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Antibiotics in ICU: The Challenges of Use, Cost and Response in a Tertiary Care Hospital

Rawshan Ara Perveen[1], Morshed Nasir[2], Nadia Farha[1] and Mohammad Ashraful Islam[3]

[1] *Assistant Professor, Department of Pharmacology, Holy Family Red Crescent Medical College, Dhaka, Bangladesh*

[2] *Professor, Department of Pharmacology, Holy Family Red Crescent Medical College Dhaka, Bangladesh*

[3] *Assistant Professor, Department of Otolaryngology, International Medical College, Dhaka, Bangladesh*

**Corresponding e-mail: rawshanperveen@gmail.com*

ABSTRACT

Antibiotic resistance can lead to increased morbidity, mortality, length of hospital stay, and healthcare expenditures. The study is designed to observe the challenges of antibiotic consumption, related costs, and their resistance pattern in critically ill patients. The study was conducted in ICU from July 2016 to December 2016, at Holy Family Red Crescent Medical College Hospital. The demographic data, antibiotic sensitivity report, the administration of different classes of antibiotics as well as individual drugs and their costs were recorded. In 216 patients, meropenem was the most commonly prescribed antibiotic followed by levofloxacin and ceftriaxone. Meropenem with one or more class of antibiotics had the higher cost (BDT 1,985 and BDT 2,800 per day per patient). Though the cephalosporins are the initial choice as the safest, cheaper antibiotics in developed countries, high rate of resistance was observed in this ICU. The overall sterilization and strict control of nosocomial infections may play a vital role in overcoming the challenges. Use of local antibiogram, narrow-spectrum antibiotics, infectious disease specialist consultation, and restricted authorization to prescribe antibiotics can effectively shift the antibiotic sensitivity and minimize the cost in ICU stay.

Keywords: Admission, Antibiotic usage, Intensive care unit, prescriptions, Treatment failure, Mortality, Antibiotics

INTRODUCTION

Patients with severe and life-threatening illnesses and injuries admitted in intensive care unit, which requires constant, close monitoring and support from specialized equipment and medications. ICUs are also different from normal hospital wards by a higher staff-to-patient ratio that specialized in critical care medicine and access to advanced medical resources and equipment that is not routinely available elsewhere. Patients may be transferred directly to an intensive care unit from an emergency department if necessary or from a general ward if they rapidly deteriorate, or immediately after invasive surgery and the patient is at high risk of complications. Intensive care service is 2.5 times more costly than other hospital stays [1].

ICU patients are more prone to develop an infection, because some of them are admitted due to infection and some of them are immunosuppressed because of critical illness and a large number of invasive devices used in them. Antibiotics are the most frequently prescribed drugs among hospitalized patients especially in intensive care and surgical departments [2]. Total Antibiotic consumption in ICU is approximately ten times higher than the general hospital wards [3]. Rational use of antibiotic is the important but actual situation is complicated because identification of microorganisms is delayed, the critical illness itself give an impact, mechanism of antibiotics, and increase the number of antibiotic-resistant strains [3].

Indiscriminate and excessive use of antimicrobial agents promotes the emergence of antibiotic-resistant organisms. Antimicrobial resistance increases already risen health care costs and also increases patient morbidity and mortality [2]. Antibiotics are the drugs compared with the other drugs, have highest costs worldwide and account for 20-30%

of total drug expenditures [4-6]. It causes a huge economic burden on patients who bear the cost of treatment in Bangladesh.

It is recommended that the number of drugs per prescription should be kept as low as possible to minimize the risk of drug interactions, development of bacterial resistance, and hospital costs [6].

The use of a computerized decision support tool and increased the number of switches to narrow-spectrum antibiotics [7], implementation of local antibiogram, infectious disease specialist consultation, and restricted authorization to prescribe antibiotics have all been reported to result in marked reductions in antibiotic consumption [8]. Here in this study, antibiotic use and their cost pattern in a general ICU ward over a 6-month period were observed. Special emphasis was given to the number of antibiotic consumption per patients, related costs, and the combinations of antibiotic use in a teaching hospital.

MATERIALS AND METHOD

Holy Family Red Crescent Medical Hospital is a 400-bed hospital with 9 bed ICU facility. It serves as a referral hospital in the center of Dhaka city. Critically ill patients from multidiscipline and trauma patients requiring hemodialysis monitoring and/or mechanical ventilation were admitted to ICU. The ICU was managed by a bunch of stuff from anesthesiology, internal medicine, surgery, neurology, neurosurgery department, with daily assistance from the departments of medical microbiology and radiology.

From May 2016 to December 2016 all adult patients (age above 14 years), with or without a mechanical ventilator, who had been admitted in ICU received at least one antibiotic were studied prospectively. Patients admitted but not prescribed with any antibiotics were excluded from the study.

Data were collected from patient's records. All collected data were analyzed by investigators.

The following parameters were recorded:

- Patient demographic profile
- Mean length of stay (LOS) in ICU
- Distribution of pattern of illness based on diagnosis
- Associated comorbidities (other illness)
- Prescription frequency of individual antibiotics
- Number of beds in ICU = 09
- The cost of antibiotics utilized in ICU
- Antibiotics sensitivity report

RESULTS

A total of 216 patients were admitted to the ICU during the 6-month study period, who met the criteria to be included in the study. Of the total, 115 were males and 101 were females. Patients were in ICU for days ranging from 2 to 15 days with an average of 5 days. During this period,62 patients died in ICU which was 30% of total admission (Table 1). Total and average number of antibiotics prescribed as shown in Table 2.

Table 1 Demographic characteristics of patients

Characteristics	Variables
Number	All (n=216)
Gender of the patient	
Male/Female	105/101
Length of stay (LOS) in ICU	
Mean (Range)	5.3 (2-15)
Medical specialty	
Medicine	89

Neuro-medicine	44
Surgery	12
Neurosurgery	15
Orthopedics	5
Gynecology	18
Cardiology	12
Nephrology	18
ENT	2
Urology	1
Mortality in ICU %	62 (30%)

Table 2 Number of antibiotics prescribed per patients

No. of antibiotic prescribed	Total no. of patients (n=216)	Percentage (%)
1	54	25%
2	115	53.24%
3	33	15.27%
4	10	4.62%
5	2	0.92%
6	1	0.46%
7	1	0.46%

In Table 3, 75% of patients who received two or more combination of antibiotics reflect that meropenem, levofloxacin and ceftriaxone play the lead role. While combination with meropenem had the highest rate BDT 1,985 per day in two-drug combination, 2800 BDT per day in three or more antibiotic combinations.

Table 3 Combination of antibiotics with their cost per day

Combinations of antibiotics	No. of patients	Cost per day (BDT)	Combinations of antibiotics	No. of patients	Cost per day (BDT)
Meropenem + Moxifloxacin	19	1280.00	Meropenem + Levofloxacin + Ceftriaxone	4	1940.00
Ceftriaxone + Metronidazole	13	760.00	Levofloxacin + Piper-Tazobac + Azithromycin	3	1303.00
Meropenem + Levofloxacin	12	1340.00	Ceftriaxone + Flucloxacillin + Co-amoxiclav	2	1425.00
Levofloxacin + Ceftriaxone	11	700.00	Meropenem + levofloxacin + Ceftazidime	2	2085.00
Levofloxacin+ Piper- tazobac	9	1103.00	Ceftriaxone + Gentamicin + Metronidazole	1	790.00
Levofloxacin +Ceftazidime	6	845.00	Levofloxacin + Ceftriaxone + Clarithromycin	1	780.00
Ceftazidime + Moxifloxacin	5	785.00	Levofloxacin + Ceftriaxone + Vancomycin	1	1250.00
Levofloxacin +Cefepime +	3	1204.00	Levofloxacin + Ceftriaxone + Azithromycin	1	900.00
Meropenem + Metronidazole	3	1400.00	Meropenem + Ceftriaxone + Moxifloxacin	1	1880.00
Meropenem + Clarithromycin	3	1280.00	Ceftriaxone + Flucloxacillin + Piper-tazobac	1	1828.00
Piper- tazobac + Moxifloxacin	2	1043.00	Meropenem + Levofloxacin + Metronidazole	1	1510.00
Piper- tazobac + Linezolid	2	1463.00	Meropenem + Cefepime + Metronidazole	1	2504.00
Piper- tazobac + Azithromycin	2	1203.00	Meropenem + Moxifloxacin + Linezolid	1	1740.00
Ceftazidime + Metronidazole	2	915.00	Meropenem + Levofloxacin + Clarithromycin	1	1380.00
Meropenem +Ceftriaxone	2	1840.00	Meropenem + Flucloxacillin + Metronidazole	1	1625.00
Ceftriaxone+ Flucloxacillin	2	825.00	Meropenem + Moxifloxacin + Clindamycin	1	1440.00
Co-amoxiclav + Clarithromycin	2	680.00	Ciprofloxacin + Co-amoxiclav + Metronidazole + Amikacin	1	316.00
Co-amoxiclav + Moxifloxacin	2	640.00	Tigecycline + Clindamycin	1	1810.00
Piper- tazobac + Ciprofloxacin	1	1353.00	Meropenem + Moxifloxacin + Metronidazole + Piper-Tazobac	1	2740.00
Imipenem + Amikacin	1	1396.00	Meropenem + Levofloxacin + Clindamycin + Piper-Tazobac	1	2800.00
Piper- tazobac + Clindamycin	1	1163.00	Levofloxacin + Ceftazidime + Ciprofloxacin +Azithromycin + Piper-tazobac	1	2695.00
Ciprofloxacin+ Metronidazole	1	510.00	Meropenem + Levofloxacin + Clarithromycin + Piper-Tazobac + Amikacin	1	2776.00

Meropenem + linezolid	1	1700.00	-	-	-
Cefepime + Azithromycin	1	1304.00	-	-	-
Meropenem + Vancomycin	1	1790.00	-	-	-
Ceftazidime + Vancomycin	1	1295.00	-	-	-
Ceftazidime + Amikacin	1	841.00	-	-	-
Meropenem + Ceftazidime	1	1985.00	-	-	-
Ceftriaxone + Moxifloxacin	1	640.00	-	-	-
Ceftriaxone + Piper-tazobac	1	1603.00	-	-	-

Among 216 admitted patients in ICU, all were advised for an antibiotic sensitivity test. But reports were found in eighty-three cases. Micro-organisms were absent in 62 cases. Six different types of the organism were found in 21 cases.

Antibiotic resistance pattern shows in next table. Majority of isolates were resistant to cephalosporin, penicillin, fluoroquinolones, streptomycin, and tetracycline. Organisms were showing sensitivity towards imipenem and meropenem (Table 4).

Table 4 Antibiotic sensitivity as per reports

Antibiotics	Resistant	Sensitive
Cefuroxime	16	5
Ceftriaxone	13	4
Ceftazidime	13	3
Cephalexin	11	5
Amoxiclav	11	2
Cloxacillin	11	-
Ciprofloxacin	11	7
Gentamicin	11	8
Azithromycin	10	3
Tetracycline	10	8
Cotrimoxazole	10	8
Amikacin	9	9
Meropenem	6	11
Imipenem	5	11
Piper-tazobac	4	6
Nitrofurantoin	3	4
Cefepime	1	1
Aztreonam	1	-
Macillinum	-	2
Vancomycin	-	1
Linezolid	-	2
Tigecycline	-	2

DISCUSSION

Antibiotics are the most frequently prescribed drugs among hospitalized patients especially in intensive care and surgical department. Appropriate and less number of antibiotic prescriptions in intensive care unit is an important element in the quality of care, infection control, and cost reduction as well as the length of hospital stays [2]. The average length of stay (LOS) in ICU was found to be 5.2 days in our study. In other studies done in ICUs of North India, South India, Nepal, and the USA, average LOS in ICU was 5.75, 6.22, 4.0, and 5.2 days, respectively [9-11]. The difference found in the mean LOS could be due to the difference in illness pattern among the population. The ICU mortality rate was found to be 30%, results are similar to several studies done in India, reported ICU mortality rate as high as around 35% [9,10,12].

In this study, only 25% of patients treated with single antibiotic and remaining 75% patients received one or more antibiotics during their ICU admission period. Drug use pattern study from an ICU in Northern India and Bengaluru, 70%, and 69% patients received more than one antibiotics [9,12] and 60% of the patients studied in a Caribbean ICU

received two antimicrobials. Majority of the patients in a Danish University Hospital ICU were on one antibiotic [13]. In another study, 36.7% of cases were treated with only one antibiotic agent, 14.1% were given a combination of 2, and 7.2% were given a combination of more than 3 antibiotic agents in a German Surgical ICU [14]. Whereas it is recommended that for minimizing the risk of drug interactions, number of drugs per prescription should be kept low. It will also reduce hospital cost and development of bacterial resistance [15].

Three highly utilized antibiotics in this study were meropenem, levofloxacin, and ceftriaxone, on reviewing similar studies from India, it was observed that five most utilized antibiotics are 3rd generation cephalosporins, meropenem, metronidazole, levofloxacin, and ceftriaxone [12]. Cephalosporins, fluoroquinolones, combinations of penicillin including β-lactamase inhibitors and carbapenems were the most frequently prescribed antibiotics in another study [16].

Increasing cost of medicines is causing a huge economic burden on patients who bear the cost of treatment in Bangladesh. In view of this, the daily cost of antibiotics combination per patient used in our ICU setup was calculated. The most prescribed drug meropenem (1240 BDT per day) with two or more combined drugs had the highest cost (1,980 and 2,800 BDT per day). A study from Turkey reported the similar result [17]. In 2007, Vandijck, et al., calculated that mean daily antimicrobial cost was 114.25€ equivalent to 11,618 BDT. The daily antimicrobial costs per infected patient with multidrug-resistant strain (165.09€ equivalent to 16,788 BDT) was 50% higher compared with those without (82.67€ equivalent to 8,406 BDT; $P<0.001$) [18]. In another study held in Turkey, Buzkart, et al., calculated that the cost of total antibacterial consumption in ICU was 40.72€ equivalent to 4,140 BDT per day in 2011 and 29.01€, 2,950 BDT per day in 2012 [12]. Compare with several studies around the world, we observed that cost of antibiotic in Bangladesh was less from abroad. One of the cause is Bangladesh was categorized as a least-developed country along with other 47 countries around the world will not be obliged, with respect to pharmaceutical products, to implement or apply the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement until 1 January 2016 but can manufacture drugs.

According to cultural sensitivity report, there were six type or organism found. Most common organism isolated was *Staphylococcus aureus, Acinetobacter,* and *Pseudomonas.* Most sensitive drugs against micro-organism were carbapenem and amikacin. From 2010 to 2014, several studies around Dhaka city and worldwide reported that carbapenem-resistant rate started to increase [19-21]. The emergence of carbapenem-resistant strains around the world is alarming and a threat to the treatment of the admitted patients in the ICUs. Most of the isolates were resistant against penicillin and cephalosporin group. Few studies reported the similar findings [19,22,23]. This might be due to the selective preference for extensive usage of these groups of drugs.

Several programs followed in ICU like infectious disease specialist intervention, the establishment of a local ambigram, the practice of de-escalation, switching to narrow spectrum antibiotic after day 3 whenever possible, restricted authorization to prescribe antibiotics could improve the quality of care, infection control, and cost containment.

CONCLUSION

Antibiotics are commonly prescribed in critically ill patients and form a significant proportion of the total drugs consumed in the ICU. Multi-drug resistant organism did the situation more difficult both for patients and physicians. It may be concluded that the high utilization rates and costs of antibiotics prescribed in the ICU are a matter of concern and need to be improved by the use of local antibiogram guidelines, continuous surveillance and antibiotic restriction policies.

DECLARATIONS

Conflict of Interest

The authors declare no conflict of interest.

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