Nosocomial sepsis and drug susceptibility pattern among patients admitted to adult intensive care unit of Ayder Comprehensive Specialized Hospital, Northern Ethiopia

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Abstract

Objective: Developing nosocomial sepsis within intensive care unit (ICU) is associated with increased mortality, morbidity, and length of hospital stay. But information is scarce regarding nosocomial sepsis in Northern Ethiopia. Hence, this study aims to determine the prevalence of nosocomial sepsis, associated factors, bacteriological profile, drug susceptibility pattern, and outcome among patients admitted to the adult intensive care unit of Ayder Comprehensive Specialized Hospital (ACSH).

Method: Facility-based cross-sectional study was conducted by reviewing the medical records of 278 patients admitted for more than 48 hours to adult ICU of ACSH from October 2016 to October 2017. Data were collected from charts, electronic medical records, and microbiology laboratory data registration book using a checklist. The collected data were subjected to descriptive statistics and multivariable logistic regression using SPSS 25. Statistical significance was declared at $p < 0.05$.

Result: Of all the patients, 60(21.6%) of them acquired nosocomial sepsis. The risk of mortality was about two times higher among those who acquired nosocomial sepsis ($RR=2.2$; 95% CI of $RR=1.3-3.5$; $p=0.003$). The odds of acquiring nosocomial sepsis among those who were on a mechanical ventilator (MV) and stayed more than a week was 5.7 and 9.3 times higher respectively than their corresponding counterparts. Among 48 isolates, *Klebsiella* was the commonest. The isolated organisms had a broad antibiotic resistance pattern for cephalosporin, penicillin, and methicillin.

Conclusion: Mortality due to nosocomial sepsis in adult ICU was higher. Use of MV and longer length of in-hospital stay were significant risk factors for nosocomial sepsis. The isolated organisms were resistant to several antibiotics. Therefore, strict application of infection prevention strategies and appropriate use of antibiotics is so crucial.

Background

Sepsis is defined as systemic inflammatory response manifested by either hyperthermia or hypothermia, tachypnoea, leukocytosis, or leukopenia in the presence of proven or presumed infection (1). Nosocomial sepsis is defined as sepsis developing after 48 hours of patient hospitalization (2). Though it varies with geography and population characteristics, the most common pathogenic Gram-positive bacteria causing nosocomial sepsis in Intensive Care Unit (ICU) setting have been reported to be *S. aureus*, while organisms such as *Klebsiella*, *Acinetobacter*, *Pseudomonas*, and *E. coli* species constituted the most common Gram-negative species (3–7).

Developing nosocomial sepsis is common in critical care units and its prevalence can range from 9.6% to 17.7% (7–9). As was mentioned in different reports this is due to immunosuppression, prolonged hospitalization, intensive use of various equipment like catheters, mechanical ventilators (MVs), and older age group which can make patients susceptible to various nosocomial pathogens (1,8,9). The commonest types of infections in the ICU are ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLABSI), urinary catheter-related infection, and surgical site infection

(SSI) (8–10). Developing nosocomial sepsis within ICU is associated with increased mortality, morbidity, and length of hospital stay (7,8).

In Ethiopia, there is scarcity of information regarding the burden of nosocomial sepsis as well as the distribution of bacteria and drug resistance profiles among patients admitted to ICUs. Particularly there is no such information in the Tigray region. Hence, this study aims to determine the prevalence of nosocomial sepsis, associated factors, bacteriological profile, drug susceptibility pattern, and outcome among patients admitted to the adult intensive care unit of Ayder Comprehensive Specialized Hospital (ACSH).

Methods

Study area, design, and period

ACSH, which is located in Mekelle city, commenced rendering its referral and non-referral services in 2008 to 8 million population in its catchment areas of Tigray, Afar, and South-eastern parts of the Amhara Regional States. It provides a broad range of medical services to all age groups. Of the services provided, adult ICU holds a role in managing critically ill patients who require at most care and life supportive machines. It is equipped with MVs, defibrillators, perfusers, and other gadgets (11). Health facility-based cross-sectional study was conducted by reviewing medical records of patients admitted to adult ICU from October 2016 to October 2017.

Study population

All patients who stayed more than 48 hours after admission to adult ICU at ACSH during the study period.

Sample size

The sample size is calculated based on the prevalence of bacteria isolated from suspected cases in Nigeria Tertiary Hospital which was reported to be 15% (8). With a 5% margin of error and 95% confidence interval ($\alpha = 0.05$), the minimum sample size for the study using single population proportion formula was calculated as follows:

$$n = \frac{(Z_{1-\alpha/2})^2 p(1-p)}{d^2} = \frac{(1.96)^2 0.15(1-0.15)}{0.05^2} = 196$$

Adding 10% contingency the minimum sample size required was 216. However, we included all the 294 patients who were admitted to adult ICU during the study period.

Data collection, source, and quality assurance

A checklist was developed and used to extract sociodemographic, clinical, and microbiological data. These were collected from charts, electronic medical records, and microbiology laboratory data registration books. Data were collected by trained internal medicine residents under the supervision of an internist.

Study variables

Our outcome variables were the acquisition of nosocomial sepsis and drug susceptibility. Age, sex, residence, length of hospital stay, MV use, and central line use were the independent variables.

Data analysis

Data analysis was aided by computer software (SPSS version 25). Frequency and percentage were employed to summarize categorical variables. Continuous variables were also described using an appropriate combination of measure of central tendency and measure of dispersion. The relationship between the acquisition of nosocomial sepsis and its predictors was analyzed using binary logistic regression. Variables with a p-value of < 0.25 in the univariate analysis were selected for the final multivariable logistic regression model. A p-value of < 0.05 is considered to yield a statistically significant result. The final multivariable model was checked for the goodness of fit and multicollinearity using Hosmer-lemeshow test and variance inflation factor (VIF) respectively.

Ethical Approval

Ethical approval of the research was obtained from the Institutional Review Board (IRB) of Mekelle University, College of Health sciences. Permission, to collect secondary data, was obtained from the chief clinical director's office of ACSH. Informed consent was not applicable since secondary data used. But deidentification was applied by removing names and medical record numbers, and finally replacing them with codes.

Results

A total of 294 patients who were admitted to the Adult ICU stayed more than 48hrs. Of this 16 were excluded due to missing or incomplete medical records and a total of 278 patient records were included in the study.

Sociodemographic and clinical characteristics

The median age of the participants was 42 (IQR=31) ranging from 17 to 90. Out of the patients included in the study, 156(56.1%) were male and 163 (58.6%) were from an urban area. Nearly one-third (32.0%) of them were on MV and only 9.0% of them required central line use. For two-third of the patients, the length of ICU stay was one week or less. Of all the patients, 60(21.6%) of them acquired nosocomial sepsis. For the patients with nosocomial sepsis, the main focuses of infections were respiratory (78.3%) and urinary

(16.7%) (**Table 1**). The risk of mortality was about two times higher among those who acquired nosocomial sepsis (Risk ratio (RR)=2.2; 95% CI of RR=1.3-3.5; p=0.003).

Table 1: *Sociodemographic and clinical characteristics of the study participants adult ICU, ACSH, 2017 (n=278).*

<i>Variables</i>	<i>Frequency</i>	<i>Percentage (95% CI)</i>
Age in years		
<40	123	44.2 (38.5-50.1)
40-64	120	43.2 (37.4-49.1)
65+	35	12.6 (9.2-17.1)
Sex		
Female	122	43.9 (38.1-49.8)
Male	156	56.1 (50.2-61.9)
Residence		
Urban	163	58.6 (52.7-64.3)
Rural	115	41.4 (35.7-47.3)
Mechanical ventilator use		
Yes	89	32.0 (26.8-37.8)
No	189	68.0 (62.2-73.2)
Central line use		
Yes	25	9.0 (6.1-13.0)
No	253	91.0 (87.0-93.9)
Length of stay		
2-7 days	188	67.6 (61.9-72.9)
>7 days	90	32.4 (27.1-38.1)
Nosocomial sepsis		
Yes	60	21.6 (17.1-26.8)
No	218	78.4 (73.2-82.9)
Focus of infection (n=60)		
Respiratory	47	78.3 (65.8-87.2)
Urinary	10	16.7 (9.0-28.7)
Thrombophlebitis	3	5.0 (1.6-14.8)
Overall outcome		
Died	51	18.3 (14.2-23.4)
Discharged	227	81.7 (76.6-85.8)
Nosocomial sepsis outcome (n=60)		
Died	19	31.6 (20.9-44.8)
Discharged	41	68.3 (55.2-79.1)

Factors associated with the acquisition of nosocomial sepsis

In the final multivariable logistic regression model, the variables MV use and length of ICU stay were significantly associated with the acquisition of nosocomial sepsis. Thus, the odds of acquiring nosocomial sepsis among those who were on MV was 5.7 (**AOR (95% CI) =5.7 (2.6-12.7), $p<0.001$**) higher than their counterparts. Those who stayed more than a week in the ICU had about nine times higher odds of nosocomial sepsis acquisition (**AOR (95% CI) =9.3 (4.3-20.4), $p<0.001$**). The final multivariable model was a good fit (Hosmer-Lemeshow test: $\chi^2=10.97$, $df=8$, $p=0.204$) and had no multicollinearity issue (max VIF=1.2, mean VIF=1.1). ROC curve analysis revealed that the final model had very good accuracy with the area under the curve of 0.873 (**Table 2**).

Table 2: *Factors associated with the acquisition of nosocomial sepsis, adult ICU, ACSH, 2017 (n=278).*

Variables	COR (95% CI)	p-value	AOR (95% CI)	p-value
Age in years				
<40	1		1	
40-64	0.7(0.4-1.4)	0.333	1.3(0.6-3.2)	0.505
65+	0.5(0.2-1.4)	0.181	0.8(0.2-3.3)	0.806
Sex				
Female	1		1	
Male	1.6(0.9-2.9)	0.119	1.4(0.6-2.9)	0.412
Residence				
Urban	1		1	
Rural	1.7(0.9-3.0)	0.069	1.6(0.8-3.4)	0.207
Mechanical ventilator use				
Yes	11.9(6.1-23.2)	<0.001	5.7(2.6-12.7)	<0.001
No	1		1	
Length of stay				
2-7 days	1		1	
>7 days	16.8(8.2-34.3)	<0.001	9.3(4.3-20.4)	<0.001
Central line use				
Yes	1.5(0.6-3.7)	0.416	1.1(0.3-3.7)	0.910
No	1		1	

Microbiological profile of isolated samples

Samples were taken from blood, urine, and tracheal secretion of septic patients in the ICU. Of the samples taken 48 isolates of organisms were found, of which 91.7% were gram-negative. The only gram-positive isolated was *Staphylococcus aureus* (8.3%). Among the samples taken *Klebsiella* was found to be the commonest organism (37.5%) (**Table 3**).

Table 3: *Isolated microorganisms from the septic patients in adult ICU, ACSH, 2017 (n=48).*

Microorganism	Frequency (n=48)	Percent (95%CI)
Klebsiella	18	37.5 (24.0-52.6)
Pseudomonas A.	8	16.6 (7.5-30.2)
Acinetobacter	7	14.6 (6.1-27.8)
E. coli	7	14.6 (6.1-27.8)
Citrobacter	3	6.3 (1.3-17.2)
Enterobacter C.	1	2.1 (0.1-11.1)
Staph. Aureus	4	8.3 (2.1-20.0)

The gram-negatives had a broad antibiotic resistance pattern for cephalosporin, penicillin, and meropenem (**Table 4**). Staphylococcus aureus was also found to be resistant to penicillin and methicillin (**Table 5**).

Table 4: *Distribution of antibiotics susceptibility pattern for isolated Gram Negative microbials from septic patients in Adult ICU, ACSH, 2017.*

Note: R=Resistant, S=Sensitive and I=Intermediate

Table 5: *Distribution of antibiotics susceptibility pattern for isolated Staphylococcus aureus from septic patients in adult ICU, ACSH, 2017.*

Antibiotic	Sensitivity pattern	Klebsiella Sensitivity %(Isolates No)	Pseudomonas Sensitivity %(Isolates No)	E. coli Sensitivity % (Isolates No)	Acinetobacter Sensitivity %(Isolates No)	Citrobacter Sensitivity %(Isolates No)
Ampicillin	R	100(17/17)	100%(5/5)	89(8/9)	100(5/5)	100(3/3)
Penicillin	S	-	-	11(1/9)	-	-
	R	-	-	100(1/1)	100%(1/1)	-
Tetracycline	R	90(9/10)	100(2/2)	83.3(5/6)	100(4/4)	100(3/3)
	S	10	-	16.7	-	-
Doxycycline	R	66.7(2/3)	100(2/2)	100(3/3)	66.7(2/3)	100(1/1)
	S	33.3	-	-	33.3	-
Chloramphenicol	R	71.4(5/7)	100(2/2)	66.7(2/3)	100(3/3)	100(3/3)
	S	28.6	-	33.3	-	-
Ciprofloxacin	R	62.5(10/16)	30()3/10)	77.8(7/9)	83.3(5/6)	100(3/3)
	S	25	50	11.1	-	-
Gentamycin	I	12.5	20	11.1	16.7	-
	R	58.3(7/12)	57.1(4/7)	60(3/5)	100(3/3)	100(3/3)
	S	16.7	14.3	20	-	-
Cotrimoxazole	I	25	28.6	20	-	-
	R	92.3(12/13)	100(2/2)	75(3/4)	100(3/3)	100(3/3)
Augmentin	R	100(13/13)	100(2/2)	100(4/4)	100(4/4)	100(3/3)
Amikacin	R	60(3/5)	25(2/8)	100(1/1)	100(3/3)	100(2/2)
	S	20	37.5(3/8)	-	-	-
	I	20	37.5(3/8)	-	-	-
Cephalothin	R	100(12/12)	100(1/1)	100(4/4)	100(2/2)	100(1/1)
Piperacillin	R	100(1/1)	25(1/3)	100(1/1)	100(2/2)	100(1/1)
Ceftriaxone	R	100(8/8)		100(1/1)	100(4/4)	100(1/1)
	S	-	100(1/1)			-
Ceftazidime	R	100(9/9)	42.9(3/7)	100(1/1)	100(5/5)	100(1/1)
	S	-	57.1	-		-
Meropenem	R	10(1/10)	50(2/2)	-	100(4/4)	100(1/1)
	S	70(7/10)	50	100(1/1)		-
	I	20	-	-	-	-
Tobramycin	R	66.7(2/3)	42.8(3/5)	-	-	-
	S	33.3	28.6	-	-	-
	I	-	28.6	-	-	-
Cefepime	R	100(3/3)	-	--	100(4/4)	-
	S	-	100(3/3)		-	-

Antibiotic	Sensitivity pattern	Staph. Aureus Sensitivity % (Isolates No)
Penicillin	R	100(3/3)
Tetracycline	S	100(1/1)
Doxycycline	R	33.3(1/3)
	S	66.7(2/3)
Chloramphenicol	R	100(1/1)
Ciprofloxacin	R	100(1/1)
Gentamycin	R	100(2/2)
Cotrimoxazole	R	100(1/1)
Ceftriaxone	R	100(2/2)
Erythromycin	R	100(2/2)
Vancomycin	R	-
	S	66.7(2/3)
	I	33.3(1/3)
Methicillin	R	100(2/2)

Discussion

Our study aimed at assessing the prevalence of nosocomial sepsis, associated factors, bacteriological profile, drug susceptibility pattern, and outcome of patients admitted at adult ICU. The prevalence of nosocomial sepsis was 21.6% developed nosocomial sepsis. MV use and length of stay were significantly associated with the acquisition of nosocomial sepsis. The microorganisms had a broad antibiotic resistance pattern for cephalosporin, penicillin, and meropenem.

The prevalence of nosocomial sepsis in our setup was higher compared to studies done in Nigeria (15%) (8) and India (9.6%-17.7%) (7,9,10). Nosocomial sepsis happens due to inadequate hand hygiene techniques, infrequent urinary catheter changes where catheters are left in situ for a prolonged time, inadequately cleaned ventilators before and after patient use, lack of programmed ICU cleaning or decontamination procedures, and lack of strict attendant visit protocol making patients susceptible for various infections (12).

Those who were on MV had a higher risk (5.7-fold) of nosocomial sepsis. This finding was in tune with studies done in India (9,10). Also, those who stayed more than a week in the ICU had about nine times higher odds of nosocomial sepsis acquisition. This higher risk of nosocomial sepsis among those who stayed more than a week could be a result of prolonged exposure to MV use. Because, in our study, the use of MV was 64.4% in those who stayed more than a week in contrast to those who stayed a week and less, which was 16.5%. This difference was statistically significant ($\chi^2=64.3$, $df=1$ and $p<0.001$). Furthermore,

longer ICU stay and MV use are thought to increase the risk of acquiring antibiotic-resistant infections (12,13).

The overall mortality of ICU patients who stayed for more than 48 hours was 18.3%. But this mortality was significantly higher in those who acquired nosocomial sepsis (31.6%). Similar results, on the mortality of patients with nosocomial sepsis, are reported from studies done in Asia, Europe, and North America (10,14–17). Hence, the presence of nosocomial sepsis contributed considerably to the poor outcome of the ICU patients by increasing mortality risk significantly ($p=0.003$). Moreover, studies report that the burden of mortality due to nosocomial sepsis is further higher in patients with organ dysfunction and had surgery on an emergency basis (15,17).

Among the body fluid samples taken, 48 isolates of organisms were found of which 91.6% were gram-negative and 8.3% were gram-positive which are consistent with studies from Nigeria, India, and Europe (8,9,14,18). *Klebsiella* was found to be the commonest organism followed by *Pseudomonas*, *E. coli*, and *Acinetobacter*. This is parallel with the studies of Nigeria, India and Fiji (8,14,18). For instance, in Fiji's study, the commonest pathogens isolated were *Klebsiella pneumoniae*, *Acinetobacter*, and *Pseudomonas* (14).

Klebsiella was resistant to ampicillin, ceftazidime, cefepime in all tested isolates and showed a broad resistance pattern to other antibiotics but was found to be sensitive to meropenem in 66.7%. *Pseudomonas* had a sensitivity of 57.1% and 50% to ceftazidime and meropenem respectively. Higher resistance to meropenem was found in *Acinetobacter*, where all 4 isolates were resistant to the antibiotic. The isolated *Staph. aureus* was also methicillin-resistant but vancomycin sensitive. These results show that although few organisms were checked against an antibiotic, there is broad resistance to penicillin, cephalosporins, and other antibiotics. Such kind of broad resistance was announced by several studies done in ICU of different countries (19,20,29,30,21–28).

The use of antibiotics to patients should be evidence-based, when there is a highly suspected infection and bacteriologic evidence of infection. Frequent use of antibiotics in patients with or without sepsis renders most organisms to be antibiotic-resistant. When indicated, the use of antibiotics should be guided with a bacteriological profile. Providing drugs to a patient harboring resistant microorganisms results in negative impacts including financial burden, longer hospital stay, deterioration, and even death of the patient (12,13).

Conclusion

There is a higher prevalence of sepsis in adult ICU. Use of MV and longer length of in-hospital stay were significant risk factors for nosocomial sepsis. Furthermore, nosocomial septicaemia had a significant effect on the mortality of admitted patients. The identified organism were mainly gram negatives.

Limitations of the study

Body fluid culture was not done for all infections, and the microbial susceptibility test was not consistent.

Recommendation

Great emphasis should be given to the high prevalence of nosocomial sepsis. Setting up motivated and persistent infection prevention techniques is required. This includes developing strict protocols and practice which is adherent to the protocol. These include adequate cleaning of mechanical ventilators and other devices before and after use in a patient. The use of antibiotics should be guided with appropriate clinical sepsis diagnosis and basing the selection on the bacteriological profile of the patient.

Abbreviations

ACSH	Ayder Comprehensive Specialized Hospital
AOR	Adjusted Odds Ratio
CLABSI	Central Line-Associated Bloodstream Infection
COR	Crude Odds Ratio
ICU	Intensive Care Unit
IQR	Inter-Quartile Range
IRB	Institutional Review Board
MV	Mechanical Ventilator
ROC	Receiver Operating Characteristic
RR	Risk Ratio
SSI	Surgical Site Infection
VAP	Ventilator-Associated Pneumonia
VIF	Variance Inflation Factor

Declarations

Ethics approval and consent to participate

Ethical approval of the research was obtained from the Institutional Review Board (IRB) of Mekelle University, College of Health sciences. Permission, to collect secondary data, was obtained from the chief clinical director's office of ACSH. Informed consent was not applicable since secondary data used. But

deidentification was applied by removing names and medical record numbers, and finally replacing them with codes. All methods are done in accordance with relevant guidelines and regulations

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TCD, MME, and HEA wrote the main manuscript as well as prepared the tables. All authors reviewed the manuscript.

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