Antibiotic Resistance Pattern in Intensive Care Unit of a Tertiary Care Hospital, Nepal

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ABSTRACT

Background

Intensive care unit (ICU) is the especial department of the hospital where critically ill patients are treated with the unique type of technologies to revert back to functional by body's own mechanism. Therefore, there are lots of external intervention with chance of getting bacterial infections. Antibiotics are medicines used to prevent and treat such bacterial infections. However, due to selective broad spectrum antibiotic pressure there is great chances to develop antimicrobial resistance at any time during hospital stay in intensive care unit.

Objective

To find out the antibiotic resistance pattern among Gram negative bacteria in Intensive Care Unit.

Method

A Descriptive cross-sectional study was conducted in Department of Microbiology of Tertiary care center for 18 months On the basis of previous sample load census method was used to include 500 sample from intensive care unit during study period. Among them only Gram negative bacteria were included in the study. All the samples were processed following standard methodology.

Result

Out of 500 samples, growth was observed in 451 (90.2%) samples. Among all the isolates *Escherichia coli* (29.6%) was predominant organism. It had shown high resistance towards Ciprofloxacin (93.5%) even in urine sample Ciprofloxacin (86.9%).

Conclusion

Our study showed *Escherichia coli* as a major organism in intensive care unit. This was resistant to commonly used oral antibiotic leaving restricted option for use of higher antibiotics. Therefore, continuous surveillance of such bacterial pathogen is warranted with implementation of effective Infection Prevention and Control measures in Health Care setting with emphasis to critical care units.

KEY WORDS

Antibiotic resistance, Escherichia coli, Intensive care unit

INTRODUCTION

Intensive Care Unit (ICU) is a special department of the Hospital where various advance techniques and technologies are applied on the vital organs of critically ill patients and are made functional until it reverts back to functional by body's own mechanism. Therefore, various external interventions may lead to the possibilities of acquiring Health Care Associated Infections (HCAI).[1-3] According to World Health Organization (WHO), out of every 100 patients in acute-care hospitals, seven patients in high-income countries and 15 patients in low- and middle-income countries will acquire at least one health care-associated infection (HAI) during their hospital stay. On average, 1 in every 10 affected patients will die from their HAI.[4]

Antibiotics are used to prevent and treat bacterial infections. However, irrational use of antibiotics has led to the development of antibiotic resistance. These resistance bacteria may infect humans or animals and the infections caused by them are difficult to treat than those caused by non-resistant bacteria.[5]

As most ICU patients are frequently on broad spectrum antibiotics, this induces selective antibiotic pressure which leads to development of antibiotic resistance among the microorganisms of ICUs which can be easily transmitted from one patient to another.

Therefore, this study was conducted to understand the AMR pattern of bacterial pathogens isolated from patients admitted in ICU of Shree Birendra Hospital (SBH), Chhauni, Kathmandu with special preference to Gram Negative isolates. This study establishes the baseline date of the various resistance patterns in our hospital.

METHODS

A descriptive cross-sectional study was conducted in Department of Microbiology, Shree Birendra Army Hospital, Chaunni which is the teaching hospital of Nepalese Army Institute of Health and Sciences (NAIHS) after taking ethical clearance from Institutional Review Board of NAIHS, Kathmandu with reference number 246. The study was conducted from February 2020 till August 2021 for 18 months. Sample size was 500 which was calculated by consensus method considering sample volume received in the Microbiology Laboratory for last three years. Among all samples (urine, wound and pus aspirate, lower respiratory tract, blood, body fluids and urogenital swab) received in the Microbiology Laboratory for diagnostic purpose. Only Gram negative bacteria were included in the study. Gram positive bacteria were excluded from the study. Convenience sampling method was used.

All these samples were processed as per standard guidelines mention in Clinical Laboratory Standard Institute (CLSI).[6] Urine samples were inoculated in Cysteine Lactose Electrolyte Deficient (CLED) media while other samples were inoculated in Blood agar, MacConkey Agar and Chocolate Agar. Quality control of Laboratory equipment, reagents and media were carried out regularly. Mueller Hinton Agar (MHA) and antibiotic disc were checked for their lot number, manufacture and expiry date and proper storage condition. For standardization of the Kirby-Bauer disc diffusion test, for performance testing of antibiotics and MHA, the control strain of *Escherichia coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 27853) were tested primarily. Quality of sensitivity testing were maintained by the thickness of MHA at 4 mm and PH at 7.2- 7.4. Identification of non-fermenters were done by using VITEK 2 Compact (bioMerieux).

Data was entered in Microsoft Excel 2016 and analysis was done using IBM SPSS Statistics version 16.0. The point estimate was calculated at a 95% CI.

RESULTS

Total of 500 samples were included in this study. Various samples were received in the laboratory during study period among which pus and pus aspirate were the most common sample followed by urine. The details of distribution of samples with growth pattern is as shown in table 1.

Table 1. Distribution of Samples with Growth Pattern

Samples	Frequency (%)	Growth (%)
Pus aspirate and wound Swab	157 (31.4)	155 (98.7)
Urine	123 (24.6)	123 (100)
Lower respiratory tract samples	116 (23.2)	109 (93.9)
Blood	75 (15.0)	52 (69.3)
Sterile body fluid	23 (4.6)	6 (26)
Urogenital swab	6 (1.2)	6 (100)
Total	500	451

Among the growth, *Escherichia coli* (29.6%) was the most common organism followed by Gram negative non fermentative bacilli (12%) distribution as shown in the table 2.

Table 2. Distribution of Gram negative bacteria

Organism	Number (%)
Escherichia coli	148 (29.6)
Non Fermenter Gram Negative Bacilli	60 (12.0)
Pseudomonas aeruginosa	54 (10.8)
Acinetobacter species	43 (8.6)
Klebsiella species	38 (7.6)
Enterobacter species	37 (7.4)

Escherichia coli was the commonest Gram negative organism in Urine, Non-fermenters were frequently isolated from Pus and pus aspirate whereas *Pseudomonas*

Table 3. Frequency and resistance percentage of isolates from pus aspirate and wound swab

Antibiotic	*Escherichia coli* (n=31)	Non fermenter GNB (n=31)	*Acinetobacter* (n=23)	*Pseudomonas aeruginosa* (n=13)	*Enterobacter* (n=18)	*Klebsiella* (n=15)
Ampicillin	11(35.4%)	31(100%)	ND	ND	18 (100%)	15(100%)
Amoxyclav	11(35.4%)	29(93.5%)	ND	ND	18(100%)	12(80%)
Piperacillin	19(61.2%)	29(93.5%)	23(100%)	06(46.1%)	14(77.7%)	13(86.6%)
Piperacillintazobactam	17(54.8%)	26(83.8%)	23(100%)	02(15.3%)	11(61.1%)	08(53.3%)
Cefoperazone	25(80.6%)	27(87%)	22(95.6%)	ND	16(88.8%)	14(93.3%)
Cefotaxime	24(77.4%)	28(90.3%)	23(100%)	ND	16(88.8%)	14(93.3%)
Cetriaxone	24(77.4%)	27(87%)	23(100%)	ND	16(88.8%)	15(100%)
Cefixime	22(70.9%)	28(90.3%)	23(100%)	ND	13(72.2%)	13(86.6%)
Cefepime	15(48.3%)	27(87%)	23(100%)	02(15.3%)	11(61.1%)	10(66.6%)
Ceftazidime	21(67.7%)	30(96.7%)	23(100%)	08(61.5%)	17(94.4%)	14(93.3%)
Amikacin	10(32.2%)	12(38.7%)	22(95.6%)	06(46.1%)	11(61.1%)	10(66.6%)
Gentamicin	08(25.8%)	12(38.7%)	23(100%)	ND	12(66.6%)	07(46.6%)
Ciprofloxacin	29(93.5%)	29(93.5%)	23(100%)	10(76.9%)	16(88.8%)	15(100%)
Ofloxacin	26(83.8%)	24(77.4%)	23(100%)	12(92.3%)	14(77.7%)	11(73.3%)
Imipenem	10(32.2%)	25(80.6%)	21(91.3%)	07(53.8%)	15(83.3%)	06(40%)
Meropenem	05(16.1%)	24(77.4%)	22(95.6%)	05(38.4%)	11(61.1%)	06(40%)
Doxycycline	14(45.1%)	13(41.9%)	21(91.3%)	ND	14(77.7%)	12(80%)
Cotrimoxazole	18(58%)	24(77.4%)	23(100%)	ND	14(77.7%)	12(80%)

ND: Not done as per CLSI guideline

Table 4. Frequency and Resistant percentage of isolates in Urine samples

Antibiotic	Escherichia. Coli (n=92)	Pseudomonas aeriginosa (n=11)	Non Fermenter GNB (n=7)	Klebsiella species (n=3)	Enterobacter species (n=3)	*Acinetobacter* species (n=3)
Ampicillin	40(43.3%)	ND	06(85.7%)	03(100%)	03(100%)	ND
Amoxyclav	49(53.2%)	ND	03(42.8%)	03(100%)	03(100%)	ND
Piperacillin	52(56.5%)	08(72.7%)	04(57.1%)	01(33.3%)	03(100%)	03(100%)
Piperacillin+ tazobactam	32(34.7%)	08(72.7%)	03(42.8%)	01(33.3%)	02(66.6%)	03(100%)
Cefoperazone	50(54.3%)	ND	05(71.4%)	02(66.6%)	03(100%)	03(100%)
Cefotaxime	62(67.3%)	ND	05(71.4%)	02(66.6%)	02(66.6%)	03(100%)
Ceftriaxone	60(65.2%)	ND	04(57.1%)	02(66.6%)	02(66.6%)	03(100%)
Cefixime	50(54.3%)	ND	03(42.8%)	02(66.6%)	01(33.3%)	03(100%)
Cefepime	25(27.1%)	09(81.8%)	04(57.1%)	02(66.6%)	01(33.3%)	03(100%)
Ceftazidime	35(38%)	10(90.9%)	03(42.8%)	02(66.6%)	01(33.3%)	03(100%)
Amikacin	44(47.8%)	10(90.9%)	06(85.7%)	00(0%)	01(33.3%)	02(66.6%)
Gentamicin	38(41.3%)	ND	04(57.1%)	00(0%)	01(33.3%)	02(66.6%)
Ciprofloxacin	80(86.9%)	10(90.9%)	07(100%)	02(66.6%)	03(100%)	03(100%)
Ofloxacin	65(70.6%)	10(90.9%)	05(71.4%)	02(66.6%)	02(66.6%)	ND
Norfloxacin	48(52.1%)	11(100%)	04(57.1%)	02(66.6%)	03(100%)	03(100%)
Imipenem	19(20.6%)	08(72.7%)	03(42.8%)	01(33.3%)	01(33.3%)	02(66.6%)
Meropenem	18(19.5%)	08(72.7%)	04(57.1%)	01(33.3%)	01(33.3%)	02(66.6%)
Nitrofurantoin	44(47.8%)	11(100%)	06(85.7%)	00(0%)	02(66.6%)	03(100%)
Doxycycline	45(48.9%)	10(90.9%)	04(57.1%)	00(0%)	02(66.6%)	ND
Cotrimoxazole	66(71.7%)	10(90.9%)	06(85.7%)	00(0%)	03(100%)	03(100%)

ND: Not done as per CLSI guideline

aeruginosa was commonly isolated from the samples from lower respiratory tract.

Among non-fermenters (n=60), *Acinetobacter* species was predominant (n=45) followed by *Stenotophomonas maltophilia* (n=8), *Burkholderia cepacia* (n=5) and *Kocuria kristinae* (n=2).

In Urine, like other studies, the most commonly isolated organism was *Escherichia coli* which was most sensitive to

Meropenem followed by fourth generation Cephalosporin like Cefepime. Frequency and Resistant percentage of isolates are as shown in table 4.

In the blood sample, *Acinetobacter* were the frequently isolated organism which were most resistant to Cefipime (100%) and Ceftazidime (100%) followed by Amikacin (92.8%), Imipenem (92.8%) and Ciprofloxacin (92.8%). Non fermenter Gram negative bacteria were successor organism which were resistant to Cefipime (100%) and Ofloxacin (100%) followed by Ciprofloxacin (90%), Piperacillin+Tazobactum (90%) and Cefoperazone (90%)

Among the lower respiratory tract sample, Non fermenter Gram negative bacilli were frequently isolated organism which were most resistant to Cefixime (96.6%) and Ciprofloxacin (93.3%) followed by Carbapenem (90%) and Cefipime (90%).

DISCUSSION

In our study, distribution of the organisms was diverse from other studies conducted in Nepal as well as different part of the world. In most of the studies conducted in different part of Nepal and other part of world *Acinetobacter spp* was found to be major organism in the ICU followed by *Klebsiella spp*.[7-9] Even in the comprehensive study conducted in different Asian countries also showed *Acinetobacter spp* as a predominant organism.[10] However, our study found *Eschericia coli* as predominant organism which was a similar to the study conducted in different part of the world.[11,12] This discrepancy of result may be due to setting of the place where the study was conducted which result into the distribution of isolated organism. Therefore, location based study should be conducted to know the distribution of the organism for that particular location as well as antibiotic resistance pattern of organisms for initiation of initial treatment.

Escherichia coli was the most common organism in pus and pus aspirate and urine samples which was similar to the other study.[11] *Escherichia coli* had shown more resistance towards Ciprofloxacin (93.5%) and Ofloxacin (83.8%) in case of pus and pus aspirate and for urinary *Escherichia coli* also resistance were more towards Ciprofloxacin(86.9%) and Ofloxacin (70.6%). Resistance pattern of E. coli towards ciprofloxacin was almost similar to the other studies (82.7%), (90.3%) and (86%) respectively from different institution of Nepal.[7,9,13] Increasing resistance pattern towards such oral antibiotic could be well explained by the fact that these antibiotics are easily accessible without prescription. Another contributor to such phenomenon in a developing nation such as ours could be because of the lack of surveillance from the stakeholders involved in the medical sector.

In the blood sample, *Acinetobacter* species were predominant organisms. The resistance patterns of the *Acinetobacter* were much more dreadful among other isolates from the blood. Unfortunately, it was resistant to almost all of the widely used antibiotics. The resistance pattern was similar with a study conducted from different part of the world.[8,9,14] The characteristic of *Acinetobacter* as MDR may be due to chance of acquisition of resistance gene and their ability to persist as well as multiply in hospital environment.[15] The rationale behind *Acinetobacter* being resistance to all most all test drug could be blood sample collected from critically ill patients from ICU who were getting treatment in ICU for longer period.

There was an interesting finding of *Kocuria kristinae* (n=2) in a blood sample. Both of the isolates were from pediatric age groups, one was even isolated from a neonate of 2 days of life. It was similar to the study conducted by Chen HM.[16]

This bacterium belongs to the member of the Micrococcus family. In Year 2008 Centers for Disease Control and Prevention/National Healthcare Safety Network surveillance defined the bacterium as healthcare-associated infections, previously which was thought to be common skin contaminants.[17] They may be pathogenic in immunocompromised host. Identification of such organism is not possible in normal setting of Microbiology Laboratory. It required especial type of automated identification System like Vitek 2 Compact. In routine laboratory procedure these type of organism might be identified as contaminant. Therefore, identification of such organism might be helpful in case of extreme of ages where immune status might be compromised. However, antibiotic sensitivity guideline is not mentioned in CLSI.

Our study revealed Non fermenter as predominant organism in samples from lower respiratory tract. The resistance pattern of this organism was towards oral Quinolone, Ciprofloxacin (93%). This result was almost similar to the study conducted (94.2%) and (92%) respectively from different parts of Nepal.[9,13] This fact is also true due to rampant use of antibiotic without prescription from local pharmacy. Upon landing at ICU for critical illness such antibiotic is already in non-responsive stage. Therefore, there is only option to choose broad spectrum antibiotics.

This study was single centric with small sample size and only ICU samples were included in the study. After getting antibiogram data, effectiveness of antibiotics upon the patient could not be assessed as we did not follow up the cases. Phenotypic as well as Genotypic mechanism of various resistance among these bacteria could not be identified. At the same time, among the non-fermenter GNB, Minimum Inhibitory Concentration (MIC) of drug could not be assessed due to limitation of resources.

CONCLUSION

MDR isolates are disseminating all over the health care setting which is much more dreadful in critically ill patients of ICU. Our study has revealed the resistant pattern of almost all of the isolates from different samples is rising at an alarmingly high rate. Among them the prevalence of resistance among Non-fermenter and *Pseudomonas aeruginosa* were at its peak. If this situation persists for a longer period, it won't leave any last resort antibiotics which will ultimately lead to an Apocalypse. Therefore, monitoring of the antibiotic consumption and its resistance pattern is the one of the most important solutions to overcome such dreadful situations.

This type of study in frequent intervals will surely help clinicians to choose appropriate antibiotics on the basis of resistance pattern of pathogens. The data collected in such a study will help strengthen the Antibiotic Stewardship of a particular Institute.

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