

## Antimicrobial Sensitivity Pattern in the Mixed Intensive Care Unit in a Tertiary Care Hospital of Eastern Nepal

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**Background:** Empirical antibiotics are used in the intensive care unit based on developing countries' guidelines due to a lack of a bacteriological profile of individual ICU and institution policy. Therefore, this study was conducted to know the antibiogram of the intensive care unit and to make institution policy for antibiotic use in ICU. **Materials and methods:** It was a prospective descriptive cross-sectional study conducted in the mixed surgical and medical intensive care unit of a tertiary care hospital for one year in 625 patients. Various clinical samples were collected aseptically and organisms were identified by the cultural characteristics, morphology, gram stain, and different biochemical test. Antimicrobial susceptibility was done with a disc diffusion test. Data collection was done in a preformed sheet that included all tested antibiotic and demographic variables. Statistical analysis was done by using statistical package for the social sciences. The result was presented as frequency and percentage. **Results:** Out of 625 samples, 135(22%) showed growth in culture. Among them, 96(71%) and 39(29%) were gram-negative bacilli and gram-positive cocci respectively. The tracheal aspirate was the most common type of specimen which comprised 49(36.29%) isolates. The most common organism was *Staphylococcus aureus* which accounts for 27(20%) isolates, followed by *Acinetobacter baumannii* 25(18.51%), *Klebsiella pneumoniae* 22(16.29%) and *Pseudomonas aeruginosa* 21(15.55%). The incidence of multidrug-resistant and extended drug resistance was 44(32.5%) and 45(33%) respectively. Meanwhile, the incidence of methicillin-resistant *Staphylococcus aureus* was 70%. However, in the case of *Acinetobacter baumannii* and *Enterobacteriaceae*, all were sensitive to polymyxin B and meropenem. **Conclusion:** Antibiotics should be prescribed based on the antibiogram of individual intensive care units that can decrease antibiotic resistance. Polymyxin B and meropenem can be prescribed for gram-negative bacilli and vancomycin for *Staphylococcus aureus*.

**Key words:** *Acinetobacter*, Antibiotic, Intensive care unit, Meropenem, Polymyxin b, *Staphylococcus aureus*

Antibiotic resistance is a common, challenging, and alarming problem in developing country including Nepal. Sepsis is the most common reason for admission to the intensive care unit.<sup>1</sup> Patients admitted to the intensive care unit (ICU) are critical and empirical antibiotics are started based on developing country guidelines due to lack of government and institution policy on antibiotic use and lack of bacteriological profile of individual ICU. Empirical

use of antibiotics may not be appropriate for different ICUs in the same country because bacteriology profile changes with the geographical region and may be different for different ICUs.

The study aimed to know the common organisms in terms of its morphology and gram staining characteristics, its sensitivity pattern; and identifying those causing multidrug and pan drug-resistance in the intensive care unit.

## Methods and Materials:

This was a prospective descriptive cross-sectional study conducted in a sixty-four bedded tertiary level mix surgical medical ICU from 7th September 2018 to 6th September 2019. Ethical approval was taken from the Institutional Review Board. A total of 625 samples (sputum, pus, urine, blood, and endotracheal tube) were obtained which yielded 135 pathogenic bacteria.

The samples received in the microbiology laboratory for culture and sensitivity were inoculated on to blood and MacConkey agar. Urine specimens were inoculated onto cysteine lactose electrolyte deficient medium and incubated at 37°C for 24 hours. A blood specimen was inoculated in brain heart infusion broth and incubated for aerobically 24 hours before sub-culturing onto blood agar, mac-Conkey agar and chocolate agar. Growths obtained on solid media after 24 hours of aerobic incubation were processed for identification and antimicrobial susceptibility. Organisms were identified using the colony characteristics, the morphology of growth, gram's stain, and different biochemical test as per standard guidelines.

### Antibiotic sensitivity testing

Antimicrobial susceptibility tests were performed on Mueller Hinton agar (MHA) plate by Kirby-Bauer disc diffusion methods following the Clinical & Laboratory Standards Institute (CLSI) guidelines. The organisms were tested against following antimicrobial discs: Amikacin, Amoxicillin-clavulanic acid, Ampicillin, Ampicillin-sulbactam, Azithromycin, Aztreonam, Cefazidime, Cefepime, Cefixime, Clindamycin, Ciprofloxacin, Cotrimoxazole, Cefoperazone, Cefoperazone-sulbactam, Cefoxitin, Ceftriaxone, Cefuroxime, Chloramphenicol, Doxycycline, Levofloxacin, Linezolid, Meropenem, Nitrofurantoin, Piperacillin-tazobactam, Penicillin Polymyxin B, Tigecycline and Vancomycin.

Category of antibiotics that were tested are Aminoglycosides, Carbapenems, Cephalosporins, Folate pathway inhibitors, Fluoroquinolones, Glycopeptides, Glycylcyclines, Penicillins, Penicillins+ $\beta$ -lactamase, Lipopeptides, Macrolides,

Monobactams, Oxazolidinones, Phenicol, Polymyxins. Tetracyclines. Multidrug-resistant (MDR) was defined as acquired nonsusceptibility to at least one agent in three or more antimicrobial categories. Extensively drug-resistant (XDR) was defined as nonsusceptibility 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). Pandrug resistance (PDR) was defined as nonsusceptibility to all agents in all antimicrobial categories.

Staphylococcus aureus was characterized into Methicillin sensitive Staphylococcus aureus (MSSA) and Methicillin-resistant Staphylococcus aureus (MRSA) by using cefoxitin disc diffusion method. Isolates with a diameter of zone of inhibition (ZOI)  $\geq 22$ mm were identified as MSSA and isolates with ZOI  $\leq 21$ mm identified as MRSA.

Data collection was done in a preformed sheet. Values are calculated as frequency, percentage, and are presented in charts and tables.

## Results:

During the study period, samples were obtained for culture and sensitivity from 625 patients out of which 135(22%) showed growth in culture. Among these growths, 96(71%) and 39(29%) were gram-negative bacilli and gram-positive cocci respectively. The highest percentage of an organism was isolated from tracheal aspirate, which is (36.29%) followed by sputum (33.33%) and urine (17%). (**Table 1**)

**Table 1. Distribution of organism based on types of specimen**

| Clinical sample   | Number of bacteria isolated (%) |
|-------------------|---------------------------------|
| Tracheal aspirate | 49(36.29%)                      |
| Sputum            | 45(33.33%)                      |
| Urine             | 23(17%)                         |
| Pus               | 7(5%)                           |
| Wound swab        | 6(4.44%)                        |
| Blood             | 3(2.22%)                        |
| Ascitic Fluid     | 2(1.48%)                        |

Staphylococcus aureus 27(20%), Acinetobacter baumannii 25(18.51%), Klebsiella pneumoniae egneuro, Volume 02, Issue 02, 2020

22(16.29%), *Pseudomonas aeruginosa* 21(15.55%), *Escherichia coli* 11(8.14%) were the commonest organisms isolated from the clinical samples. (Table 2)

The antibiotic resistance pattern of predominance microorganisms was shown in table 3. Ampicillin was resistant to all the microorganism isolates. However, in the case of *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacteriaceae*, all were sensitive to Polymyxin B and Meropenem (Table 3).

**Table 2: Distribution of bacterial isolates in the clinical sample**

| Organism                            | Trachial aspirate | Sputum     | Blood    | Urine      | Pus      | Wound Swab | Ascitic fluid | Total      |
|-------------------------------------|-------------------|------------|----------|------------|----------|------------|---------------|------------|
| Gram positive cocci                 |                   |            |          |            |          |            |               |            |
| <i>Staphylococcus aureus</i> n(%)   | 5(3.7%)           | 6(4.44%)   | 3(2.22%) | 2(1.48%)   | 6(4.44%) | 5(3.7%)    | 0(0%)         | 27(20%)    |
| <i>Streptococcus Pyogens</i> n(%)   | 0(0%)             | 6(4.44%)   | 0(0%)    | 0(0%)      | 0(0%)    | 0(0%)      | 0(0%)         | 6(4.44%)   |
| <i>Enterococcus Faecalis</i> n(%)   | 0(0%)             | 4(2.96%)   | 0(0%)    | 2(1.48%)   | 0(0%)    | 0(0%)      | 0(0%)         | 6(4.44%)   |
| Gram negative bacilli               |                   |            |          |            |          |            |               |            |
| <i>Acinetobacter Baumannii</i> n(%) | 10(7.40%)         | 9(6.66%)   | 0(0%)    | 4(2.96%)   | 0(0%)    | 0(0%)      | 2(1.48%)      | 25(18.51%) |
| <i>Klebsiella Pneumonia</i> n(%)    | 11(8.14%)         | 8(5.92%)   | 0(0%)    | 3(2.22%)   | 0(0%)    | 0(0%)      | 0(0%)         | 22(16.29%) |
| <i>Pseudomonas Aeruginosa</i> n(%)  | 11(8.14%)         | 6(4.44%)   | 0(0%)    | 2(1.48%)   | 1(0.74%) | 1(0.74%)   | 0(0%)         | 21(15.55%) |
| <i>Escherichia Coli</i> n(%)        | 5(3.7%)           | 0(0%)      | 0(0%)    | 6(4.44%)   | 0(0%)    | 0(0%)      | 0(0%)         | 11(8.14%)  |
| <i>Citrobacter Freundii</i> n(%)    | 5(3.7%)           | 2(1.48)    | 0(0%)    | 1(0.74%)   | 0(0%)    | 0(0%)      | 0(0%)         | 8(5.92%)   |
| <i>Enterobacter Aerogenes</i> n(%)  | 2(1.48%)          | 2(1.48%)   | 0(0%)    | 0(0%)      | 0(0%)    | 0(0%)      | 0(0%)         | 4(2.96%)   |
| <i>Proteus Vulgaris</i> n(%)        | 0(0%)             | 0(0%)      | 0(0%)    | 3(2.22%)   | 0(0%)    | 0(0%)      | 0(0%)         | 3(2.22%)   |
| <i>Klebsiella Oxytoca</i> n(%)      | 0(0%)             | 2(1.48%)   | 0(0%)    | 0(0%)      | 0(0%)    | 0(0%)      | 0(0%)         | 2(1.48%)   |
| <b>Total</b>                        | 49(36.29%)        | 45(33.33%) | 3(2.22%) | 23(17.03%) | 7(5.18%) | 6(4.44%)   | 2(1.48%)      | 135(100%)  |

**Table 3: Antibiotics resistance pattern of predominance microorganism of patients admitted in ICU of tertiary care hospital (%)**

| Antibiotics             | A. Baumannii (n=25) | P. Aeruginosa (n=21) | K. Pneumoniae (n=22) | E. Coli (n=11) | Proteus Vulgaris (n=3) | E. Aerogenes (n=4) | C. Freundii (n=8) | S. Aureus (n=27) | Strep. Pyogens (n=6) | E. Faecalis (n=6) |
|-------------------------|---------------------|----------------------|----------------------|----------------|------------------------|--------------------|-------------------|------------------|----------------------|-------------------|
| Amikacin                | 69                  | 17                   | 40                   | 42             | 34                     | 34                 | 0                 | 0                | 0                    | 0                 |
| Amoxyclav               | 100                 | 89                   | 82                   | 100            | 100                    | 100                | 100               | 0                | 0                    | 0                 |
| Ampicillin              | 100                 | 100                  | 100                  | 100            | -                      | 100                | 100               | 100              | 100                  | 100               |
| Ampicillin-Sulbactam    | 71                  | 88                   | 56                   | 80             |                        | 34                 | 34                | 67               | 100                  | 100               |
| Azithromycin            | 100                 | 100                  | 93                   | 100            |                        | 100                | 100               | 0                | 75                   | 75                |
| Aztreonam               | 85                  | 100                  | 34                   | 100            |                        | 50                 | -                 | -                | -                    | -                 |
| Cefepime                | 100                 | 100                  | 89                   | 100            | 100                    | 100                | -                 | 100              | -                    | -                 |
| Cefixime                | 100                 | 100                  | 100                  | 100            | 34                     | -                  | 100               | 100              | -                    | -                 |
| Cefoperazone            | 100                 | 40                   | 67                   | 100            | -                      | -                  | -                 | -                | -                    | -                 |
| Cefoperazone-sulbactam  | 65                  | 35                   | 42                   | 85             | -                      | -                  | -                 | -                | -                    | -                 |
| Cefoxitin               | 100                 | -                    | -                    | -              | -                      | -                  | -                 | 70               | 100                  | 100               |
| Ceftazidime             | 89                  | 65                   | 67                   | 100            | 34                     | 67                 | 100               | -                | -                    | -                 |
| Ceftriaxone             | 89                  | 58                   | 60                   | 100            | 34                     | 34                 | 50                | 60               | 100                  | 100               |
| Cefuroxime              | 100                 | 100                  | 69                   | 100            | 34                     | 34                 | 100               | 50               | -                    | -                 |
| Chloramphenicol         | 73                  | 100                  | 43                   | 20             | -                      | 0                  | -                 | 89               | 0                    | 0                 |
| Ciprofloxacin           | 62                  | 20                   | 43                   | 100            | 100                    | 50                 | 18                | 91               | 50                   | 50                |
| Clindamycin             | -                   | -                    | -                    | -              | -                      | -                  | -                 | 64               | 0                    | 0                 |
| Cotrimoxazole           | 35                  | 20                   | 59                   | 60             | 100                    | 25                 | 22                | 85               | 40                   | 40                |
| Doxycycline             | 50                  | 100                  | 32                   | 46             | 0                      | -                  | 0                 | 36               | 34                   | 17                |
| Levofloxacin            | 62                  | 42                   | 48                   | 82             | 100                    | 0                  | 15                | 77               | 40                   | 24                |
| Linezolid               | -                   | -                    | -                    | -              | -                      | -                  | -                 | 61               | 0                    | 60                |
| Meropenem               | 0                   | 0                    | 0                    | 50             | 0                      | 0                  | 0                 | 0                | -                    | -                 |
| Nitrofurantoin          | 100                 | -                    | 100                  | 50             | 100                    | -                  | 0                 | 100              | -                    | 100               |
| Penicillin              | -                   | -                    | -                    | -              | -                      | -                  | -                 | 100              | 100                  | 100               |
| Piperacillin Tazobactam | 53                  | 17                   | 0                    | 0              | -                      | 0                  | 0                 | 30               | 0                    | 0                 |
| Polymyxin B             | 0                   | 0                    | 0                    | 0              | 0                      | 0                  | 0                 | -                | 0                    | 0                 |
| Tigecycline             | 0                   | 100                  | 0                    | -              | -                      | 0                  | 0                 | -                | -                    | -                 |
| Vancomycin              | -                   | -                    | -                    | -              | -                      | -                  | -                 | 0                | 0                    | 0                 |

Overall, the Incidence of multidrug-resistant and extended drug resistance was 44(32.5%) and 44(32.6%) respectively (**Figure 1**). Furthermore, MDR in gram-positive cocci and gram-negative bacilli was 13(33.33%) and 31(32.2%) respectively.

Also, XDR in gram-positive cocci and gram-negative bacilli was 11(28.2%) and 34(34.3%) (**Table 4**). Meanwhile, the incidence of methicillin-resistant staphylococcus aureus was 70%.

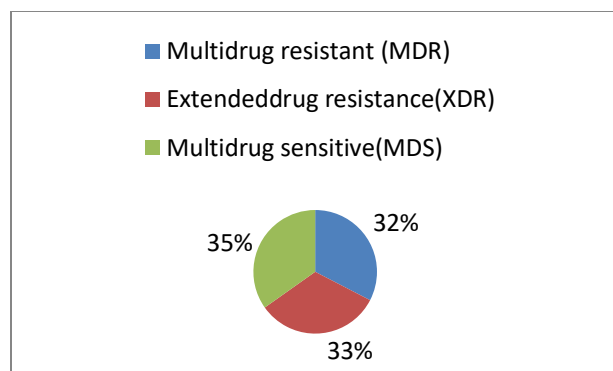


Fig 1: Incidence of MDR and XDR in the Intensive care unit

Table 4. Distribution of MDR, XDR, and MDS bacterial isolates in ICU.

| Types of isolates | Gram-positive cocci | Gram-negative |
|-------------------|---------------------|---------------|
|                   | N(%)                | bacilli N(%)  |
| MDR               | 13(33.33%)          | 31(32.2%)     |
| XDR               | 11(28.2%)           | 34(34.3%)     |
| MDS               | 15(38.4%)           | 31(33.3%)     |

**Table 3** Shows that *Acinetobacter* showed 100% resistance to Amoxicillin-clavulanic acid, Ampicillin, Azithromycin, Cefoxitin, Cefoperazone, Cefuroxime, Cefixime, Nitrofurantoin, and Cefepime. It showed high rate of resistance to Ceftriaxone (89%), Ceftazidime (89%), Aztreonam (85%), Chloramphenicol (73%), Ampicillin-sulbactam (71%), Amikacin (69%), Cefoperazone-sulbactam (65%), Ciprofloxacin and Levofloxacin (62%), Piperacillin-tazobactam (53%). Doxycycline and Cotrimoxazole showed 50% and 30% resistance to *Acinetobacter*. It showed a 100% sensitivity to Meropenem, Polymyxin, and Tigecycline.

The *Klebsiella pneumoniae* showed 100% resistance to Ampicillin, Cefixime and Nitrofurantoin. It showed high rate of resistance to Azithromycin (93%), Cefepime (89%), Amoxicillin-clavulanic (82%), Cefuroxime (69%), Cefoperazone (67%), Ceftazidime (67%), Ceftriaxone (60%), Cotrimoxazole (59%), Ampicillin-sulbactam (56%). *Klebsiella pneumoniae* showed

resistance to Cefoperazone-sulbactam, Levofloxacin, Ciprofloxacin, Chloramphenicol, Aztreonam, Doxycycline, and Amikacin in less than 50% of patients. It showed 100% sensitivity to Meropenem, Polymyxin B, Tigecycline, and Piperacillin-tazobactam.

The *Pseudomonas aeruginosa* showed 100% resistance to Ampicillin, Azithromycin, Aztreonam, Cefuroxime, Cefixime, Cefepime, Chloramphenicol, Doxycycline, and Tigecycline. It showed a high rate of resistance to Amoxicillin-clavulanic (89%), Ampicillin-sulbactam (88%), Ceftazidime (65%), Ceftriaxone (58%). *Pseudomonas aeruginosa* showed resistance to Cefoperazone-sulbactam, Cefoperazone, Levofloxacin, Ciprofloxacin, Amikacin, Cotrimoxazole, Piperacillin-tazobactam in less than 50% of patients. It showed a 100% sensitivity to Meropenem and Polymyxin B.

Enterobacteraceae showed 100% resistance to Ampicillin, Amoxicillin-clavulanic, Azithromycin, Cefixime, and Cefepime. It showed resistance to Amikacin, Ceftriaxone, Ceftazidime, Cefoperazone-sulbactam in less than 50% of patients. It showed 100% sensitivity to Meropenem, Polymyxin B, Tigecycline, and Piperacillin-tazobactam.

### Discussion:

The intensive care unit is called a hub of infection. Infection can be primary or secondary. Secondary infection is more common than primary infection in ICU.<sup>2</sup> The main aim of ICU care is to have a decrease in antimicrobial resistance. This will ensure the healthy outcome, decrease in length of stay, and antibiotic cost in ICU. Therefore, it is important to know the bacterial profile and antibiogram of a particular ICU in any hospital.<sup>3</sup>

Modern critical care is a multi-disciplinary team lead by the intensivist, clinical microbiologist, and supported as required by other specialties. A combined effort of the intensivist and the clinical microbiologist is required for better clinical outcomes and a decrease in antibiotic resistance.<sup>4,5</sup>

This study showed that culture was positive in 135(22%). while in other studies percentage varied from 28% to 67%.<sup>1-7</sup> This difference may be due to

the collection of samples after the administration of antibiotics, bacteria may be sensitive to empirically administered antibiotics, different patient populations in different studies, maintenance of aseptic precaution, antibiotic stewardship.

This study showed that gram-negative infection is more common than gram-positive which is similar to other studies from developing country whereas gram-positive infection is more common in developed country.<sup>1-8</sup>

The present study shows that tracheal aspirate 49(36.26%) was a common sample which is similar to other studies.<sup>1,3,7,9</sup> Studies conducted by Raval et al<sup>10</sup> and Sarkar et al<sup>11</sup> have shown that urinary tract infection was more common than respiratory tract infection.

*Staphylococcus aureus* 27(20%) was most common bacteria isolated in our study while in other studies from Asian countries<sup>1,3-7,9,10,12</sup> percentage varied from 2% to 17% and in western study percentage varied from 20% to 25%<sup>8</sup> Our ICU receives patients not only from our center itself but also from other hospitals and most of the time these patients are usually with high Acute Physiology And Chronic Health Evaluation (APACHE) scores and are already on multiple antibiotics. This might explain the reason we have a higher incidence of *Staphylococcus aureus* in our study, unlike others.

Our study revealed that *Acinetobacter* 25(18.5%) followed by *Klebsiella pneumoniae* 22(16.5%) and *Pseudomonas aeruginosa* were the most common gram-negative bacilli in our study that is similar to other studies.<sup>1,6,7,13</sup> Studies conducted by Sanjana et al, Singh et al and Raval et al showed *Pseudomonas* was common bacteria followed by *Klebsiella*. This difference may be because the organism can vary within the country, state, and different hospitals.

Our study showed 100% resistance to Ampicillin among *Acinetobacter*, *Klebsiella*, *Pseudomonas*, *Enterobacteriaceae*, *Staphylococcus*, *Streptococcus pyogenes*, and *Enterococcus faecalis*. This may be due overuse of this antibiotic.

This study has shown that *Acinetobacter*, *Pseudomonas* *Klebsiella* were resistant to most of the commonly used antibiotic and were sensitive to

*Meropenem* and *Polymyxin B* that is similar to other studies.<sup>6-13</sup>

Our study showed an incidence of MRSA to be 70% which is similar to the study conducted by Sapkota et al<sup>14</sup> while in other studies percentage varied from 10% to 60%.<sup>7-10</sup> This difference may be due to the overuse of antibiotics, high prevalence of MRSA in this region of the country.

The incidence of MDR and XDR was 61.5% and 66.5% respectively in our study that is similar to other studies.<sup>5,9,13,15</sup> Studies conducted by Shrestha et al<sup>1</sup>, Bhandari et al<sup>7</sup>, Raval et al<sup>10</sup> that percentage varied from 70-85%. This difference may be due to early use of higher antibiotic for a common infection, lack of use of antibiotic based on antibiogram.<sup>17,18</sup>

This study showed that *Acinetobacter*, *Klebsiella*, *Enterobacteriaceae* showed 100% sensitive to *Polymyxin B* and *Meropenem* that is similar to a study conducted by Basnet et al.<sup>19</sup>

Our study has limitations like it was a single-center study and the outcome of the patient was excluded. Multiple trauma patients were included in this examination. This investigation was directed in a private tertiary care center consequently the patient population may not be illustrative of all socioeconomic status. All disease was incorporated whether it was primary or secondary.

## Conclusion:

It tends to be presumed that antibiotics ought to be prescribed based on the antibiogram of individual intensive care units that can diminish antibiotic resistance. Antibiotic stewardship programs ought to be followed in each hospital.

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