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Original Investigation

Antibiotic Resistance among Gram Negative Bacilli Isolated from the ICU Admitted Patients Attending Chitwan Medical College Teaching Hospital

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ABSTRACT

INTRODUCTION: Antimicrobial therapy is the main stone in treatment. Gram negative bacilli are common cause of sepsis, pneumonia and urinary tract infections in ICU patients. Their treatment becomes more challenging due to the evolution of multiple drug resistant strains. The findings of this study would be useful in the formation of effective diagnostic approaches and policy of antimicrobial therapy for the treatment of infections in a similar intensive care hospital setting. **MATERIALS AND METHODS:** A Laboratory based descriptive cross-sectional study was conducted at the department of clinical microbiology of the Chitwan Medical College Teaching Hospital based on the reports of 129 bacterial isolated of various clinical specimens from different ICUs of hospital between April 2018 to September 2018. **RESULTS:** Among the 129-gram bacilli isolated mono bacterial growth were 116(89.92%) while remaining 13(10.08%) had poly bacterial or mixed organisms isolated. The most frequently isolated organisms were *Acinetobacter spp.* 51(39.55%), *Escherichia coli* 25(19.37%), *Klebsiella spp.* 27(20.93%), *Pseudomonas aeruginosa* 17(13.95%) and *Enterobacter spp.* 8(6.2%). Antibiotic resistance was observed in many organisms with multidrug resistance 97(75.2%) among them. High level of resistance was observed to Cefotaxime (98.04%), Ceftriaxone (96.08%), Imipenem (80.39%), Ampicillin/sulbactam (72.55%) and Amikacin (70.59%). Ciprofloxacin (68.63%), Levofloxacin (27.45%) and Meropenem (28.21%) were found to be relatively effective against *Acinetobacter spp.* Isolated. **CONCLUSIONS:** Most of the frequently isolated organisms are multi drug resistant.

Keywords: Antibiotic resistance, Intensive care units, multi drug resistance.

INTRODUCTION

Antimicrobial therapy is the main stone in treatment. Intensive care units (ICUs) are specialized sections of a hospital with comprehensive and continuous care, hi-tech medicine, mechanical ventilator support; hemodynamic monitoring; total parenteral nutrition; innovative forms of surgery; and a huge arsenal of drugs, specially anti-infective of every genre [1,2]. They are important for the control and treatment of the most variable and severe illness that effect the human body, representing a powerful tool in modern medicine [3]. Inspite of their invaluable and well-established role, ICU often is called the epicenter of infections due to its extremely vulnerable population and increased risk of becoming infected through multiple procedures and use of invasive devices distorting the anatomical integrity protective barriers of patients [5]. Patients in the ICU have a 5-7 fold higher risk of a nosocomial infection compared with the average patient and 20-25% of all nosocomial infections develop in ICUs [6,7]. Infections due to Gram negative organisms continue to be one of the leading causes of morbidity and mortality.

Gram negative bacilli are common cause of sepsis, pneumonia and urinary tract infections in ICU patients [10-12]. Their treatment becomes more challenging due to the evolution of multiple drug resistant strains [13]. Globally, ICUs are encountering emergence and spread of antibiotic

resistant pathogens and for some pathogens, only a few therapeutic options are available [14]. The burden of resistance, however, is probably more due to the higher rate of inappropriate empirical antimicrobial treatment associated with infections caused by multi drug resistant pathogens than with the virulence of particular MDR strains [15].

Due to lack of local data, western guidelines on initial antibiotic selection are generally applied in Nepalese ICUs and the empirical choice made for serious ICU related infections. This descriptive cross-section study was carried out in ICU to obtain more information on the characteristics and outcomes of infections in our ICU population. The findings of this study would be useful in the formation of effective diagnostic approaches and policy of antimicrobial therapy for the treatment of infections in a similar intensive care hospital setting.

MATERIALS AND METHODS

Study design and setting

A laboratory based descriptive cross sectional study was conducted at the department of clinical microbiology of the Chitwan Medical College Teaching Hospital based on the reports of bacterial isolated of various clinical specimens from different ICUs of hospital between April 2018 to September 2018.

Sample and procedure

The clinical isolates of 129 GNB recovered from Blood, Body fluid, Endotracheal aspirate, Pus, Sputum and Urine samples were inoculated into suitable media according to their requirements and analyzed, identified using standard microbiological techniques and differentiation to species level using biochemical reactions [1]. The specimens were collected appropriately and transported to the clinical microbiology laboratory with minimal time delay. Specimens that strictly meet the criteria recommended by the American Society for Microbiology (ASM) [1] were selected for further processing and those specimens not fulfilling the ASM criteria and duplicate specimens from the same patients are excluded in this study.

The antibiotic susceptibility testing of the 129 pathogens isolated from the clinical specimens against different antibiotics were done using Muller Hinton Agar (MHA) by the standard disk diffusion technique of Modified Kriby-Bauer method as recommended by CLSI [1]. For this purpose following antibiotics (Hi-media disc in µg) were used; Amikacin (30), ampicillin/sulbactam (10/10), Carbenicillin (100), Cefotaxime (30), Ceftazidime (30), ceftriaxone (30), ciprofloxacin (5), Imipenem (10), levofloxacin (5), Meropenem (10), Piperacillin (100), Piperacillin/Tazobactam (100/10) and tobramycin (10). Quality control of disc diffusing tests was performed using ATCC control strains of *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853.

Multidrug resistance (MDR) bacterial isolates were identified according to the criteria recommended by International expert committee of the European Centre for Disease Control (ECDC) and the Centers for Disease Control and Prevention (CDC) [1]. According to this study, the isolate resistant to at least one antimicrobial from three different group of first line drugs tested was regarded as multidrug resistant (MDR).

Statistical analysis and data management

Data were entered into Microsoft excel for analysis. Frequencies and percentages were used to present the findings.

Ethical considerations

Ethical approval was taken from CMC-IRC (Chitwan Medical College - Institutional Review Committee) and Department of Laboratory Medicine, CMCTH. The reference number for this approval is CMC/ADM/075/076/246, Tuesday November 13, 2018 A verbal informed consent was taken from the patient prior to his/her inclusion in research. All required data for my research was taken form test that was prescribed by clinicians and patients were not extra charged for my research purpose.

RESULTS

A total of 129 isolates of GNB were isolated from the ICU admitted patients. One hundred and sixteen samples (89.92%) had single growth organism, while the remaining thirteen (10.08%) had poly bacterial or mixed organisms isolated. Growth is found to be highest in endotracheal aspirate 63 (48.8%) followed by sputum 27 (20.9%), Urine 21 (16.3%), blood 12 (9.3%), pus 5 (3.9%) and

Table 1| Distribution of different gram-negative bacilli in various specimens

Organisms	Blood	Body fluid	E.T.	Pus	Sputum	Urine	Total
Acinetobacter sps.	2	0	36	2	7	4	51
E. coli	2	1	4	2	4	12	25
Enterobacter sps.	2	0	2	0	4	0	8
Klebsiella sps	5	0	11	0	7	4	27
Pseudomonas aeruginosa	1	0	10	1	5	1	18
Total	12	1	63	5	27	21	129

Table 2| Antibiotic resistance pattern of predominant microorganisms isolated from the specimens of the patients admitted in ICUs of CMCTH (in %)

Antibiotics	*Acinetobacter sps (51)*	*Escherichia coli (25)*	*Klebsiella sps. (27)*	*Pseudomonas aeruginosa (18)*	*Enterobacter sps. (8)*
Amikacin	70.59	22.22	42.31	35.29	50.0
Ampicillin/sulbactam	72.55	-	-	-	-
Carbenicillin	-	-	-	47.06	-
Cefotaxime	98.04	88.89	81.48	82.35	100.0
Ceftazidime	-	-	-	82.35	-
Ceftriaxone	96.04	88.89	80.77	82.35	100.0
Ciprofloxacin	68.63	80.0	80.0	83.33	75.0
Imipenem	80.39	18.52	42.31	35.29	50.0
Levofloxacin	27.45	73.33	60.0	29.41	50.0
Meropenem	28.21	11.11	42.31	35.29	50.0
Piperacillin	-	-	-	47.06	-
Piperacillin/Tazobactam	-	30.77	61.90	-	50.0
Tobramycin	-	-	-	29.41	-

lowest number from body fluid1(0.8%)(Table1). The organisms most frequently isolated were *Acinetobacter sps* 51 (39.55%), *Escherichia coli* 25 (19.37%), *Klebsiella sps* 27 (20.93%), *Pseudomonas aeruginosa* 18 (13.95%) and *Enterobacter sps* 8 (6.2%). Acinetobacter sps was the most commonly isolated organism from the respiratory tract while *E. coli* was the most frequently isolated organism from urine (Table 1).

The antimicrobials tested and the percentages of isolates determined to be resistant are listed in Table 2. Rates of resistance to most antibiotics were significantly increased among the isolated organisms. Entire isolates of the organisms were mostly resistance to the cephalosporins. Fluoroquinolones and Meropenem is effective against the *Acinetobacter sps* isolated. The antibiotic sensitivity pattern of *Pseudomonas aeruginosa* shows that most of the isolates are resistant to cephalosporins. Among the *Pseudomonas aeruginosa*, Tobramycin has the highest susceptibility rate followed by fluoroquinolones and Carbapenem as shown in Table 2.

Most of the frequently isolated organisms like *Escherichia coli*, *Klebsiella pneumonia* and *Enterobacter sps* are mostly resistance to cephalosporins. They are more sensitive to fluoroquinolones, Carbapenem and aminoglycosides as presented in Table 2. Among the isolated organisms 97 (75.2%) were found to be multi drug resistance

DISCUSSION

Globally, the resistance rate to the multiple antibiotics used for microbes is in increasing sequence which is a leading cause of the treatment failure in ICUs patients. The actual situation of ICU related infections in Nepal is difficult to assess because high quality data on the local conditions are scarce in the literature. Due to lack of local data, western guidelines on initial antibiotics selection are generally applied in Nepalese ICUs and the empirical chance made for serious ICU related infections. This study aimed to evaluate the antibiotic resistance patterns and changes among gram negative bacilli recovered from the ICU patients. Thus, identification of the underlying pattern of drug resistance among microorganisms in every hospital is the key to success in the appropriate treatment of the ICU patients empirically. It's of most important in the Nepalese situation on the treatment of frequently isolated antibiotic resistance organisms from the ICU.

In the current study, the most common type of infection prevalent in ICU patients was respiratory tract infections (69.70%), urine (16.30%), blood (9.30%), pus (3.90%) and body fluid (0.8%) (Table1). Similar findings were reported from the study conducted in Turkey which results as Respiratory tracts (76.5%), blood cultures (12.1%)and urine (11.4%) [1]. In the study conducted in 5 European countries, it was found that main sources of infections were respiratory tract (42%), urine (26%), blood (14%), abdomen (11%) and skin and soft tissue (7%) [21].

The monobacterial growth of gram negative bacilli was found in 89.92% clinical specimens and remaining 10.08% gram negative bacilli were associated with polybacterial growth and isolated along with different gram negative bacilli in our study. A surveillance study from Turkey found that 57.9% were single isolates, whereas 23.4% were mixed. 7.9% isolates were initial growth of multi re-isolation and 10.8% were obtained from repeated cultures [22]. Another retrospective study conducted in CMC-TH shows that 75.5% had single organism while the remaining 24.4% had two or more organisms isolated [23].

In our study, Acinetobacter sps, Escherichia coli and Klebsiella sps were the most common microorganisms isolated from ICU patients, similarly the study conducted in intensive care unit of Tribhuvan University Teaching Hospital, Kathmandu. Our study revealed that Acinetobacter sps is the most common organism (39.55%) followed by Klebsiella spp. (20.9%), Escherichia coli (19.37%),Pseudomonas sps (13.95%) and Enterobacter sps (6.2%). The spectrum of pathogens in ICUs may change from country with time and by the hospital, type of ICU, and specific patient populations [24-29]. But in some studies conducted Pseudomonas aeruginosa was found to be predominant isolate from the ICU acquired infections [11,23,30].

Our study indicates a rising pattern of antibiotic resistance among the majority of the ICU isolates. The most dramatic change was observed for Acinetobacter spp; the isolates showed an increasing trend of resistant to most of the antibiotics (Table 2). Accordingly, the resistance for cephalosporins, Carbapenem and fluoroquinolones increased overtime. On the other hand, Pseudomonas aeruginosa resistance rates were lower overall than Acinetobacter spp. Resistance rates for the antibiotics tested. Acinetobacter isolates, usually acquired in the ICU, are multi drug resistant and may cause severe infections associated with a high mortality rate. In this study, high level of resistance was observed to Cefotaxime (98.04%), ceftriaxone (96.04%0, Imipenem (80.39%). Fluoroquinolones and Meropenem were found to be relatively effective against Acinetobacter spp isolated. High resistance rates to these drugs were also revealed in a similar study conducted before [20,23]. We observed a high level of resistance among the cephalosporins (82.35%). Tobramycin, Amikacin and Carbenicillin were found to be relatively effective against Pseudomonas aeruginosa. High resistance rate to cephalosporin and fluoroquinolones was in concord with the study done before [23,31].

We observed a significant increase in resistance trend to cephalosporins and fluoroquinolones among enterobacteriaceae isolates, but amikacin was broadly active against Enterobacteriaceae. One of the most important findings from our study was the decrease of cephalosporin and fluoroquinolones susceptibility over the study period. These results are consistent with the results of other surveillance studies from Turkey [24,32]. An alarming finding is increase in the resistance to the third generation cephalosporins used. Similar observations are

found in the study of other surveillance study conducted before [33-35].

CONCLUSIONS

Maximum participants prefer private health care services as compared to government health services for their treatment. The study found significant association between healthcare facility utilizations for diabetes and waiting time at the health facility. Even though in our study there was not found significant association of various variable with healthcare facility utilization, majority of participants utilized private health facilities than public health facilities.

Therefore, additional community-based studies are needed to include larger study populations in order to help healthcare providers develop proper health care programs for these patients. Health care professionals should emphasize the impact of the chronic illness on patients.

ADDITIONAL INFORMATION AND DECLARATIONS

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Data Availability: Data will be available upon request to corresponding authors after valid reason.

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