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Original Article

Bacteriologic Profile, Antibiotics Resistance Pattern, and Outcomes of Patients Admitted to Lancet General Hospital from June 2022 to June 2023: A Retrospective Cohort Study

Zekewos Demissie[1], Serkalem Nurlegn[1], Nahom Zemedkun[2], Yidnekachew Demssis[1], Bethel Mekuriya[2], Eyob Beyene[3], Seifemichael Getachew[4], Desalew Mekonnen[3], Yohannes Birhanu[3], Brook Alemayehu[1], Nebiyat Sileshi[1], Gelila Sintayehu[1], Dawit Admasu[5], Kibruyisfaw Zewdie[6]

[1]Department of Internal Medicine Lancet General Hospital, Addis Ababa, Ethiopia
[2]Lancet General Hospital, Addis Ababa, Ethiopia
[3] Department of Internal Medicine, Addis Ababa University, Addis Ababa, Ethiopia
[4] Department of Internal medicine, St. Paul Millennium Medical College, Addis Ababa, Ethiopia
[5] Department of Surgery, Lancet General Hospital, Addis Ababa, Ethiopia
[6] Department of Neurosurgery, Addis Ababa University, Addis Ababa, Ethiopia

Corresponding authors*: zakdem61@gmail.com

Abstract

Background *Prior studies indicated increased antimicrobial resistance in Ethiopia, with related health, economic, and environmental costs. Knowing an institutions and population microbiologic profile allows for proper antibiotic treatment, which substantially impact patients' outcomes such as healthcare related costs, morbidity, and mortality. The current study assessed the bacteriologic profile, resistance pattern, and treatment outcome in Lancet General Hospital.*

Method *A retrospective cohort study on the bacteriologic profile, antibiotics resistance pattern, and outcome of patients was done on 128 eligible patients who were admitted to Lancet General Hospital from June 2022 to June 2023. Data from all hospitalized patients with culture-confirmed infection were analyzed. SPSS version 26.0 was used to analyze the data. Association between independent and dependent variables was analyzed using binary logistic regression model.*

Results *Gram-negative bacteria were recovered in 77% of the cases. Extended-spectrum beta-lactamase producing Enterobacteriaceae was found in 37.5% (54) isolates and carbapenem resistant bacteria were identified in 27.8% of patients. In-hospital mortality from multidrug resistant bacterial infection was 14.8%. Age ≥ 65 years, presence of septic shock, and presence of carbapenem-resistant bacteria were independently associated with increased in-hospital mortality.*

Conclusion *High number of resistant microorganisms was isolated, and increased mortality was documented from infections caused by carbapenem-resistant bacteria. Multi-center studies should be done to determine the extent of resistant organisms in health facilities throughout the country.epidemiology, and the findings should be factored into clinical decision making and program design for disease prevention, screening, and treatment. It also calls for further prospective research to learn more about the conditions in the context of additional relevant personal and clinical characteristics*

Keywords: *Bacteriologic profile, Antimicrobial resistance, carbapenem resistance, extended-spectrum beta-lactamase,methicillin-resistant S. aureus, vancomycin-resistant enterococcus*

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Introduction

Treatment with antibiotics is one of the main armaments of modern medicine, with the discovery of antibiotics in the 1930s to 1960s drastically reducing infectious disease mortality. In the absence of discovering new classes of antimicrobials and the increasing emergence and reemergence of resistant pathogens, mortality from infectious disease is increasing [1].
Due to this concerning rise in antimicrobial-resistant pathogens, the WHO has identified twelve species of bacteria as priority pathogens based on their antimicrobial resistance. These priority pathogens are grouped into critical, high, and medium priority groups [2].

Collectively antimicrobial resistance causes at least 700,000 deaths each year according to a report in 2019, making common diseases fatal and lifesaving medical procedures risky. The problem is expected to rise barring extensive interventions resulting in 10 million deaths by 2050. The highest impact is expected to be in Africa, accounting for 4.2 million deaths annually and Asia [3, 4].

A study published in 2023 on situational analysis of antimicrobial resistance in Ethiopia found a rising antimicrobial resistance with associated health, economic, and environmental burdens [5].

A multicenter study evaluated emerging pathogens at four referral hospitals in Ethiopia and found the contribution of gram-negative bacteria for the majority of culture results with Klebsiella species and E. coli being the most frequently identified bacteria and an alarmingly higher frequency of multidrug resistance among the isolated bacteria. [6].

In another study from St. Paul Millennium Medical College and Abet Trauma Center, gram-negative bacteria were the most common isolates in 68% of cases, and drug-resistant pathogens were frequently isolated [7].

Cultures obtained from inanimate objects in the Tikur Anbessa Specialized Hospital intensive care unit showed an even a scarring picture of nosocomial infection risks. The results from this study isolated both gram-positive and gram-negative bacteria with a high drug resistance pattern [8].

Multiple risk factors were linked with acquisition of infection from Multi-drug resistant (MDR) pathogens. These risk factors are variable for different MDR pathogens. The most important risk factors for MDR gram negative bacteria include hospitalization in the past 03 month, antibiotics use in the past 01 month, presence of central venous catheter, and presence of indwelling urinary catheter[9].

Knowing the microbiologic profile of an institution and population tailors the initial empiric antibiotic management of patients, which significantly affects patient's outcome, including health-related costs, morbidity, and mortality. The objective of the current study was, therefore, to assess the bacteriologic profile, resistance pattern, and patient's outcome in Lancet General Hospital.

Methodology

Materials and Method

We conducted a hospital-based, retrospective cohort study on the bacteriologic profile, antibiotics resistance pattern, and outcome of patients admitted to Lancet General Hospital from June2022 to June2023 G.C. Lancet General Hospital is one of the largest private hospitals in Ethiopia. It currently offers complete specialist care through a variety of specialty and subspecialty departments.

Study participants

The study included participants who fulfilled the eligibility criteria. Patients ≥18 years (age 18 and above with known culture-proven microbiologic profiles, and admitted to the medical ward, surgical wards, and adult ICU and received treatment for infection were included in this study. Patients with incomplete medical records and unknown outcome were excluded from the study.

Sampling and Data collection

We included all patients with a known culture-proven microbiologic profile who received inpatient treatment for infection at Lancet General Hospital Medical and Surgical Ward and Adult Intensive Care Unit using a convenient sampling method. Participants were identified using registries for admission logbooks and culture results. Data were collected using pretested and structured questionnaire. Clinical data were collected from electronic medical records, and microbiologic data were collected from culture registries.

Bacterial and antimicrobial resistance identification
The same microbiology lab received all culture specimens, and same method was utilized to examine the results. All cultures were taken after initiation of antibiotics to tailor further management. All culture results were defined by their Gram stain reaction and colony characteristics. Bacterial species were confirmed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI TOF).A disc diffusion test was used to assess the antimicrobial resistance pattern of the isolated species.

Data Analysis

The acquired data were verified, cleaned up, and then given a final analysis. IBM SPSS Statistics software

package version 26.0 was used for analysis. To evaluate the relationship between each independent variable and the treatment outcome, binary logistic regression model was used. Univariable logistic regression analysis was performed to determine the association of each independent variable with patient outcome and variables which showed association at p-value of ≤ 0.2 were analyzed in multivariate analysis. A P-value less than 0.05 was considered to determine the statistical significance of the association, and an odds ratio with a 95% confidence interval will be used to determine the presence, strength, and direction of association between covariates and the outcome variable.

Operational definitions

Bacterial identification and species confirmation: All culture results were defined by their Gram stain reaction and colony characteristics. Bacterial species were confirmed by matrix-assisted laser desorption/ ionization time-of-flight mass spectrometry (MALDI TOF).

Extended-spectrum beta-lactamase-producing Enterobacteriaceae: defined by phenotypic detection of resistance to cefotaxime (oxyimino-beta-lactam substrate) on a disc diffusion test.

Carbapenem resistance:Carbapenem resistance was defined by phenotypic detection of resistance to carbapenem antibiotics on a disc diffusion test and confirmed by the laboratory MIC cutoff value.

Septic shock: It was defined by the need for a vasopressor to maintain a patient's mean arterial pressure (MAP) ≥ 65 mmHg or blood pressure ≥ 90/60 [9].

Patient outcome: Patient outcome was defined as in hospital mortality from any cause in patients with culture-proven bacterial infections.

Ethical Consideration

Ethical clearance was obtained from the institutional review board, and consent was not needed from the patients because wavier was obtained from the IRB of the institution. All the information obtained was confidential and used only for the intended purpose. The obtained data were documented and analyzed anonymously.

Results

A total of 174 patients were identified during the study period, and 46 were excluded for incomplete medical records (24) and unknown outcomes (22). A total of 144 microbiological culture isolates were identified from 128 patients and included in the final analysis.

Sociodemographic characteristics of study participants

The mean [± standard deviation] age of the participants was 54.38 ± (54). The majority of the study participants were male (57%). Two-third of the study participants were from Addis Ababa.

The socio-demographic characteristics of study participants are shown in Table 1.

Characteristics		No	%
Sex	Male	73	57
	Female	55	43
Age Category	< 65	84	65.6
	>/65	44	34.4
Region	Addis Ababa	81	63.3
	Somali	30	23.4
	Oromia	7	5.1
	Amhara	4	3.1
	Tigray	2	1.6
	Sidama	1	0.8
	SWP	1	0.8
	Foreginers	2	1.6

The genitourinary system was the most frequently documented site of infection followed by the pulmonary system, wound site, and soft tissue. Blood stream infection was identified only in 4 patients.

More than two-thirds (88) of the study participants had at least one risk factor for the MDR pathogen, and among those patients, 69.3% (61) had more than one risk factor. The two most often found risk factors were hospitalization within the previous three months and usage of antibiotics during the previous month.

Forty-six (35.9%) research participants had imaging evidence of an abscess and the most frequent locations were the liver, lung, and chest wall, followed by soft tissue and joint spaces.

Clinical characteristics of study participants are shown in Table 2.

Table 2: Clinical Characteristics of Study Participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023.

Characteristics		No	%
Identified focus of infection	Lung	39	30.5
	Gastrointestinal Tract	10	7.8
	Genitourinary system	42	32.8
	Central Nervous System	3	2.3
	Wound and soft tissue infection	28	21.9
	Surgical site	2	1.6
	CRBSI	4	3.1
Identified risk factors for MDR pathogen	Yes	88	68.75
	No	40	31.25
Hospitalization in the past 03 months?		50	39
Antibiotics use in the past 01 month?		53	41.4
Recurrent surgery?		33	25.8
On hemodialysis in the past 01 month?		22	17.2
Presence of central venous catheter?		20	15.6
On immunosuppressive therapy?		12	9.4
Others		10	7.8
Comorbidities	No	37	28.9
	Hypertension	57	44.5
	Diabetes	35	27.3
	Chronic Kidney Disease	35	27.3
	Acute Kidney Injury	24	18.8
	Stroke	10	7.8
	HIV	9	7
	Heart Failure	9	7
	Cancer	20	15.6
	Chemotherapy	12	9.4
Presence of septic shock		16	12.5
Mean WBC Count (± SD)	15,756.98 ± 15,850		
Mean CRP (±SD)	103.92 ± 52.30		
Imaging Evidence of Abscess		46	35.9
Location of Abscess n=46	Soft tissue and Joint	25	54.3
	Liver	7	15.2
	Lung and chest wall	5	10.9
	Renal	3	6.5
	Surgical site	2	4.3
	CNS	2	4.3
	Others	2	4.3

CRBSI: catheter-related blood stream infection

Microbiologic profile of study participants

In this study, a total of 144 specimens from 128 patients generated positive culture results. Among the study participants, 42 (32.8%) had positive blood culture results, and 102 (79.7%) had positive culture results from specimens other than blood. Gram-negative bacteria constituted 77.1% (111) of the isolated microorganism. *E. coli* was the most prevalent bacteria overall and among gram-negative isolates found in 48 (33.3%) cultures followedby *K. pneumoniae.S. aureus* was the most prevalent gram-positive bacteria

isolated in 20 (13.9%) cases. In this study, numerous bacterial isolates with a multidrug resistance pattern were discovered. Gram-negative isolates displayed a higher number of resistance compared to gram-positive isolates. ESBL-PE was found in 37.5% (54) isolates, while carbapenem resistance was found in 27.8% (40). There was no discernible resistance pattern among *S. aureus.*
Microbiologic profile and drug resistance pattern of bacteria isolates from study participants are shown in Table 3 and Figure 1.

Treatment-related characteristics of study participants

Two or more antimicrobial drugs from various classes were administered to all participants in the study. Meropenem was the most commonly used antibiotic followed by cefepime. In accordance with the findings of the culture, a higher class of antimicrobial drugs (polymyxin-B and ceftazidime-avibactam) was prescribed. MRSA coverage was used in 98 (76.6%) cases.
In 55 (43%) patients, source control was indicated.

Table 3: Microbiologic profile and drug resistance pattern of isolates from blood and non-blood culture specimens of the study participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023.

Characteristics		**Number (n)**	**Percentage (%)**
Antibiotics Used	Ceftriaxone	13	10.2
	Ceftazidime	2	1.6
	Cefepime	43	33.6
	Meropenem	68	53.1
	Ceftazidime-Avibactum	12	9.4
	Polmyxin-B	4	3.1
	Ampicillin-sulbactum	2	1.6
Gram positive coverage	No	30	23.4
	Vancomycin	91	71.1
	Linezolide	7	5.5
Intervention for Source control	No	73	57
	Surgical incision and drainage	22	17.2
	Percutaneous ultrasound guided drainage	7	5.5
	Debridement	13	10.2
	Surgery	9	7
	CVC removal	4	3.1
Mean duration of antibiotics use (± SD)	11.14 ± 4.98		
Mean duration of hospital stay (± SD)	20.52 ± 18.49		
Patient outcome	Discharge Improved	109	85.2
	In-hospital Mortality	19	14.8

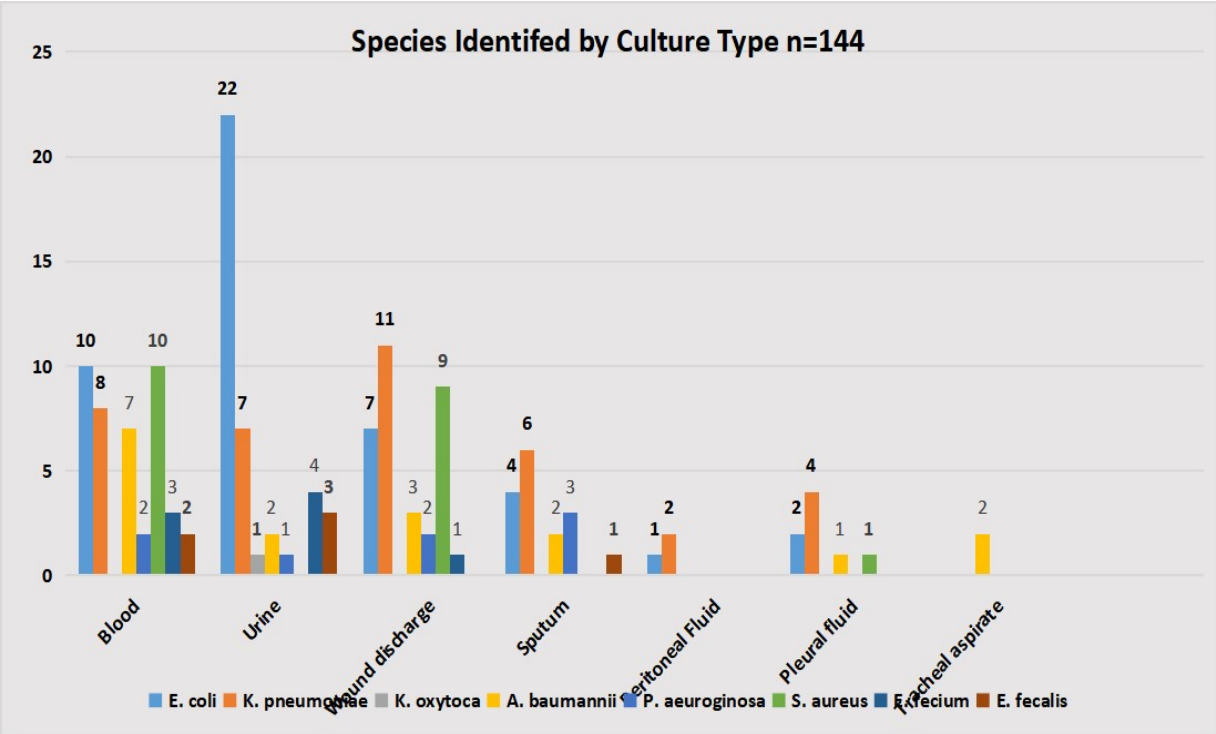

Figure 1: Species identified from blood and non-blood culture specimens of study participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023.

Incision and drainage, debridement, major surgical operations, and percutaneous ultrasound-guided drainage were the most frequently performed procedures.
The mean duration of antibiotic use and the mean duration of hospital stay was 11 and 20.5 days, respectively. Antibiotics were modified based on culture result in 54 (43.7%) patients. In 38 (29.7%) patients' 3rd and 4th generation cephalosporin were changed to Meropenem and In 16 (12.5%) patients Meropenem was changed in to Ceftazidime-Avibactum and Polymyxin-B.

From 128 patients admitted and received inpatient treatment, 109 (85.2%) of the patients completed their course of antibiotics and were discharged. In-hospital mortality was found to be 14.8% (15) in the study.
Treatment-related characteristics of study participants are shown in Table 4

Multivariate analysis of factors associated with in-hospital mortality of patients admitted for treatment of infection at Lancet General Hospital

A logistic regression analysis of the risk factors for in-hospital mortality was performed. Six variables were found to be significantly associated with in-hospital mortality on univariate analysis with a p value of ≤ 0.2. These include age ≥ 65 years, presence of risk factor for MDR pathogen, presence of comorbidities, presence of septic shock, type of bacteria identified, and presence of carbapenem-resistant bacteria.

At a p value ≤ 0.05, the final multivariate regression model revealed that 3 factors had a statistically significant association with in-hospital mortality. These include age ≥ 65 years, the presence of septic shock, and the presence of carbapenem-resistant bacteria. Compared to patients under 65 years old, patients over 65 years old had a 7.5-fold greater chance of mortality in the hospital (adjusted odds ratio (AOR 7.649), 95% confidence interval (CI): 2.018–18.986, p=0.003). In the presence of septic shock, in-hospital mortality was seven times greater than in its absence (AOR 7.051, 95% CI: 1.618-21.732, p=0.009). In-hospital mortality is five times more likely when carbapenem-resistant bacteria are present (AOR 5.062, 95% CI: 1.310-19.566, p=0.019).

Binary logistic regression analysis of factors associated with in-hospital mortality is shown in Table 5.

Table 4: Treatment-related characteristics and outcomes of study participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023

Characteristics		Number (n)	Percentage (%)
Antibiotics Used	Ceftriaxone	13	10.2
	Ceftazidime	2	1.6
	Cefepime	43	33.6
	Meropenem	68	53.1
	Ceftazidime-Avibactum	12	9.4
	Polmyxin-B	4	3.1
	Ampicillin-sulbactum	2	1.6
Gram positive cover-age	No	30	23.4
	Vancomycin	91	71.1
	Linezolide	7	5.5
Intervention for Source control	No	73	57
	Surgical incison and drainage	22	17.2
	Percutaneous ultrasound guided drainage	7	5.5
	Debridemnet	13	10.2
	Surgery	9	7
	CVC removal	4	3.1
Mean duration of antibiotics use (± SD)	11.14 ± 4.98		
Mean duration of hospital stay (± SD)	20.52 ± 18.49		
Patient outcome	Discharge Improved	109	85.2
	In-hospital Mortality	19	14.8

Discussion

Antimicrobials play a crucial role in the treatment of many infectious diseases, saving millions of lives while also easing the burden of the disease and enhancing patients' quality of life [10]. Compared to infections caused by nonresistant pathogens, hospitalization due to infection caused by drug-resistant microbes is associated with a longer hospital stay and increased healthcare expenses, morbidity, and mortality. Previous research conducted in Ethiopia indicated a trend toward an increase in the prevalence of drug-resistant pathogens [5, 11].

The study participants in this study were older on average than those in other studies. The increasing proportion of elderly participants in our study may be attributable to a greater number of older patients receiving follow-up care at the hospital's chronic outpatient services [7, 12].

The genitourinary system was the most common documented focus of infection followed by the pulmonary system. This outcome is different compared with studies conducted at adult intensive care units at Abet Trauma Center, and the Iran ICU. The difference in study populations and study settings might have contributed for the difference in the focus of infection observed in the various studies [7, 13].

Gram-negative bacteria were discovered in 77% of the cases, and E. coli and K. pneumoniae were the most frequent species found and 70% of A.baumannii isolates exhibited carbapenem resistance. This is comparable with other studies [6, 7].

The delivery of adequate empiric antibiotics, the utilization of culture data for individualized antibiotic modification, appropriate imaging surveillance to identify collections, and prompt source control interventions could all contribute to this higher discharge rate in this study.

Three factors were identified in the present study as independent predictors of in-hospital mortality. These include age ≥ 65 years, the presence of septic shock, and the presence of carbapenem-resistant bacteria.

The increased prevalence of comorbidities in this age group may be the cause of the higher mortality. When septic shock was present, fatality rates were greater. The findings from septic shock investigations demonstrated a 30 to 50% greater risk of mortality [14, 15]. The delayed identification of the bacteria from clinical specimens and the lack of higher classes of antimicrobials in our scenario may be the causes of increased mortality brought on by the presence of carbapenem-resistant bacteria.

Discussion

Antimicrobials play a crucial role in the treatment of many infectious diseases, saving millions of lives while also easing the burden of the disease and enhancing patients' quality of life [10]. Compared to infections caused by nonresistant pathogens, hospitalization due to infection caused by drug-resistant mi-

Table 5: Multivariate analysis of factors associated with in-hospital mortality of study participants at Lancet General Hospital, Addis Ababa, Ethiopia, June 2022 – June 2023.

Variables	In-Hospital Mortality		COR (95% CI)	P value	AOR (95% CI)	P value
	Yes	No				
Age Category						
<65	4	80	1	1		
>/=65	15	29	10.345 (3.173 - 18.731)	0.0001	7.649 (2.018 - 18.986)	0.003
Presence of risk factor for MDR pathogen						
Yes	16	72	2.741 (0.750 - 10.009)	0.127	1.570 (0.232 - 5.049)	0.939
No	3	37	1	1		
Presence of comorbidities						
Yes	18	73	4.315 (0.957 - 19.929)	0.057	1.639 (0.287 - 9.354)	0.578
No	2	35	1	1		
Presence of Septic shock						
Yes	8	8	9.182 (2.876 - 21.315)	0.0001	7.051 (1.618 – 21.732)	0.009
No	11	101	1	1		
Type of Bacteria Identified						
Gram Positive	2	27	1	1		
Gram Negative	17	82	2.799 (0.607 - 12.904)	0.187	1.526 (0.254 – 9.177)	0.644
Presence of Carbapenem Resistance						
Yes	12	22	6.779 (2.389 - 19.236)	0.0003	5.062 (1.310-19.566)	0.019
No	7	87	1	1		

crobes is associated with a longer hospital stay and increased healthcare expenses, morbidity, and mortality. Previous research conducted in Ethiopia indicated a trend toward an increase in the prevalence of drug-resistant pathogens [5, 11].

The study participants in this study were older on average than those in other studies. The increasing proportion of elderly participants in our study may be attributable to a greater number of older patients receiving follow-up care at the hospital's chronic outpatient services [7, 12].

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Three factors were identified in the present study as independent predictors of in-hospital mortality. These include age $\geq$ 65 years, the presence of septic shock, and the presence of carbapenem-resistant bacteria. The increased prevalence of comorbidities in this age group may be the cause of the higher mortality. When septic shock was present, fatality rates were greater. The findings from septic shock investigations demonstrated a 30 to 50% greater risk of mortality [14, 15].

The delayed identification of the bacteria from clinical specimens and the lack of higher classes of antimicrobials in our scenario may be the causes of increased mortality brought on by the presence of carbapenem-resistant bacteria.

Conclusion

Gram-negative bacteria were the most frequent isolates, and an increasing number of drug-resistant organisms were identified in clinical specimens from patients in this study. Age greater than or equal to 65 years, the prevalence of septic shock, and the presence of bacteria resistance to carbapenem were all independently associated with greater in-hospital mortality. In regard to selecting antibiotics and directing improved antimicrobial stewardship programs, adequate monitoring and antimicrobial data are crucial. Results from appropriate culture specimens tailors antimicrobial choice. Primary care physicians should use higher classes of cephalosporin and carbapenem with proper indication. Ministry of Health and hospital administrations should ensure a proper infection prevention programs and a controlled mechanism should be established to control appropriateness of antimicrobial prescriptions.

Recommendations

We recommend our institution to advocate antimicrobial stewardship program and prepare antibiogram based on available data. Strengthening infection prevention measures and application of proper use of antibiotics help in mitigating the rising public health concern from MDR pathogens. We also recommend a large multicenter prospective study with pre-specified aims to analyze the microbiologic culture profile, resistance pattern of isolates, outcomes, and factors associated with the outcomes because this is a single-center, retrospective investigation with a small sample size. We also advise institutions to properly prepare for and adhere to infection prevention, as well as to conduct regular surveillance of their antimicrobial data and stewardship programs.

Strengths and Limitations of the Study

To the best of the authors' knowledge, this is the first study on microbiologic profiles and medication resistance patterns from a private facility; therefore, it can serve as a reference and baseline for future research. Because it is a retrospective study, the observer is unable to directly gauge the study variables and timing of infection or new infection that developed after admission.

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Conflict of Interest

All authors state that they have no conflicts of interest.

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