



Antimicrobial sensitivity patterns among sepsis patients in intensive care unit of Dhaka Medical College Hospital, Bangladesh

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ABSTRACT

Background: Sepsis is a leading cause of mortality in Intensive Care Unit (ICU) patients. Rapid initiation of effective empirical therapy lessens both patient mortality rates and time spent in ICU. Objective of the study was to identify microorganisms isolated from sepsis patients in ICU and determine the antimicrobial sensitivity patterns.

Methodology: Hospital based cross-sectional study was conducted among 80 culture positive sepsis patients in the ICU of Dhaka Medical College Hospital (DMCH).

Results: Most commonly source of isolated organisms were from respiratory (30.0%), genitourinary (23.8%), blood (18.8%) and gastrointestinal (16.3%) sources. Overall gram negative organisms (70.0%) were more common than gram positive organisms (22.5%). The most common organisms in respiratory, genitourinary, gastrointestinal, blood, CSF and pus were *Acinetobacter* sp. & *Streptococcus pneumoniae* (25.0%), *E. coli* (31.6%), *E. coli* (46.2%), *Pseudomonas* sp. (60.0%), *Neisseria meningitis* (60.0%), *Staphylococcus aureus* (100.0%), respectively. The highest susceptibility was for Colistin (100.0%), Imipenem (73.0%), Moxifloxacin (31.4%) and Piperacillin (68.0%). Gram negative bacteria were found most sensitive to Colistin (100.0%), Imipenem (82.1%), Moxifloxacin (71.43%), Piperacillin (68.14%) and Amikacin (65.85%) whereas gram positive bacteria to 100% sensitive to Cloxacillin, Azithromicin, Vancomycin and Piperacillin.

Conclusion: Judicious practice of antimicrobial agents for empirical therapy is essential for effective management of sepsis patients in ICU.

Key Words: Antimicrobial sensitivity pattern, Sepsis and ICU

Cite Article: Khan, A. M., Jannat, F. T. and Ahasan, M. F. (2017). Antimicrobial sensitivity patterns among the sepsis patients in the intensive care unit of Dhaka Medical College Hospital, Bangladesh. *Journal of Molecular Studies and Medicine Research*, 02(01), 80-87. **Crossref:** <https://doi.org/10.18801/jmsmr.020117.10>

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I. Introduction

Sepsis is one of the leading causes of morbidity and mortality; the incidence of which about 18 million per year globally (Lyle et al., 2014). It develops in 1-2% of hospitalized patients and occupies about 25% of intensive care unit (ICU) beds (Balk, 2000; Dries, 2005; Ely and Goyette, 2005). Sepsis is

responsible for the majority of the mortality in patients who are hospitalized (Dellinger et al., 2013; Martin et al., 2003). Antimicrobial resistance is a major public health concern resulting in substantial morbidity and mortality especially in hospitalized patients (Mehta et al., 2005). The association of health service cost, duration of hospital stay and patient mortality with the resistance has been established. It is an alarming problem for the ICU setting (Lockhart et al., 2007). Rapid administration of effective empirical antimicrobial therapy is the prerequisite for successful management of septic patients in the ICU (Diekema et al., 1999; Ibrahim et al., 2000; Kollef et al., 1999). Culture of the sample from the patients to identify the microorganisms, is a highly specific indicator of sepsis, and the results of antimicrobial testing may help to select proper antimicrobial treatment (Bohte et al., 1995). Antimicrobial resistance may differ from region to region due to the pattern of antibiotic use in a particular region. The present study is designed to determine the present antimicrobial sensitivity patterns of microorganism isolated from ICU patients in Dhaka Medical College Hospital (DMCH). The antibiotic sensitivity patterns may guide the physicians for initiation empiric therapy with antibiotics and also may help in revising the antibiotic policy of this country.

II. Materials and Methods

This hospital based cross-sectional study was carried out in the ICU of DMCH which is one of the renowned tertiary hospitals of Bangladesh. The total study period was a period of six months from July 2015 to December 2015. A total of 80 patients admitted in ICU and diagnosed as sepsis by positive culture performed were the study participants. Conventional methods of culture of different samples employed at the hospital were carried out to identify the organisms. Only the first isolate of a particular species was considered for each patient. The samples of blood, CSF, urine, pus, bronchoscopic or nasogastric aspirate were collected under aseptic precautions following standard procedures. Blood samples were inoculated into bile- and glucose-broth containing bottles, incubated overnight at 37°C and sub-cultured on MacConkey agar and blood agar which was repeated for up to 7 days (Forbes et al., 1998). CSF samples were streaked on blood and chocolate agar culture media and inoculated into Fildes broth, and incubated in at 37°C up to 7 days and sub-cultured on blood and chocolate agar plates (Kennedy et al., 2007). The bronchoscopic, nasogastric aspirates and pus samples were plated, processed and observed the colony characteristic on the blood and MacConkey agar plate (Forbes et al., 1998). Urine samples were processed by a surface streak procedure on both blood and MacConkey agar using calibrated loops for semi-quantitative method and incubated at 37°C for upto 48 hours and considered positive if a single organism was cultured at a concentration of $>10^5$ CFU/ml (Bonadio et al., 2001). The isolates found from the samples were further processed as per the standard procedures to identify pathogens (Forbes et al., 1998) and disc diffusion methods were followed to determine their antibiotic susceptibility (Reller et al., 2009). Antibiotics tested included penicillin, amikacin, gentamicin, imipenem, ciprofloxacin, ceftazidime, vancomycin, meropenem, piperacillin, tobramycin, cefepime, cefixime, cefotaxime, metronidazole, ceftriaxone, levofloxacin, clindamycin, azithromycin, clarithromycin, colistin, moxifloxacin, cloxacillin and cefuroxime. A set of structured questionnaire was used for data collection. Data were collected interviewing the attendants of the patients and the laboratory investigations. Before the interview, the detail of the study was explained to each eligible respondent and written informed consent was taken. After completion of data collection, data analysis was done using SPSS version 21. Frequency distribution and percentage were calculated.

III. Results and Discussion

Socio-demographic characteristics

Age of the patients ranged between 12 and 85 days with a mean of 50.26 ± 21.37 years. Proportion of male patients (62.50%) was relatively more than female patients (37.50%) with the male-female ratio was 1.67: 1. Majority of the patients were illiterate (41.3%) followed by patients who were in class 1-5 level (33.7%). Majority of the respondents were from lower socioeconomic class (86.2%) and rest were from middle class (13.8%).

Organisms isolated from the patients

Among the 80 culture positive samples, majority of the isolated micro-organisms were gram negative bacteria (70.0%) followed by gram positive bacteria (22.5%) and others (7.5%) including

Mycobacterium tuberculosis, *Mycoplasma pneumonia* and *Candida albicans*. Out of 56 gram negative bacteria 26 (46.43%) were enterobacteriaceae (Table 01).

Table 01. Organisms isolated from the patients (n=80)

Organisms	Frequency	Percent
Gram negative		
<i>Pseudomonas</i> sp.	13	16.3
<i>E. coli</i>	12	15.0
<i>Acinetobacter</i> sp.	10	12.5
<i>Klebsiella</i> sp.	4	5.0
<i>Salmonella</i> sp.	4	5.0
<i>Neisseria meningitis</i>	3	3.8
<i>Proteus</i> sp.	2	2.5
<i>Shigella</i> sp.	2	2.5
<i>Citrobacter</i>	2	2.5
<i>Bacteroides</i>	2	2.5
<i>Acnitomyces</i>	2	2.5
Gram positive		
<i>Staphylococcus aureus</i> (MRSA)	8	10.0
<i>Streptococcus pneumonia</i>	8	10.0
<i>Clostridium defficile</i>	2	2.5
Others		
<i>Mycobacterium tuberculosis</i>	2	2.5
<i>Mycoplasma pneumonia</i>	2	2.5
<i>Candida albicans</i>	2	2.5
Total	80	100.0

Organism isolated in relation to source

The proportion of gram positive and gram negative organisms was equal (41.7%) from the sample of respiratory source. Gram negative organism was more prevalent (89.5%) in the genitourinary sample. From all the samples of gastrointestinal source gram negative organisms (100.0%) were isolated. Gram negative organism (86.7%) was more common than gram positive organism (13.3%) in blood samples. The proportion of gram positive and negative organisms was more or less equal in CSF samples. From all the pus samples (100.0%) gram positive organisms were isolated (Table 02).

Table 02. Types of organism isolated in relation to source (n=80)

Source	Gram positive N (%)	Gram negative N (%)	Others N (%)	Total N (%)
Respiratory	10 (41.7)	10 (41.7)	4 (16.7)	24 (100.0)
Genitourinary	0 (0.0)	17 (89.5)	2 (10.5)	19 (100.0)
Gastrointestinal	0 (0.0)	13 (100.0)	0 (0.0)	13 (100.0)
Blood	2 (13.3)	13 (86.7)	0 (0.0)	15 (100.0)
CSF	2 (40.0)	3 (60.0)	0 (0.0)	5 (100.0)
Pus	4 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)
Total	18 (22.5)	56 (70.0)	6 (7.5)	80 (100.0)

Most commonly isolated organisms from the respiratory tract were *Acinetobacter* sp. (25.0%), *S. pneumonia* (25.0%) and *S. aureus* (16.7%). From the genitourinary source commonly isolated organisms were *E. coli* (31.6%) and *Klebsiella* sp. (15.8%). The most prevalent gastrointestinal isolates were *E. coli* (46.2%), *Salmonella* sp. (23.1%) and *Shigella* sp. (15.4%). *Pseudomonas* sp. (60.0%), *Acinetobacter* sp. (13.3%) and *Clostridium defficile* (13.3%) were the common blood isolates. From CSF the commonly isolated pathogens were *Neisseria meningitis* (60.0%) and *S. pneumonia* (40.0%). *S. aureus* (MRSA) was isolated from 100% of pus culture (Table 03).

Table 03. Name of organisms isolated in relation to source (n=80)

Organism	Source of infection					
	Respiratory (%)	Genitourinary (%)	GI (%)	Blood (%)	CSF (%)	Pus (%)
<i>Acinetobacter sp.</i>	25.0	10.5	0.0	13.3	0.0	0.0
<i>Acnitozymes</i>	8.3	0.0	0.0	0.0	0.0	0.0
<i>Bacteroides</i>	0.0	0.0	15.4	0.0	0.0	0.0
<i>Candida albicans</i>	0.0	10.5	0.0	0.0	0.0	0.0
<i>Citrobacter</i>	0.0	10.5	0.0	0.0	0.0	0.0
<i>Clostridium defficile</i>	0.0	0.0	0.0	13.3	0.0	0.0
<i>E. coli</i>	0.0	31.6	46.2	0.0	0.0	0.0
<i>Klebsiella sp.</i>	0.0	15.8	0.0	6.7	0.0	0.0
<i>M. tuberculosis</i>	8.3	0.0	0.0	0.0	0.0	0.0
<i>M. pneumonia</i>	8.3	0.0	0.0	0.0	0.0	0.0
<i>Neisseria meningitis</i>	0.0	0.0	0.0	0.0	60.0	0.0
<i>Proteus sp.</i>	0.0	10.5	0.0	0.0	0.0	0.0
<i>Pseudomonas sp.</i>	8.3	10.5	0.0	60.0	0.0	0.0
<i>Salmonella sp.</i>	0.0	0.0	23.1	6.7	0.0	0.0
<i>Shigella sp.</i>	0.0	0.0	15.4	0.0	0.0	0.0
<i>S. aureus (MRSA)</i>	16.7	0.0	0.0	0.0	0.0	100
<i>S. pneumonia</i>	25.0	0.0	0.0	0.0	40.0	0.0
Total	100	100	100	100	100	100

Antimicrobial sensitivity pattern to bacteria in relation to type of bacteria

Antibiogram of the isolated pathogens is shown in Table 04. The highest susceptibility was for Colistin (100.0%), Imipenem (73.0%) Moxifloxacin (71.4%) and Piperacillin (68.0%). On the other hand the lowest susceptibility was for Cefuroxim (11.1%), Metronidazole (11.4%) Azithromicin (11.8%), Penicillin (12.3%), Ceftriaxone (12.5%) and Ciprofloxacin (13.7%) for all the bacteria isolated. Gram negative bacteria were found most sensitive to Colistin (100.0%), Imipenem (82.1%), Moxifloxacin (71.4%), Piperacillin (68.2%) and Amikacin (65.9%). Among the gram negative bacteria enterobacteriaceae was shown 100% sensitivity to Tobramycin, Cefepime and Colistin. Gram positive bacteria were most sensitive to Cloxicillin (100.0%), Azithromicin (100.0%), Vancomycin (100.0%), Piperacillin (100.0%) and Clindamycin (60.0%). Acid fast bacilli *Mycobacterium tuberculosis* was isolated from two patients of respiratory which was sensitive to Rifampicin, Isoniazid, Ethambutol, Rifabutin and Amikacin. *Candida albicans* was isolated from two patients of genitourinary source of two patients which was sensitive to Fluconazole and Amphotericin-B.

Antimicrobial sensitivity pattern to bacteria in relation to source of isolation

The antibiogram of the isolated bacteria in relation to source of isolation is shown in Table 05. Organisms isolated from respiratory source were most sensitive to Vancomycin (83.3%) and Levofloxacin (66.7%). Genitourinary organisms were Colistin (100.0%), Moxifloxacin (100.0%), Tobramycin (100.0%) and Imipenem (88.2%). Bacteria isolated from gastrointestinal source were shown highest sensitivity pattern to Piperacillin (77.8%), Cefutaxime (75.0%), Imipenem (69.2%) and Amikacin (60.0%). Blood isolated bacteria were most sensitive to Cefuroxime (100.0%), Colistin (100.0%), Gentamicin (90.0%), Imipenem (86.7%), Piperacillin (85.7%) and Amikacin (64.3%). Organisms isolated from CSF were shown 100% sensitivity pattern to Penicillin, Imipenem, Piperacillin, Cefotaxime, Clindamycin and Moxifloxacin. Organisms from pus was shown highest sensitivity to Gentamicin (100.0%), Vancomycin (100.0%), Piperacillin (100.0%) and Cloxacillin (100.0%).

Table 04. Antimicrobial sensitivity pattern to in relation to type of bacteria (n=76)

Antibacterial agents	Sensitivity patterns (%)			
	All bacteria	Gram negative bacteria	Enterobacteriaceae	Gram positive bacteria
Penicillin	12.3	11.6	0.0	20.0
Amikacin	47.5	65.9	50.0	0.0
Gentamicin	44.7	54.2	25.0	28.6
Imipenem	73.0	82.1	92.3	50.0
Ciprofloxacin	13.7	18.0	29.4	0.0
Ceftazidime	23.5	26.7	47.1	0.0
Vancomycin	33.3	5.3	0.0	100.0
Meropenem	41.9	44.6	69.2	37.5
Piperacillin	68.0	68.2	85.7	100.0
Tobramycin	35.7	41.7	100.0	0.0
Cefepime	23.3	22.7	100.0	25.0
Cefixime	12.1	13.8	21.1	0.0
Cefotaxime	34.4	45.8	61.5	0.0
Metronidazole	11.4	8.0	0.0	20.0
Ceftriaxone	12.5	16.7	13.3	0.0
Levofloxacin	48.0	47.1	40.0	42.9
Clindamycin	23.5	9.1	0.0	60.0
Azithromycin	11.8	0.0	0.0	100.0
Clarithromycin	23.1	14.3	0.0	50.0
Colistin	100.0	100.0	100.0	-
Moxifloxacin	71.4	71.4	50.0	-
Cloxacillin	16.7	0.0	0.0	100.0
Cefuroxime	11.1	20.0	20.0	0.0

Table 05. Antimicrobial sensitivity pattern to bacteria in relation to source of isolation (n=76)

Antibacterial agents	Sensitivity patterns (%)					
	Respiratory	Genitourinary	GI	Blood	CSF	Pus
Penicillin	14.3	0.0	0.0	16.7	100.0	0.0
Amikacin	45.5	36.4	60.0	64.3	0.0	0.0
Gentamicin	33.3	22.2	-	90.0	0.0	100.0
Imipenem	50.0	88.2	69.2	86.7	100.0	50.0
Ciprofloxacin	12.5	18.2	33.3	7.7	0.0	0.0
Ceftazidime	33.3	18.2	45.5	8.3	0.0	-
Vancomycin	83.3	0.0	0.0	15.4	40.0	100.0
Meropenem	20.0	52.9	53.9	40.0	60.0	50.0
Piperacillin	33.3	60.0	77.8	85.7	100.0	100.0
Tobramycin	-	100.0	-	25.0	-	-
Cefepime	50.0	50.0	-	0.0	33.3	0.0
Cefixime	0.0	0.0	42.9	33.3	-	0.0
Cefotaxime	0.0	22.2	75.0	0.0	100.0	0.0
Metronidazole	0.0	0.0	18.2	50.0	0.0	0.0
Ceftriaxone	0.0	0.0	0.0	50.0	33.3	-
Levofloxacin	66.7	38.5	45.5	0.0	0.0	50.0
Clindamycin	33.3	0.0	0.0	0.0	100.0	0.0
Azithromycin	20.0	0.0	-	0.0	-	-
Clarithromycin	33.3	0.0	0.0	0.0	0.0	-
Colistin	-	100.0	-	100.0	-	-
Moxifloxacin	-	100.0	0.0	-	100.0	-
Cloxacillin	0.0	0.0	0.0	-	-	100.0
Cefuroxime	0.0	0.0	-	100.0	-	-

Discussion

Mean age of the study population was 50.26 ± 21.37 years in the study and about 62.50% were male. Almost similar findings were observed in a study of the epidemiology of severe sepsis in India which found the mean age 54.9 ± 17.6 years, of which 67% were male (Todi et al., 2007). Male gender was reported as a risk factor for developing sepsis by Wafaisade et al. (2011). In a cohort study measuring incidence and risk factors for sepsis in surgical patients found the mean age was 53.2 ± 18.8 years (Georgeto et al., 2011). Most commonly source of isolated organism was from respiratory source (30.0%), followed by genitourinary (23.8%), blood (18.8%) and gastrointestinal source (16.3%). CSF (6.3%) and pus (5.0%) source were relatively less common source of sepsis. Almost same finding were noticed in a study of US in which specimen sources included the lower respiratory tract (52.1%), urine (17.3%), and blood (14.2%) (Lockhart et al., 2007). Majority of the isolated micro-organisms were gram negative bacteria among which common organisms were *Pseudomonas sp.* (16.3%), *E. coli* (15.0%) and *Acinetobacter sp.* (12.5%). Among the gram positive bacteria *Staphylococcus aureus* (10.0%) and *Streptococcus pneumoniae* (10.0%) were quite common. Lockhart identified 11 organisms most frequently isolated majority of which was identified in this study (Lockhart et al., 2007). However, Annane et al. (2005) reported common pathogens for septic shock were gram positive bacteria 30-50% and gram negative bacteria 25-30%. Annane also identified *Candida albicans* 1-3% as cause of sepsis consistent to the present study. Proportion of gram positive and gram negative organisms was almost equal from the respiratory isolates in the study. This finding was contradictory to a study of intensive care unit of India which reported about 95% organisms were gram negative bacilli (GNB). The most common organisms in order of frequency were *Pseudomonas aeruginosa* (35%), *Acinetobacter baumannii* (23.6%) and *Klebsiella pneumoniae* (13.6%) (Goel et al., 2009). However, in the current study, the common organisms were *Acinetobacter spp.* (25%), *Streptococcus pneumoniae* (25%) and *Staphylococcus aureus* (16.7%). Gram negative organisms i.e. *Pseudomonas sp.* (60.0%), *Acinetobacter sp.* (13.3%) and *Clostridium defficile* (13.3%) were the most frequently isolated (86.7%) from the blood samples. This finding is consistent with a study conducted in a teaching hospital in North India which reported about 81% gram negative bacteria where *Pseudomonas sp.*, *E. coli*, *Klebsiella sp.* and *Salmonella sp.* were most commonly isolated organisms (Mehta et al., 2005). From the genitourinary source commonly isolated organisms were *E. coli* (31.6%), *Klebsiella sp.* (15.8%) and *Candida albicans* (10.5%). The isolation rates of urinary pathogens are almost similar to the reports of some studies (Abu, 1999; Das et al., 2006; Jones et al., 1999; Navaneeth et al., 2002). The most prevalent gastrointestinal isolates were *E. coli* (46.2%), *Salmonella sp.* (23.1%) and *Shigella sp.* (15.4%). According to a study on gut origin of sepsis, the most common enteric organism cultured was *E. coli* (20%) (MacFie et al., 1999). From CSF the commonly isolated pathogens were *Neisseria meningitidis* and *S. pneumoniae*. *S. aureus* (MRSA) was isolated from all of pus culture. The percentage of organisms isolated from CSF or pus was relatively less than previously discussed sources of sepsis. Antibiotic resistance is the most important problem in ICU admitted patients. This might be due to the extensive and irrational usage of these drugs. This study noticed the lowest susceptibility was for Cefuroxim (11.11%), Metronidazole (11.43%) Azithromicin (11.76%), Penicillin (12.28%), Ceftriaxone (12.50%) and Ciprofloxacin (13.73%) for all the bacteria isolated. In this study Gram negative bacteria were found most sensitive to Colistin (100.00%), Imipenem (82.14%), Moxifloxacin (71.43%), Piperacillin (68.18%) and Amikacin (65.85%). Goel et al. (2009) reported a very high resistance (80-100%) among predominant GNB to ciprofloxacin, ceftazidime, co-trimoxazole and amoxicillin/clavulanic acid. High sensitivity was noted to meropenem and doxycycline. According to the study in North India, amikacin showed higher activity (76.6%) against *Enterobacteriaceae* and ciprofloxacin (65.2%) against non-fermenters (Mehta et al., 2005). In the present study, gram positive bacteria were most sensitive to Cloxicillin (100%), Azithromicin (100%), Vancomycin (100%), Piperacillin (100%) and Clindamycin (60.00%). Mehta et al. (2005) reported vancomycin (100.0%), ciprofloxacin (89.74%) highest activity against gram positive organisms.

IV. Conclusion

Gram negative organisms were more common than gram positive organisms and it was related to source of organisms isolated. Most common organisms in respiratory, genitourinary, gastrointestinal, blood, CSF and pus were *Acinetobacter sp.* and *Streptococcus pneumoniae*, *E. coli*, *E. coli*, *Pseudomonas sp.*, *Neisseria meningitidis*, *Staphylococcus aureus*, respectively. Highest susceptibility was for Colistin, Imipenem, Moxifloxacin and Piperacillin. Gram negative bacteria were found most sensitive to

Colistin, Imipenem, Moxifloxacin, Piperacillin and Amikacin whereas gram positive bacteria to Cloxacillin, Azithromycin, Vancomycin, Piperacillin and Clindamycin. Judicious use of antimicrobial agents for empirical therapy is essential for better management of sepsis patients in ICU.

Acknowledgements

The authors would like to acknowledge all respected respondents for their zealous participation in this research work. The authors also thank the authorities of DMCH to allow them to carry out the research in their institution.

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