Microbiological Profile, Antimicrobial Susceptibility, and Outcome Among Patients Admitted to Addis Ababa Intensive Care Units; a Cross-sectional Study.

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Abstract

Background: ICU infections are major health care problems affecting millions globally each year. ICU mortality of infectious patients is increasing and as high as 14.31% to 45.4%. The objective of this study was to determine microbiological culture profile, their antimicrobial susceptibility and treatment outcome of patients admitted to intensive care units.

Methods and materials: An institutional based cross sectional study was conducted in all patients with microbiological culture and susceptibility results after admission to intensive care units from January 2019 to December 2019. A modified, pretested questionnaire was used to collect data and analyzed using SPSS version 25. Correlation and regression analysis was done for association. P value of <0.05 with CI of 95% was taken as clinically significant.

Results: A total of 106 patients with 173 culture results were analyzed. Majority 68(64.2%) were males and the mean age of the patients were 35.08 ± 1.6 years. The most common source of infection was the pulmonary system 84(54.5%) followed by urinary tract infection 26(16.9%). Forty-four (25.43%) of cultures had growth. Gram negative microorganisms were identified in 35(68.63%) of isolates and *Acinetobacter species* accounts for 10(28.57%) followed by *Klebsiella pneumonia* and *E. coli* 7(13.725%) each. Generally, higher resistance was observed with cephalosporins and penicillins, whereas sensitivity to carbapenems, PIP/TAZ, and amikacin was satisfactory. The mortality associated with intensive care infections was found to be 32.1%.

Conclusion: This study revealed that the mortality rate associated with ICU infection was 32.1%. Early identification, targeted provision of antimicrobials based on microbiological culture and susceptibility result has to be implemented to have better outcome. Designs of future multicenter and large studies are crucial to improve outcome of critically ill patients.

1. Introduction

Intensive care unit infections are among the most serious infections and leading causes of morbidity and mortality in hospitalized patients, where indiscriminate and inadequately prolonged use of antimicrobials is common and leads to emerging proliferation of resistant strains (1, 2).

Notable among these resistant microorganisms are *methicillin-resistant s. aureus* (MRSA), and *vancomycin-resistant enterococcus* (VRE) which pose increased mortality and morbidity (4, 5).

Knowledge of antimicrobial susceptibility in ICU is crucial and far more important for giving effective treatment and decreasing the spread of drug resistant microorganisms. And it is crucial step for early intervention, decrease health-care costs, improve outcome of patients and increase treatment provider satisfaction.

Nevertheless, there was no study done in the ICU setting, both institutionally and country wise. So, this study on the assessment of microbiological culture profile, antimicrobial susceptibility and outcome of ICU patients will be a great input in addressing the gap.

2. Objectives

The objective of this study was to determine microbiological culture profile, their antimicrobial susceptibility and treatment outcome of patients admitted to intensive care units of Saint Paul's hospital millennium medical college and AaBET hospital ICUs.

3. Methods And Materials

Institutional based cross-sectional study was conducted at Saint Paul's hospital millennium medical college and AaBET hospital ICUs. SPHMMC is a referral teaching hospital in Addis Ababa, Ethiopia. And AaBET hospital is a branch of SPHMMC in Addis Ababa, Ethiopia which is an emergency complex which gives services for emergency, burn and trauma cases. SPHMMC has 14 bedded ICU and AaBET hospital has 11 bedded ICU. Both are general ICUs admitting both surgical and medical patients.

Data was collected from patients chart using pretested and structured questionnaire, after receiving ethical clearance from the college's institutional review board. All microbiological culture and susceptibility results of patients sent after intensive care unit admission from January 2019 to December 2019 were studied. Data was collected by trained data collectors using pretested standardized checklists developed by the principal investigator. Socio-demographic data, comorbidities, sites of infection, causative micro-organisms, ICU admission category, associated organ failure, type of culture sent, antimicrobials given prior to culture sampling and based on susceptibility result, and patient outcome to ICU was retrieved. All data was taken from patient record chart with collected laboratory culture and susceptibility results after selecting their MRN from ICU registration book.

Data was entered and statistical analysis performed using SPSS version 25. Chi-square test was used for categorical variables and mean, median and standard deviation (SD) for continuous variables. Associated risk factors were determined using logistic regression and correlation.

4. Results

4.1. Demographic characteristics

A total of 106 patients having culture result after admission to ICU over a period of one year were analyzed. Majority 68(64.2%) were males and the median age was 30.5 years, within the range of 3-82 years. Most of the patients 75(70.8%) were admitted from the emergency department. The median length of ICU stay was 31 days (interquartile range of 3-128 days). And the hospital length of stay prior to ICU admission was 6.89 ± 10.52 (mean $\pm$ SD). More than 99% of the patients have met the SIRS criteria.

4.2. Clinical characteristics of patients

Underlying comorbidities were identified in 49(46.2%) of patients. The most common comorbidity was hypertension 14(28.6%) followed by coronary artery disease and congestive heart failure 10(20.4%) combined. Majority of deaths 22(64.70%) were associated with comorbidity. Coronary artery disease and congestive heart failure being the most common comorbidity 6(17.6%) followed by hypertension 5(14.70%). The most common site of infection was the pulmonary system 84(54.5%) followed by urinary tract infection 26(16.9%), skin/soft tissue infection 18(11.7%), CNS 16(10.4%), and 10(6.5%) intra-abdominal focus. Pulmonary and urinary focus was higher in male patients 55(65.47%) and 18(69.23%) respectively, whereas intra-abdominal focus was higher in females 9(90%). Organ failure occurred in majority 94(88.7%) of patients, with the respiratory system comprised 84(44.7%) of organ failures followed by neurologic system 60(31.9%).

As shown in Table 1.

Table 1

Outcome to ICU (discharge and death) among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019 with regard to comorbidity, infection site, and organ failure (N= number of patients).

Variable	Total (N=106)	Discharge (N=65)	P value	Death (N=34)	P value
Comorbidity	49(46.2%)			22(64.7%)	
- RVI	3(6.1%)	1(1.5%)	.317	2(5.9%)	.196
- DM	8(16.3%)	5(7.7%)	.944	3(8.8%)	.735
- HTN	14(28.6%)	8(12.3%)	.733	5(14.7%)	.757
- CAD/CHF	10(20.4%)	4(6.15%)	.149	6(17.6%)	.047
- COPD/Asthma	2(4.1%)	1(1.5%)	.743	1(2.9%)	.588
- CKD	6(12.2%)	3(4.6%)	.562	3(8.8%)	.338
- CLD	1(2.0%)	-	.210	1(2.9%)	.146
- Malignancy	2(4.1%)	-	.073	1(2.9%)	.588
Infection site	154	95		59	
- Pulmonary	84(54.5%)	51(53.7%)	.804	27(45.8%)	.977
- Urinary	26(16.9%)	18(18.9%)	.345	4(6.8%)	.036
- CNS	16(10.4%)	9(9.5%)	.655	7(11.9%)	.282
- Skin/soft tissue	18(11.7%)	9(9.5%)	.283	9(15.25%)	.075
- Gastrointestinal	10(6.5%)	8(8.4%)	.206	2(3.4%)	.395
Organ failure	188	105		71	
- Neurologic	60(31.9%)	33(31.4%)	.129	23(32.4%)	.117
- Respiratory	84(44.7%)	48(45.7%)	.086	30(42.25%)	.119
- Renal	31(16.5%)	17(16.2%)	.383	13(18.3%)	.165
- Cardiovascular	13(6.9%)	7(6.7%)	.559	5(7.0%)	.603

RVI- Retroviral Infection, DM- Diabetes Mellitus, HTN- Hypertension, CAD/CHF- Coronary artery disease/congestive heart failure, COPD- Chronic Obstructive Pulmonary Disease, CKD- Chronic Kidney Disease, CLD- Chronic Liver Disease, CNS- central nervous system.

4.3. Microbiological profile and antimicrobial susceptibility

Out of 173 cultures analyzed 84(48.55%) were blood cultures, urine 69(39.88%), pus 6(3.47%), CSF and body fluid 5(2.89%) each, and 2(1.16%) of the cultures were tracheal aspirate and stool culture each. Forty four (25.43%) of cultures had growth of 51 microorganism isolates. *Gram negative microorganisms*

were identified in 35(68.63%) of isolates (Table 2) and *Acinetobacter species* accounts for 10(28.57%) followed by *Klebsiella pneumonia* and *E. coli* 7(13.725%) each and *proteus mirabilis* 4(7.84%). Ten (19.60%) of microorganisms were *gram positive microorganisms*, of which 5(50%) were *coagulase negative staphylococci*, 2(20%) enterococci and *staphylococcus aureus* each and 1(10%) *Streptococcus pneumoniae*. Six (11.76%) of the microorganisms grown were fungal, all from urine culture (Figure 1).

Acinetobacter species had shown sensitivity to meropenem 5(55.6%), ceftazidime 1(50%), amikacin 3(42.9%), gentamicin 2(40%), amoxicillin/clavulanate and cotrimoxazole 1, 2(33.3%) respectively, and ciprofloxacin and tobramycin 2, 1(25%) respectively, but resistant at all test times to other cephalosporins (cefazoline, ceftriaxone, cefepime, cefotaxime), TTC, nitrofurantoin and piperacillin.

Klebsiella pneumoniae was sensitive to imipenem 1(100%), piperacillin/tazobactam 1(50%), chloramphenicol 1(50%), meropenem 3(42.9%), ciprofloxacin 1(20%), but resistant at all test times to all cephalosporins (cefuroxime, ceftazidime, cefepime, and cefotaxime), nitrofurantoin, ampicillin, and gentamicin.

Escherichia coli had shown sensitivity to meropenem 4(100%), amikacin 1(100%), chloramphenicol and nitrofurantoin 2(100%) each, gentamicin 4(80%), piperacillin/tazobactam 1(50%), ciprofloxacin 2(33.3%), and TMP/SMX 1(25%). Whereas, resistant to cephalosporins (cefazoline, cefotaxime, and cefuroxime), augmentine, piperacillin and tetracycline at all test times.

Pseudomonas aeruginosa was sensitive to ciprofloxacin 2(100%), amoxicillin, cefepime and piperacillin 1(100%) each, meropenem and tobramycin 1(50%) each.

Table 2

Type of microorganism isolates on microbiological culture among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019 (N=number of microorganism isolates).

Type of culture	Number of Microorganism isolates (N=51)				
	Gram negative (N=35)	Percentage % (68.7)	Gram positive (N=10)	Percentage %(19.6)	Fungus (N=6) 11.7%
Blood	5	9.80	7	13.73	-
Urine	23	45.10	1	1.96	6
Pus	3	5.90	2	3.92	-
Body fluid	1	1.96	-	-	-
Tracheal aspirate	3	5.90	-	-	-

Microorganisms isolated from urine culture which were resistant to all tested antimicrobials were like *Klebsiella ozaena* (ceftriaxone, gentamicin, nitrofurantoin, piperacillin, cotrimoxazole, and tobramycin), and *rhizobium radiobacter* (ampicillin, amoxicillin/clavulanate, ceftriaxone, cefepime, ciprofloxacin, nitrofurantoin, TTC, cotrimoxazole, and tobramycin).

A single *citrobacter species* isolated from urine culture was only sensitive to amikacin, but resistant to cephalosporins (ceftriaxone and cefuroxime), tmp/smx, ciprofloxacin, gentamicin, amox/clav, TTC, and piperacillin. And also enterococcus species from urine culture had shown sensitivity to ciprofloxacin, daptomycin, and vancomycin, intermediate activity against erythromycin, but resistant to penicillin G.

Proteus mirabilis from urine cultures were sensitive to levofloxacin 1(100%), piperacillin/tazobactam 2(66.7), intrapenem 1(50%), gentamicin 1(33.3%), and intermediate to tobramycin 1(50%). But, resistant to ciprofloxacin 4(100%), ceftriaxone 4(100%), tmp/smx 4(100%), and meropenem 1(100%).

Generally, higher resistance was observed with cephalosporins and penicillins, whereas sensitivity to carbapenems, PIP/TAZ, and amikacin was satisfactory (Table 3) and (Figure 2).

Table 3
 Antimicrobial resistance and sensitivity frequency among patients
 admitted to SPHMMC and AaBET ICUs from January 2019 to
 December 2019 (N= number of tests).

Antimicrobials	Resistance: N (%)	Sensitive: N (%)
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Antimicrobials	Resistance: N (%)	Sensitive: N (%)
Ampicillin	10(100%)	-
Amikacin	6(42.8%)	8(57.2%)
Amoxicillin/Clavulanate	12(80%)	3(20%)
Ceftriaxone	14(100%)	-
Cefotaxime	10(100%)	-
Cefepime	11(91.7%)	1(8.3%)
Cefuroxime	4(100%)	-
Ceftazidime	5(71.4%)	1(14.3%)
Cefazoline	4(100%)	-
Ciprofloxacin	23(76.7%)	7(23.3)
CAF (chloramphenicol)	5(62.5%)	3(37.5%)
Clindamycin	1(50%)	1(50%)
Daptomycin	-	2(100%)
Erythromycin	1(33.3%)	-
Gentamycin	10(52.6%)	8(42.1%)
Imipenem	1(16.7%)	4(66.7%)
Intrapanem	1(33.3%)	2(66.7%)
Meropenem	4(25%)	11(68.7%)
Nitrofurantoin	13(86.7%)	2(13.3%)
Norfloxacin	1(50%)	1(50%)
Oxacillin	2(100%)	-
Penicillin	2(100%)	-
Piperacillin	9(81.8%)	2(18.2%)
Piperacillin/Tazobactam	2(18.2%)	6(54.6%)
SMX/TMP (cotrimoxazole)	19(86.4%)	3(13.6%)
TTC (Tetracycline)	9(90%)	1(10%)
Tobramycin	10(62.5%)	3(18.7%)
Vancomycin	2(66.7%)	-

A single *staphylococcus aureus* isolated from pus culture shown sensitivity to gentamicin, vancomycin, clindamycin, and TMP/SMX, but resistant to penicillins, piperacillin, and cloxacillin.

Enterococcus species had shown sensitivity against vancomycin 2(100%), daptomycin 1(100%), pip/taz 1(100%), imipenem 1(100%), and ciprofloxacin 1(50%). Intermediate activity against erythromycin; but resistant to amikacin, cephalosporins (ceftriaxone and cefotaxime), amox/clav, piperacillin, and ampicillin/sulbactam.

Streptococcus pneumoniae from blood culture was only sensitive to pip/taz, and resistant to penicillins (amoxicillin, amikacin, and amox/clav), cephalosporins (ceftriaxone, ceftazidime, and cefepime), and nitrofurantoin.

A single *klebsiella species* from blood culture was sensitive to amox/clav, ciprofloxacin, gentamicin, TTC, imipenem, and norfloxacin. But, resistant against cephalosporins, piperacillin, and TMP/SMX.

Staphylococcus aureus from pus culture was sensitive to cotrimoxazole, vancomycin and clindamycin but resistant to oxacillin, penicillin, and ciprofloxacin.

4.4. Antimicrobial use and outcome of patients to ICU

Almost all patients, 103(97.3%) took antimicrobials before ICU admission or prior to culture sampling, and ceftriaxone was used in 67(62.3%) patients, followed by vancomycin in 62(58.5%), and metronidazole in 56(52.8%) patients. The most common indications were pulmonary infection in 68(37.2%), followed by empiric therapy in 26(14.2%), and urosepsis in 25(13.7%) patients (Table 4).

Fourteen (13.2%) patients took meropenem based on culture and susceptibility result, followed by ciprofloxacin 3(2.8%), and cotrimoxazole and gentamycin in 2(1.9%) patients each.

Sixty five (61.3%) patients were discharged, whereas thirty four (32.1%) patients died during their ICU stay. And patients with urinary tract infection and septic shock before admission were significantly associated with higher risk of death.

Table 4

Comparison among outcome to ICU and indication for antimicrobial use before admission or prior to culture sampling among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019.

Indication	N (%)	Death	P value	Discharge	P value
- Bacterial sepsis	14(13.2%)	3(21.4%)	.364	9(64.3%)	.809
- Septic shock	5(4.7%)	1(20%)	.019	4(80%)	.053
- CNS infection	11(10.4%)	6(54.5%)	.093	5(45.5%)	.258
- Urosepsis	25(23.6%)	5(20%)	.036	16(64%)	.086
- Pulmonary	68(64.2%)	24(35.3%)	.347	39(57.4%)	.266
- Intra-abdominal	8(7.5%)	1(12.5%)	.221	7(87.5%)	.255
- Soft-tissue/skin	16(15.1%)	7(43.75%)	.282	9(56.3%)	.655
- Infective endocarditis	1(0.9%)	-	.495	-	.430
- Empiric	26(24.5%)	6(23.1%)	.262	18(69.2%)	.345
- Prophylaxis	9(8.5%)	2(22.2%)	.513	7(26.9%)	.294

5. Discussion

Majority of the patients were males 68(64.2%) similar to a study by Dahmesh et. al. (51.4%), but different from a study done in septic shock patients at TASH at which 60% were females (24, 34).

The mean age and median length of stay in the ICU was 35.8±1.6 years and 31 days respectively, different from TASH septic shock patients' 47.99±16.5 years and 4 days respectively. And, most of our patients (70.8%) were admitted directly from the emergency, >99% met SIRS criteria different from a study done in TASH which revealed in only 60% of patients (34). It could be because AaBET hospital is a trauma center, and trauma victimizes the young, also a reason for prolonged ICU admission.

Underlying comorbidity was found in 49(46.2%) of patients, hypertension being the most common comorbidity in 14(28.6%), lower than and different from TASH ICU septic shock patients which revealed 89.5% associated comorbidity and immunosuppression being the most common in 33.9% of patients and that of US study which showed 55.5% comorbidity with COPD accounting 12.3% (34, 40). This can be from epidemiologic shift that NCDs are affecting the young.

Organ failure occurred in majority (88.7%) of our patients, which were lower than TASH study in septic shock patients, but the most frequently failing organs were similar (34). This can be from the nature of our patients, which are not only septic shock patients, and the prolonged ICU stay.

Of the 106 patients studied 173 cultures sent were analyzed, and only 44(25.43%) of cultures had growth of microorganisms with 51 isolates, which was similar with a study in eastern Ethiopia hospitals with

isolation rate of 27.9%, but higher than that of a study done in TASH 16.5% and lower than a study done in Nepal 39.6% (32, 33, 34).

The most common source of infection was the pulmonary and urinary tract similar with a study in five ICUs of Imam Reza hospital and TASH ICU septic shock patients, but different from Jimma university hospital Ali et.al. from which surgical site infection being the most common source (29, 34, 36).

Pulmonary and urinary focus was higher in male patients 55(65.47%) and 18(69.23%) respectively, while intra-abdominal focus was higher in females 9(90%) in our study. Also a study in organisms causing UTI in ICU patients of Kenyatta national hospital reveal higher incidence in male patients (31).

Gram negatives were the most commonly identified microorganisms similar with other studies, but the isolated species were different (32, 33, 34).

And patients with CAD/CHF, urinary tract source of infection and septic shock before admission had greater risk of death which was different from other studies which revealed high risk of death with different factors such as infection with *acinetobacter* species, renal replacement therapy, use of mechanical ventilation, COPD, malignancy, pulmonary cause of infection and antibiotic use before admission (39–44).

The study found 32.1% mortality with ICU infections which was similar to other different studies 14.31–45.4%, lower than that of an African study 47.2% (17–22, 39).

High antibiotic resistance rate (>60%) was observed with ciprofloxacin, cephalosporins, piperacillin, cotrimoxazole, chloramphenicol, tetracycline, nitrofurantoin, tobramycin and penicillins including oxacillin similar to a study in Chad-Ndjamena general hospital and other studies (26, 27, 28, 30). Good sensitivity (>65%) was shown with carbapenems and vancomycin, daptomycin (100%) with two tests, amikacin (57.2%), and piperacillin/tazobactam (54.5%) similar with other studies (26, 28, 30, 31, 32).

Almost all patients 103(97.3%) studied took antimicrobials before ICU admission, which contributes to antimicrobial resistance that was directly proportional to the volume of antimicrobials consumed (13).

Whereas, the use of antimicrobial based on culture and susceptibility result showed only at 13.2% which needs improvement to have better outcome, reduce adverse events and their attendant costs, and prevent the emergence and dissemination of resistant microorganisms (12).

6. Strengths And Limitations

Data was collected retrospectively, which predisposed to lack of complete and clear data especially with the duration of antimicrobials provided before and after ICU admission, no clear date of culture sampling, and onset of infection. It was studied in different two institutional, multidisciplinary ICU settings which makes it a strong study.

7. Conclusion And Recommendation

Our study had shown patients with urinary source of infection, septic shock, and patients with comorbid illness especially coronary artery disease or congestive heart failure had significant risk of death. Resistant *gram negatives* were the predominant microorganisms identified which pose greatest challenges to ICU quality of care and prolonged ICU stay complications.

Designs of future multicenter and large studies are crucial to improve outcome of critically ill patients and targeted provision of antimicrobials based on microbiological culture and susceptibility results has to be implemented.

Abbreviations

AaBET- Addis-Ababa Burn Emergency and Trauma Hospital, CSF- Cerebro Spinal Fluid, ICU- Intensive and Critical care Unit, MRN- Medical Registration Number, SIRS- Systemic Inflammatory Response Syndrome, SPHMMC- Saint Paul's Hospital Millennium Medical College, TASH- Tikur Anbessa Specialized Hospital.

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Figures

Figure 1

Type of microorganisms grown per type of culture among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019.

Figure 2

Antimicrobial resistance and sensitivity distribution among patients admitted to SPHMMC and AaBET ICUs from January 2019 to December 2019.

TTC- Tetracycline, SMX/TMP- Sulfmethoxazole/Trimethoprim, PIP/TAZ- Piperacillin/Tazobactam, CAF- Chloramphenicol.

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