Impact of Pretransplant Infections on Clinical Course in Liver Transplant Recipients

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ABSTRACT

Background. Uncontrolled infections are known to be an absolute contraindication for liver transplantation; however, the posttransplant prognosis of recipients treated for pretransplant infection is unclear. The aim of this study was to analyze pretransplant infections among liver transplant recipients and to determine their impact on posttransplant clinical outcomes.

Methods. This study retrospectively analyzed 357 subjects who had undergone living-donor liver transplantation between January 2008 and May 2014.

Results. Among 357 recipients, 71 patients (19.8%) had 74 episodes of infectious complications before liver transplantation. These complications consisted of pneumonia (n = 13), spontaneous bacterial peritonitis (n = 12), catheter-related infection (n = 10), urinary tract infection (n = 12), biliary tract infection (n = 6), and skin and soft-tissue infection (n = 3). Twenty-six patients experienced 29 episodes of bacteremia, and the most common pathogens were coagulase-negative staphylococci (n = 8), followed by *Klebsiella pneumoniae* (n = 7), *Staphylococcus aureus* (n = 4), and *Streptococcus* species (n = 3). Twenty-one bacteremic episodes (70%) occurred within 1 month before transplantation (n = 4). Recipients with pretransplant infections had significantly more frequent posttransplant infections (71.8% [51 of 71] vs 47.2% [35 of 286]; $P = .0001$), posttransplant bacteremia (33.8% [24 of 71] vs 20.3% [58 of 286]; $P = .015$), and longer posttransplant intensive care unit stays (11.2 ± 10.7 days vs 7.3 ± 4.2 days; $P = .0004$) than those without pretransplant infections. However, episodes of rejection ($P = .36$), length of hospitalization ($P = .10$), 28-day mortality ($P = .31$), and 1-year mortality ($P = .61$) after transplantation were not significantly different between the 2 groups.

Conclusions. Pretransplant infection had an impact on posttransplant morbidity, although not on rejection and mortality. Alertness for posttransplant infection and proper management (including effective antimicrobial coverage) would improve patient morbidity.

LIVER transplantation is the only therapeutic modality for acute and chronic end-stage liver disease. Patients with end-stage liver disease are at risk of developing numerous infectious complications while they await transplantation because of their impaired immune function, surgical procedures, multiple episodes of hospitalization, and malnutrition [1–3]. Infections in transplant recipients remain the main cause of mortality and morbidity despite advances in surgical techniques, the development of new suppressive agents, and the use of prophylactic antibiotics. Uncontrolled sepsis outside the biliary tract is a known absolute contraindication for liver transplantation [4];

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Table 1. Pretransplant Infections and Causative Organisms

Infection Site	No. (%)	Pathogen Isolated
Pneumonia	13 (18.3)	*Staphylococcus aureus* (3), *Klebsiella pneumoniae* (1), *Pseudomonas aeruginosa* (1), *Acinetobacter baumannii* (1), *Escherichia coli* (1), NTM (1)
Spontaneous bacterial peritonitis	12 (16.9)	*Enterococcus* spp (2), *Streptococcus* spp (2), *K pneumoniae* (2), *E coli* (1), *S aureus* (2), *A baumannii* (1)
Catheter-related infection	10 (14.1)	CNS (6), MRSA (2), *A baumannii* (1), *Stenotrophomonas maltophilia* (1)
Urinary tract infection	12 (16.9)	*E coli* (5), *Klebsiella* spp (2), *Enterococcus* spp (2), *Enterobacter* (1), MRSA (1)
Biliary tract infection	6 (8.5)	*Klebsiella* spp (3), *Enterococcus* spp (2)
Skin and soft-tissue infection	3 (4.2)	*S aureus* (1), CNS (2)
Others	12 (16.9)	*P aeruginosa* (1), *K pneumoniae* (1), *Streptococcus* spp (1), TB (2)
Unknown source	3 (4.2)	

Abbreviations: CNS, coagulase-negative stapylococci; MRSA, methicillin-resistant *S aureus*; NTM, nontuberculous mycobacteria.

however, the posttransplant prognosis of patients treated for pretransplant infection is unclear. The aim of the present study was to analyze pretransplant infections among liver transplant recipients and their impact on posttransplant clinical outcomes.

PATIENTS AND METHODS

We reviewed the medical records of 357 subjects who underwent living-donor liver transplantation at Seoul St. Mary's Hospital, a 1200-bed tertiary care university hospital, in Seoul, Republic of Korea, between January 2008 and May 2014. Information was collected on demographic characteristics, preoperative infections, and clinical outcomes. Patients were divided into 2 groups depending on whether they had pretransplant infections. These infections were diagnosed based on clinical, laboratory, microbiology, and/or imaging findings before transplantation, and they were defined according to standard criteria proposed by the Centers for Disease Control and Prevention [5].

The Student t test or the Mann-Whitney U test were used for the analysis of continuous variables, and the χ^2 test or Fisher exact test was used for the analysis of categorical variables. Statistical analysis was performed by using SPSS version 13.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, United States), and P values $< .05$ were considered statistically significant.

RESULTS

Among 357 recipients, 71 patients (19.8%) had 74 episodes of infectious complications before liver transplantation; these consisted of pneumonia (n = 13), spontaneous bacterial peritonitis (n = 12), catheter-related infection (n = 10), urinary tract infection (n = 12), biliary tract infection (n = 6), and skin and soft-tissue infection (n = 3) (Table 1). Causative pathogens are listed in Table 1 according to the infection site. Gram-positive cocci, primarily *Enterococcus* species and *Streptococcus* species, were the major pathogens of spontaneous bacterial peritonitis, and gram-negative bacilli, including *Escherichia coli* and *Klebsiella pneumoniae*, were the major pathogens of urinary tract infections.

Thirty infectious episodes (42.3%) occurred within 1 month before transplantation. Among 71 patients with infectious complications, 26 (33.8%) experienced 29 episodes of bacteremia, and the most common pathogens were coagulase-negative staphylococci (n = 8), followed by *K pneumoniae* (n = 7), *Staphylococcus aureus* (n = 4), *Streptococcus* species (n = 3), *Acinetobacter baumannii* (n = 2), *E coli* (n = 2), *Pseudomonas aeruginosa* (n = 2), *Enterococcus faecium* (n = 1), and *Enterobacter cloacae* (n = 1). Twenty-one bacteremic episodes (70%) occurred within 1 month before transplantation, and the remaining 30% occurred within 1 month to 1 year before transplantation.

Table 2 presents a comparison of demographic characteristics between patients with and without pretransplant infections. Age, diabetes mellitus, and underlying liver disease were not significantly different between the 2 groups. However, recipients with pretransplant infections had higher Model for End-Stage Liver Disease (MELD) scores (21.3 ± 11.3 vs 15.8 ± 9.5, respectively; $P = .0001$), a more extensive intensive care unit (ICU) history (28.2% [20 of 71] vs 8.7% [25 of 286]; $P = .0001$), and were more likely to have undergone pretransplant dialysis (14.1% [10 of 71] vs 6.3% [18 of 286]; $P = .0001$) than those without pretransplant infections.

Table 3 displays the clinical outcomes of patients with and without pretransplant infections. Recipients with pretransplant infections had significantly longer posttransplant ICU stays (11.2 ± 10.7 days vs 7.3 ± 4.2 days; $P = .0004$), more posttransplant infections (71.8% [51 of 71] vs 47.2% [35 of 286]; $P = .0001$), and more cases of posttransplant bacteremia (33.8% [24 of 71] vs 20.3% [58 of 286]; $P = .015$) than those without pretransplant infections. Rejection (21.1% [15 of 71] vs 16.5% [47 of 286]; $P = .36$) and the length of hospitalization (32.2 ± 26.2 days vs 26.8 ± 15.7 days; $P = .10$) did not differ between the 2 groups. Overall mortality at 28 days' posttransplantation was 3.6% (13 of 357); this finding was subdivided into 5.6% (4 of 71) in patients with pretransplant infections and 3.1% (9 of 286) in those without pretransplant infections ($P = .31$). At 1 year posttransplant, overall mortality increased to 7.0% (25 of 357), and there was no significant difference in 1-year mortality between the 2 groups (5.6% [4 of 71] vs 7.3% [21 of 286]; $P = .61$).

DISCUSSION

Patients with end-stage liver disease are vulnerable to infection because of their impaired immunity, bacterial