/453 (34.8%) samples were isolated from Intensive Care Unit (ICU) patients in whom 59 were from Surgical Intensive Care Unit (SICU), 50 from Medicine Intensive Care Unit (MICU), 18 from Intensive Coronary Care Unit (ICCU), 19 from Accident & Trauma Centre Intensive Care Unit (ATC-ICU), 7 from Pediatric Intensive Care Unit (PICU), 5 from Neonatal Intensive Care Unit (NICU) shown in **Fig 3.**The most frequently identified isolates were *Escherichia coli* at 206 (25.43%) followed by *Staphylococcus aureus* 199 (24.56%), *Klebsiella pneumoniae*, 153 (18.88%) and in ICU patients *Pseudomonas aeruginosa* at 78 (9.6%) was the highest.From urine culture, altogether 373 bacterial isolates were isolated. Gram-negative isolates at 254 were predominant. Of these, *E. coli* at 170 (45.57%) followed by *K. pneumoniae* at 45 (12.06%) were the common ones. *Salmonella typhi* was identified only from blood cultures and stool cultures.Altogether 286 isolates were GPC. Among these, *Staphylococcus aureus* at 199 (24.56%) was the major isolate followed by *Enterococcus fecalis* at 65 (8.02%),

Coagulase Negative Staphylococcus at 22 (2.7%). Of a total of 123 bacterial isolates from pus samples, maximum were Gram positive bacteria at 82 (70%).

The overall AMR profile of the isolates is presented in **Table 3**. In this study, the resistance rate of Gram-negatives for ceftriaxone, ciprofloxacin, levofloxacin, norfloxacin, ceftazidime, nitrofurantoin, gentamicin, azithromycin, cefoperazone-tazobactum, piperacillin-tazobactum, meropenem was between 10% and 65% and only 1(one) *Pseudomonas aeruginosa* was found resistant to Colistin shown in **Table 3**. On the other hand, the resistance rate of Gram-positive isolates for ciprofloxacin, levofloxacin, vancomycin, teicoplanin, cefriaxone, linezolid was between 6% and 65%. 2% *Enterococcus fecalis* were resistant to vancomycin (Vancomycin Resistant Enterococci i.e, VRE) and 30% *Staphylococcus aureus* were resistant to cefoxitin (Methicillin Resistant Staphylococcus aureus i.e MRSA) shown in **Table 3.**

Table 1: **Age and Gender Distribution Chart**

Age in years	Male	Female	Total
0-10	20	33	53
11-20	29	45	74
21-30	28	76	104
31-40	53	82	135
41-50	69	74	143
51-60	44	83	127
>60	74	100	174
Total	317	493	810

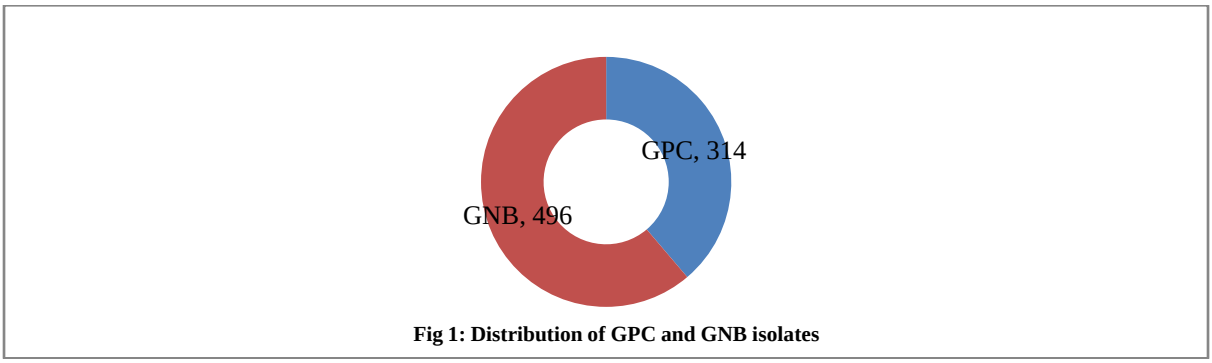

Fig 1: Distribution of GPC and GNB isolates

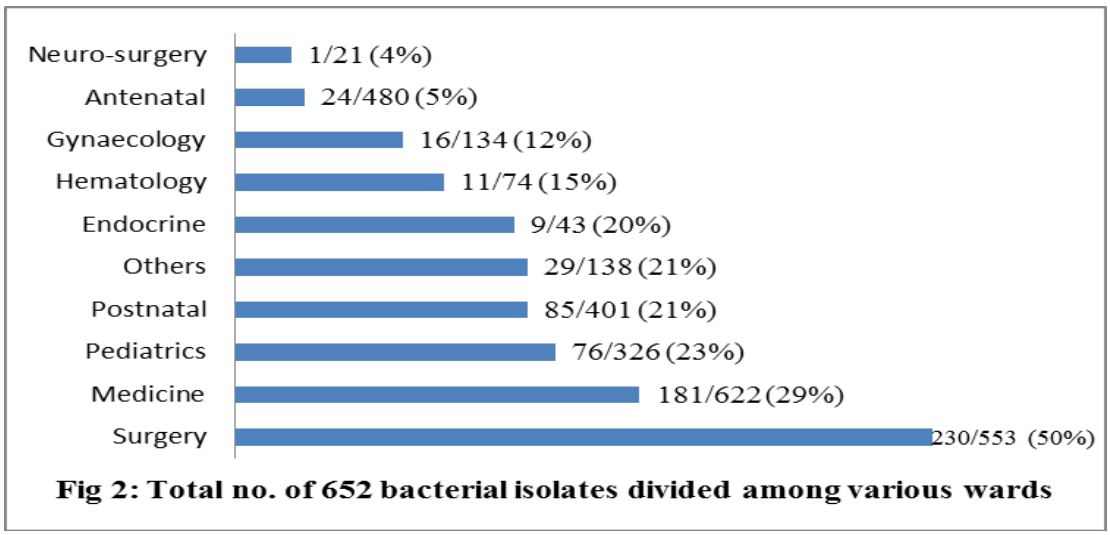

Fig 2: Total no. of 652 bacterial isolates divided among various wards

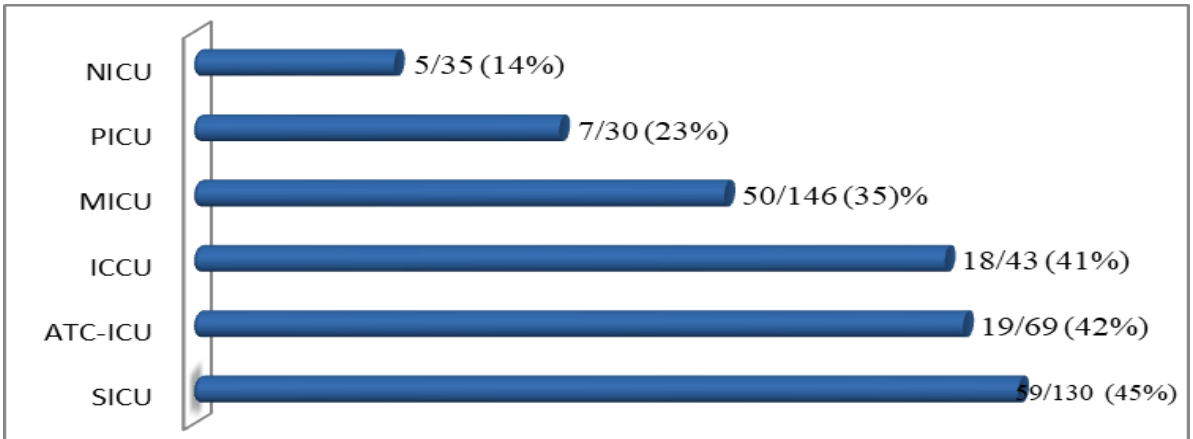

Fig 3: Distribution of 158 clinical isolates in different ICU(intensive Care Unit) SICU-Surgical ICU, MICU-Medical ICU, ICCU-Intensive Coronary CU, ATC-ICU-Trauma Centre ICU, PICU-Perinatal ICU, NICU-Neonatal ICU

Table 2: Distribution of clinical samples for various bacterial isolates

GNB	**Urine**	**Stool**	**Blood**	**Pus**	**Sputum**	**Catheter tip**	**Endotracheal tube tip**	**Body fluid**	**Total no. of bacterial isolates**
Escherichia coli	170	8	22	-	6	-	-	-	206
Klebsiella pneumoniae	45	-	28	-	62	8	6	4	153
Enterobacter cloacae	6	-	-	-	-	-	-	-	6
Citrobacter freundii	2	-	-	-	-	1	-	-	3
Proteus mirabilis	5	-	-	-	-	-	-	-	5
Salmonella typhi	-	5	15	-	-	-	-	-	20
Pseudomonas aeruginosa	19	-	10	31	-	15	-	3	78
Acinetobacter baumanni	7	-	7	10	17	12	-	-	53
GPC									
Staphlococcus aureus	67	-	23	70	39	-	-	-	199
CONS (Coagulase Negative Staphylococcus)	9	-	6	-	-	7	-	-	22
Enterococcus fecalis	43	-	5	12	-	5	-	-	65
Total no. of samples	373	13	116	123	151	48	6	7	810

Table 3: Anti-microbial Resistance pattern of different bacterial clinical isolates

GNB	**CIP**	**LE**	**NX**	**NIT**	**CIT**	**CST**	**CZM**	**AZM**	**GEN**	**PIT**	**MRP**	**COL**
Escherichia coli	86	59	38	26	58	52	29	21	51	36	28	0
Klebsiella pneumonia	63	48	66	18	62	49	12	19	32	43	22	0
Enterobacter cloacae	5	2	3	2	3	4	1	1	3	2	3	0
Citrobacter freundii	2	1	1	1	3	3	1	1	3	2	2	0
Proteus mirabilis	2	1	3	-	2	4	2	-	3	2	2	0
Salmonella typhi	12	-	5	-	13	9	4	-	11	6	4	0
Pseudomonas aeruginosa	20	11	-	-	-	19	53	-	51	32	29	1
Acinetobacter baumanni	12	6			-	17	22		39	11	17	0
GPC				**LZ**	**CIT**	**NV**	**VAN**	**TEI**	**COT**	**CX**	**HLG**	

Staphylococcus aureus	36	47	-	14	12	-	28	29	53	59	-
CONS (Coagulase Negative Staphylococcus)	12	6	-	9	10	6	5	-	14	-	-
Enterococcus sp.	22	11	-	8	-	-	1	1	-	-	12
CIP-Ciprofloxacin, LE-Levofloxacin, NX- Norfloxacin, NIT-Nitrofurantoin, CIT-Ceftriaxone, CST-Cefoperazone-Tazobactum, CZM-Ceftazidime, AZM-Azithromycin, GEN-Gentamicin, PIT-Piperacillin-Tazobactum, MRP-Meropnem, COL-Colistin, LZ-Linezolid, NV-Novobiocin, VAN-Vancomycin, TEI-Teicoplanin, COT-Cotrimoxazole, Cx-Cefoxitin, HLG-High Level Gentamicin											

IV. Discussion

In the present study, majority of isolates were from urine samples. Females were affected more than males because they have short urethra and are more prone to have urinary tract infections. We can correlate these findings with similar findings obtained by Abebe *et al*[18] and Chakrapani *et al*[19]. The age group suffering most in our study was above 60 years as elderly individuals do not respond to infection with an immune challenge as robustly as the young. In this study among 496 Gram-negative bacteria strains, the most commonly isolated bacteria was *Escherichia coli* (41.53%) followed by *Klebsiella pneumonia* (30.84%). Our study findings correlated well with other studies done by Aly and Balkhy[20]. *Salmonella typhi* was isolated mostly (75%) from blood samples and this finding is in tandem with what is known from *Sastry et al*[10] that blood sample gives upto 90% positivity for enteric fever in the first week of illness.

The most common resistant bacteria in ICU were *Pseudomonasa eruginosa* followed by *Acinetobacter baumannii* and *Staphylococcus aureus*. They are the leading cause of nosocomial infection. These findings correlated well with Tan *et al.*[21] Among different wards highest number of samples were isolated from Surgery (205), similar findings have been observed by Basak *et al.*[22] Among the ICUs, it has been found that SICU has maximum (45%) bacterial isolates probably due to breach in the skin or operative wound or due to presence of pre-operative indwelling urinary catheter which has been kept for too many days leading to Catheter Associated Urinary Tract Infection (CAUTI). Similar findings of CAUTI has been seen in study done by Tedja *et al*[23], so aseptic techniques during surgical procedure, regular dressing, early removal of catheter, encouraging fluid intake, using condom catheter and avoiding irrigation of the bladder can prevent such infections. In Intensive Care Unit (ICU), bacterial resistance is mainly due to cross-infectivity from other patients and the hospital environment. Improper techniques and poor hand hygiene before and after touching the patient and patients surrounding by the health care professionals are the key factors for the cross-infection which leads to increase in multi-drug resistance. This can be prevented by infection prevention and control (IPC) trainings especially proper hand washing.

Analysis of the AMR profile of bacterial isolates was done to sort out the ones with MDR. MDR organisms are described as superbugs with very limited treatment options. Patients with MDR organisms have increased risk of mortality and the cost of care for these patients can be more than double. Since the patient's condition is critical in ICU, clinicians tend to prescribe multiple antimicrobials for longer periods of time and this increases the chances of development of MDR in them. So, it is essential to minimize and de-escalate antibiotics at the right time. In this study, commonest GNB-MDR was *E.coli* and GNB-XDR was *P. aeruginosa* which correlated well with studies done by Aly [19], Qadri et al [22], and Basak et al [21]. *E.coli* strains isolated from the whole blood specimen were found to be resistant to ceftriaxone and cefoperazone-tazobactum. Similar findings were found by *Gashe et al.*[24] *Salmonella typhi* showed maximum resistance towards ciprofloxaxin and ceftriaxone. *P.aeruginosa* and *A. baumanii* has maximum resistance towards gentamicin and ceftazidime. Similar findings can be found with a study done by Aloush *et al.*[51] Among Gram positive bacteria 30% *Staphylococcus aureus* were found to be methicillin resistant *Staphylococcus aureus* (MRSA), and this correlated well with Al-Zoubi *et al.*[26] The resistance rate of Enterococcus sp. for vancomycin (VRE) was found to be 2% and similar findings were shown by Surbhi M.[27]

V. Conclusion

The leading bacterial isolates showing MDR was E.coli and those showing XDR was P. aeruginosa among patients admitted at this tertiary care hospital. For detection of change in AMR resistance patterns, irregular Ward-ICU based surveillance need to be replaced with laboratory-based ward-liaison surveillance by the infection control doctors and nurses working in close co-ordination. This is the most commonly used and best method.

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