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Health care-associated infections in pre-transplant liver intensive care unit: Perspectives and challenges

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ABSTRACT

Background: Health care-associated infections (HAIs) threaten patient's safety worldwide especially in the intensive care units (ICU). In end-stage liver disease (ESLD), the condition is much more complicated. Data regarding HAIs among ESLD patients is lacking. We aimed to assess the incidence of HAIs, risk factors, causative micro-organisms, antimicrobial susceptibilities and mortality rates among patients with end-stage liver disease (ESLD) admitted to pre-transplant liver intensive care unit (LICU).
Method: This prospective observational study included 337 ESLD patients admitted to LICU, Al-Rajhi liver center, Assiut University Hospital, Assiut, Egypt between January 2016 and June 2016 and they were followed up for the development of HAI manifestations. The medical history, physical examination and severity of underlying disease were determined. Clinical samples were taken from patients who developed HAIs for microbiological diagnosis and antimicrobial susceptibility testing.
Results: A total of 57 (16.9%) ESLD patients developed HAIs with the incidence density of 26.8 per 1000 patient-days. Blood stream infection was the most common (49.1%). *Escherichia coli* (21.1%) followed by methicillin-resistant *Staphylococcus aureus* (MRSA) (15.8%) were the commonest bacteria. Multidrug resistant organisms were reported in 52.6% of the isolates. Fungal causes were 15.8% with *Candida* species dominance. *Sphingomonas paucimobilis* and *Achromobacter dentrificans* were reported for the first time as pathogens for HAIs in LICU. Prolonged hospital stay, intravenous line duration, prolonged use of proton pump inhibitors and paracentesis were predictors for HAIs. No significant difference between ESLD patients with and without HAIs regarding mortality (36.8% vs. 48.6%, P = 0.2).
Conclusion: High HAI rate among ESLD patients is a matter of worry. Effective surveillance program, active infection control measures and national antibiotic policies are necessary to reduce the burden of HAIs.

Introduction

Health care-associated infections (HAIs) cause significant morbidity and mortality threatening patient's safety worldwide. In developing countries, HAI prevalence is two- to threefold higher than Europe or USA [1,2]. In general, the incidence is particularly high in intensive care units (ICUs) compared to non-ICU wards in the hospital as ICU patients have severe co-morbidities and greater use of invasive devices [3]. In end-stage liver disease (ESLD), the condition is much more complicated as its dysimmunoregulation state, co-morbidity e.g. diabetes mellitus, renal impairment, and malignancy, hyperammonemia, and hyponatremia thus increased susceptibility to infections [4,5]. However, to our knowledge, studies on HAIs in pretransplant Liver intensive care unit (LICU) are deficient especially from our region. So, we aimed to measure HAI rates among patients admitted to pre-transplant LICU, their risk factors, the causative micro-organisms, their antimicrobial susceptibilities and mortality rates.

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Materials and methods

Study design

This prospective observational study was carried out at Assiut University Hospital (AUH), Egypt, from January 2016 to June 2016.

Study population

Patients with ESLD admitted to the pre-transplant LICU, Tropical Medicine and Gastroenterology Department, Al-Rajhi liver center, AUH, Egypt between January 2016 and June 2016 were followed up for the development of HAI manifestation according to the CDC definitions [6].

Methods

During hospitalization, thorough clinical history and examination were taken. The severity of underlying diseases was assessed using Child-Pugh, MELD and the Acute Physiology and Chronic Health Evaluation II (APACHE II) scores [7–9].

Clinical specimens were collected from patients according to the suspected site of infection (e.g. blood, urine, ascitic fluid, sputum or endotracheal aspirates). In-hospital mortality was assessed.

Microbiologic studies

With universal safety precautions and standard laboratory protocols [10], clinical samples were collected from patients then transported and processed in the Medical Microbiology and Immunology Department, Faculty of Medicine, AUH, for initial identification by conventional methods then sent to the Microbiology laboratory of the Clinical Pathology Department, AUH, for automated confirmation. For blood and ascitic fluid samples, 2 blood culture bottles (aerobic and anaerobic) were incubated in Bact/Alert system (bioMerieux Inc, Mercy L'etoil, Fransa) according to its manufacturer. Gram staining was done for positive culture bottles and subculture was performed onto appropriate solid media. For other specimens, Gram staining, viable count estimation for urine samples, followed by inoculation onto blood agar, MacConkey agar, chocolate agar, bile esculin azide agar and plates were incubated at 37 °C for 24 h. Also, two plates of saboroud's dextrose agar were inoculated for each sample; one incubated at 37 °C and the other at 25 °C for two weeks and were examined daily, all under aerobic condition. For blood agar, incubation was done at 37 °C in an anaerobic jar for 3 days. Cultures were confirmed and antimicrobial susceptibility testing was performed with VITEK 2 COMPACT-15 automated system (bioMerieux Inc, Mercy L'etoil, Fransa). Isolates resistant to more than two different classes of antibiotics were considered as multidrug resistant organisms (MDROs) [11].

We used ID-GNB and AST-N073 cards for Gram −ve bacilli, ID-GP and AST cards for Gram +ve cocci, IDYST and AST-Yeast07 cards for yeasts and the ID-ANC card for anaerobes.

Outcomes were interpreted according to the Clinical and Laboratory Standards Institute standards [12].

Statistical analysis

Statistical analyses were conducted using SPSS for windows version 16 (SPSS Inc., Chicago, IL, USA). The continuous data was expressed as means ± standard deviation (SD) and was compared using Student's t test. Categorical variables were expressed as percentage and compared using chi-squared. Significant factors on univariate analysis were considered for inclusion in multiple regression analysis to predict HAI development. Kaplan–Meier curves were constructed to study the effect of HAIs on LICU stay and difference between two curves was analyzed using the log-rank test. In addition, multivariable Cox regression model was used to determine independent factors for case fatality. For all analyses, P-value < 0.05 was considered statistically significant.

The infection and mortality rates were calculated using WHO formulas [13].

Results

Distribution of HAIs in the study patients

Between January 2016 and April 2016, 337 ESLD patients (243 males and 94 females with mean age of 57.9 ± 9.5 years) were admitted to LICU for different indications: hepatic encephalopathy (n = 197), bleeding varices (n = 90), fulminant hepatitis (n = 12) and others (n = 38). HAIs were suspected in 36.5% (123/337) of patients (85 males and 38 females with mean age of 58.1 ± 6.6 years) with an incidence density of 57.9 patients per 1000 patients-days. Of 123 patients, 57 cases of infection were confirmed bacteriologically with cumulative incidence rate (57/337, 16.9%). These cases were 23 females and 34 males, with a mean age of 59.1 ± 5.3 years and an incidence density of 26.8 per 1000 patient-days. The remaining 66 patients (15 females and 51 males with a mean age of 57.4 ± 7.4 years) had negative cultures. The most frequent bacteriologically confirmed HAIs according to the CDC definitions [6] were blood stream infection (BSI, 49.1%), followed by urinary tract infection (UTI, 31.6%), pneumonia (12.3%) and lastly spontaneous bacterial peritonitis (SBP, 7%). The mean stay length in patients with and without HAIs was 11.5 ± 3.8 versus 5.1 ± 3.7 days respectively (P < 0.05).

The most frequent Gram-positive bacteria causing HAIs was *Staphylococcus* species (20/57, 35.1%) with *Staphylococcus aureus* being the commonest (12/20, 60%). The most common Gram-negative bacteria was *Escherichia coli* (12/57, 21.1%). Fungal infections were reported in 15.8% (9/57) with *Candida* species being the predominant (12.3%). No anaerobic infection could be detected. The details are shown in Table 1.

Out of 337 admitted patients, 231 (68.5%) had a history of receiving empirical antibiotics, 62.7% of them for prophylactic purposes. The most commonly prescribed antibiotic in the LICU was third generation cephalosporin "cefotaxime" for prophylactic (105/337, 31.2%) and therapeutic indications (45/337, 13.4%) followed by ciprofloxacin for prophylaxis (25/337, 7.4%) and levofloxacin (29/337, 8.6%) and cefepime (24/337, 7.1%) for therapeutic use.

Concerning patients with HAIs, 57.9% received empirical antibiotics (33/57) mostly for prophylactic indications (16/33, 48.5%), and 36.4% (12/33) for therapeutic indications. Patients who received prophylactic followed by therapeutic antibiotics constituted 15.2% (5/33). Cefotaxime was the commonest antibiotic used for prophylactic and therapeutic treatment for patients with HAIs (n = 14 and 3 respectively).

Antimicrobial resistance

Multidrug resistant organisms (MDROs) were reported in 52.6% of the isolates. The majority of *S. aureus* isolates (75%) were methicillin-resistant (*MRSA*). For Gram-negative isolates, 20% were ESBL-producers (25% of *E. coli*, 33.3% of *Enterobacter aerogenes* and 100% of *Pseudomonas aeruginosa* isolates). Amp C production was found in 16% of Gram-negative isolates (16.7% of *E. coli*, 33.3% of *E. aerogenes* and 100% of *P. aeruginosa isolates*). In addition, 48% of Gram-negative isolates were carbapenemase-producers. The antimicrobial resistance patterns of isolated microorganisms are shown in Tables 2–4.

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