Early Bacterial Pneumonia After Hepatic Transplantation: Epidemiologic Profile

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ABSTRACT

Background. Postoperative pulmonary complications are major cause of morbidity and mortality in patients receiving liver transplantation (LT), particularly bacterial pneumonia occurring within the first 100 days after transplantation. Our aim in this study was to determine the incidence, microorganisms involved, associated factors, and morbidity of bacterial pneumonia presenting in the first 100 days posttransplant.

Methods. We performed a cohort study in which patients receiving liver transplantation were included prospectively in our national database (Database of Infections in Transplantation of Solid Organs). The study period was from July 14, 2009 to July 24, 2015.

Results. One hundred six patients were transplanted during the 6-year period. We documented 9 bacterial pneumonia cases with an incidence of 8.5 per 100 patients; 2 patients had hospital-acquired pneumonia (HAP) and 7 had ventilator-associated pneumonia (VAP). In 4 of the 9 bacterial pneumonia cases, patients presented with bacteremia. Eleven microorganisms were isolated these 9 patients. Microbiologic diagnosis methods included 5 cases of alveolar bronchoalveolar lavage (BAL), 1 case of BAL and pleural fluid puncture, 1 case of pleural fluid puncture, and 1 case through sputum study. Of the 11 isolated organisms, 9 corresponded to Gram-negative bacilli (GNB): *Klebsiella* spp, n = 3; *Acinetobacter baumannii*, n = 4; *Morganella morganii*, n = 1; and *Pseudomonas aeruginosa*, n = 1. Regarding the resistance profile, 7 presented with a multiresistance profile (MDR) and extreme resistance (XDR). Univariate analysis identified the Model for End-Stage Liver Disease (MELD) pretransplant score as a factor associated with developing pneumonia ($P < .001$, 95% confidence interval [CI] 2.872–10.167), and early extubation, before 8 hours posttransplant, as a protective factor ($P = .008$; relative risk [RR] 0.124; 95% CI 0 .041–0.377). Hospital stay was longer in patients with pneumonia compared to those without pneumonia ($P < .0001$, 95% CI 17.79–43.11 days). There was also an increased risk of death in patients with pneumonia (RR 17.963; 95% CI 5106–63,195).

Conclusions. Early bacterial pneumonia after hepatic transplantation is associated with higher morbidity and mortality. At our center, 4 of 9 patients had bacteremia. GNB cases with MDR and XDR profiles are predominant. Early extubation is a protective factor.

POSTOPERATIVE pulmonary complications represent a major cause of morbidity and mortality and increased hospital stays in liver transplant patients [1]. These complications are classified as "infectious" (eg, pneumonia) or "noninfectious," as well as "early" (in the

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Table 1. Overview of the Population Having Received a Liver Transplant (n = 106)

Variables	
Median age (P25–P75) years	45.91 (35–58)
Male, n (%)	68 (64.2)
MELD pretransplantation, median (P25–P75)	19.813 (15.75–22)
Illness that determined organ failure, n (%)	
Alcoholic cirrhosis	26 (24.5)
Autoimmune	17 (16.0)
Chronic hepatitis C	12 (11.3)
Primary biliary	7 (6.6)
More than 1 cause	7 (6.6)
Others*	37 (34.9)
Transplanted organ, n (%)	
Liver	101 (95.3)
Liver/kidney	5 (4.7)
Surgical information, mean (P25–P75)	420 (364–505)

Abbreviation: MELD, Model for End-Stage Liver Disease; P25, 25th percentile; P75, 75th percentile.

*Includes cryptogenic (6 patients), non-alcoholic steatohepatitis (4 patients), hepatitis B (5 patients), acute liver failure (4 patients), primary sclerosing cholangitis (4 patients), polycystic (3 patients), biliary atresia (2 patients), Wilson desease (2 patients), hemangioendothelioma (2 patients), hemochromatosis, deficit of α_1-antitrypsin, portal cavernoma, secondary biliary cirrhosis, Budd–Chiari syndrome, and acute-on-chronic failure (1 patient each).

Data from the Bi-institutional Unit for Complex Liver Diseases (Hospital Militar, Hospital de Clinicas), Uruguay, July 14, 2009 to July 24, 2015.

first 100 days) or "late" (after 100 days). Globally, early complications (both infectious and noninfectious) have a high incidence (59%) and high morbidity and mortality rates, as described by Ulubay et al [2] and Pirat et al [3].

Posttransplant pneumonia in the first 100 days is a postoperative complication that results in greater morbidity and mortality, manifested as the need for prolonged use of mechanical ventilation, extended stay in the intensive care unit, and the need for a tracheotomy, among other complications [4–6]. Despite the use of antibiotic prophylaxis, improved surgical techniques, and optimization of immunosuppression, the incidence of pneumonia remains high, being the second-most frequent complication after intraabdominal surgery. Its incidence has been described to vary from 5% to 48% [6], depending on reporting institution.

Risk factors associated with posttransplant pneumonia in the first 100 days after liver transplantation include pretransplant conditions (intraoperative recipient age, restrictive respiratory pattern, Model for End-Stage Liver Disease [MELD] score, hemoglobin level, diabetes mellitus, and intraoperative factors [blood loss >10 L]) and posttransplantation circumstances (the need for surgical reintervention, retransplantation, and the duration of mechanical ventilation) [1–4,6]. Gram-negative bacilli (GNB) bacteria are the predominant microorganisms involved in posttransplant pneumonia, accounting for up to 84% [3–8].

The objectives of this study were to determine the incidence and morbidity/mortality associated with bacterial pneumonia in the first 100 days after liver transplantation at our center, as well as the microorganisms involved and the associated factors.

METHODS

We performed a cohort study with data obtained from a national database BaDaInTOS. Patients who had undergone liver transplantation were included prospectively. All episodes of bacterial pneumonia occurring within the first 100 days posttransplant were included. The study period was from July 14, 2009 to July 24, 2015, and included patients in the Liver Transplant Program at the Bi-Institutional Unit of Complex Liver Diseases (Hospital Militar and Hospital de Clínicas) in Uruguay.

Liver transplant recipients (LTs) who had bacterial pneumonia within the first 100 days after transplantation were included in our study. Liver transplant recipients who died within the first 48 hours posttransplant were excluded.

A data collection form was designed for this work, the results of which were entered into an SPSS version 22 (IBM SPSS, Armonk, NY) database coded for the analysis.

The data collected for this work in the pretransplant period included: age; sex; transplanted organ; type of disease that determined organ failure; lymphocytosis; diabetes mellitus; MELD score; and immunosuppressive drugs. At the time of transplantation, we recorded whether the donor had an infectious process and whether surgical prophylaxis had been implemented in the recipient. Posttransplant data obtained included: time of extubation postsurgery; length of hospital stay; survival at discharge; early

Table 2. Form of Presentation, Diagnosis, and Microorganism Isolated (n = 9)

Number Transplanted	Form of Presentation	Diagnosis	Bacteremia	MO Isolated	Day of Presentation
15*	VAP	BAL	No	*Estreptococo beta hemolítico*	1
18*	VAP	BAL	Yes	*Acinetobacter baumannii*	1
23	VAP	BAL	No	*Acinetobacter baumannii*	5
27	VAP	BAL	Yes	*Acinetobacter baumannii*	72
33	VAP/empyema	BAL + pleural fluid puncture	Yes	*Acinetobacter baumannii/Klebsiella*	12
42	VAP	BAL	No	*Enteroccocus faecium/Morganella morganii*	9
52†	VAP	BAL	No	*Sin MO aislado*	2
56	HAP	Sputum	Yes	*Klebsiella*	9
62	HAP/empyema	Pleural fluid puncture	No	*Klebsiella/Pseudomonas aeruginosa*	30

Abbreviations: BAL, bronchoalveolar lavage; HAP, hospital-acquired pneumonia; MO, microorganism; VAP, ventilator-associated pneumonia.

*Ventilated 24 hours before liver transplant.

†No isolated microorganism, but patient had compatible signs with VAP and favorable evolution under antibiotic treatment.

Data from the Bi-Institutional Unit for Complex Liver Diseases (Hospital Militar, Hospital de Clinicas), Uruguay, July 14, 2009 to July 24, 2015.