INFECTIONS IN THE INTENSIVE CARE UNIT FOLLOWING LIVER TRANSPLANTATION: PROFILE OF A SINGLE CENTER

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Introduction. Despite the advances in antibiotherapy and critical care management, infectious complications remain among the leading complications after liver transplantation related with mortality and morbidity. This study analysis the incidence and pattern of infections and possible prognostic factors of infectious complications retrospectively in a single center. **Patients and Methods.** Results of 30 consecutive patients with a primary liver transplantation history in a single center between August 2011 and August 2012 and a positive culture result in the first month in the ICU were analysed retrospectively. **Results.** During the first 1 month stay in the ICU postoperatively 30 (13,63%) patients had at least 1 infection. Total number of infections were 68. Mortality rate of the infected patients was 53,3% (n = 16). Among these infections, 25 (36,76%) of them were in deep surgical sites. Eighteen of the 30 patients (60%) were infected with a single microorganism. Eleven patients (36,66%) had a single infection episode. Microorganism were gram negative in 52 (76,47%) of the infections, gram positive in 14 (20,58%) of the infections, rest of the 2 (2,94%) infections were due to Candidiasis. Among the possible risk factors contributing to mortality, there was a statistically significant difference ($p < 0,001$) between the platelet counts of the mortality and surviving groups of the patients. **Conclusion.** Infections are among the preventable risk factors for mortality and morbidity after liver transplantation. Our data reveals a significant relation between trombocytopenia and mortality among the infected patients. Further studies focusing on this relation would expose the mechanisms and any possible contribution in clinical management of the patients.

Key words: liver transplantation, infection, immunosuppression, intensive care.

INTRODUCTION

Liver transplantation (LT) is the curative treatment option for end stage liver disease. Despite the advances in immunosuppressive treatment and antibioprophylaxy regimes, infectious complications remain to be the most frequent complication associated with significant increase in mortality and morbidity [1]. Vulnerability of the liver transplant patients to infections is related with technical difficulty of the procedure, preoperative abdominal contamination and underlying disease [1]. Most of the bacteremia episodes occur in first 3 months following transplantation with a rate of 33–68% [1, 2].

Following LT, overall mortality in relation with infection is reported from 30 to 53 % [3, 4].

The aim of this study was to examine the incidence and pattern of infections and prognostic factors associated with mortality following LT.

PATIENTS AND METHODS

We retrospectively analyzed 220 patients who had undergone liver transplantation between August 2011 and August 2012. Results of 30 consecutive patients with a primary liver transplantation history between August 2011 and August 2012 and a positive culture result in the first month in the ICU were included to the study.

Patients already under antibiotherapy with a history of preoperative infection and patients postoperatively hospitalised out of ICU were excluded from the study.

Data of age, gender, aetiology of the liver disease, type of transplantation (deceased, cadaveric), timing of surgery (emergent or elective), immunosuppressive regime, WBC, PLT, liver function rest results on day of positive culture result, model for end stage liver disease (MELD) score, history of diabetes mellitus (DM), preoperative hospitalisation history, isolated microorganisms and infection sites were analysed retrospectively.

Immunosuppressive and Antibioprophylaxy Protocol

Without a history of ongoing infection therapy, periopertaive antibioprophylactic regimen consisted of 1000 mg Ampicillin/sulbactam administered intraveously every 4 hours. Same regimen is continued postoperatively twice daily for 48 hours and discontinued in cases with no clinical signs for infection.

Immunosuppressive methylprednisolone treatment is initialised in the ICU at a dose of 100 mg/day is tapered according to the greft function status. On postoperative day 3, without any contraindication, tacrolimus 2 mg/day and cyclosporin 200 mg/day are initiated.

Microbiological Analysis

Blood culture testing was carried out with an automated microbiology growth and detection system (BACTEC™ Instrumented blood culture systems Sparks, MD. USA). Conventional methods were used for rest of the specimens. Antibiotic susceptibility was determined by minimum inhibitory concentration test.

RESULTS

Among 220 patients, 121 of them male (55%) and 99 were female (45%) with a mean age of 41,07 ± 17,89. Number of patients underwent living donor liver transplantation (LDLT) was 166 (75,45%) and cadaveric liver transplantation was 54 (24,54%). Among these liver transplantation operations, indication was acute liver failure in 132 (60%) patients and rest of the 88 patients (40%) underwent surgery as a result of elective conditions. During the first 1 month stay in the ICU postoperatively 30 (13,63%) patients had at least 1 infection. Total number of infections were 68. Seventeen (56,7%) of these patients were male and 13 (43,3%) were female with a mean age of 37,77 ± 21,08. Mortality rate was 53,3% (n = 16) among the infected patients. Among these infections, 25 (36,76%) of them were in deep surgical sites. Eighteen of the 30 patients (60%) were infected with a single microorganism. Eleven patients (36,66%) had a single infection episode. Microorganism were gram negative in 52 (76,47%) of the infections, gram positive in 14 (20,58%) of the infections, rest of the 2 (2,94%) infections were due to Candidiasis. Infection site disturbance and microbiological disturbance details of the infections are given in table 1 and 2.

Table 1

Infection site disturbance

Site of Infection	n	%
Deep surgical site	25	36,76
Superficial surgical site	3	4,41
Bloodstream	24	35,29
Urinary	7	10,29
Sputum	4	5,88
Catheter	5	7,35
Total	68	100

Among the pre-, intra- and post-operative conditions contributing to mortality; microbiological disturbance details are given in table 3–9.

Discussion

Bacterial infections following liver transplantation remain among the leading preventable factors contributing to morbidity. More than half of the bacterial infections occur within the 1 st month after transplantation [5, 6]. In our study, rate of infection in the 1 st month among patients in the ICU was 13,63%. This relatively lower rate is thought to be related with the study design, where patients already under antibiotherapy with a history of preoperative infection and patients postoperatively hospitalised out of ICU were excluded.

Although gram-positive bacteria have a predominance, there is a notable increase in incidence of blood-stream infections due to gram-negative organisms following liver transplantation [7–9]. Our study results reveal a significant gram-negative infections dominancy with a rate of 76,47%. Among blood-stream

Table 2

Microbiological disturbance

Microorganism (gram stain + or –)	Sputum n (%)	Bloodstream n (%)	Urine n (%)	Surgical Site Infection		Catheter n (%)	Total n (%)
				Deep n (%)	Superficial n (%)		
Pseudomonas (–)	1 (1,47)	3 (4,41)	–	–	–	–	4 (5,88)
E. coli (–)	–	3 (4,41)	1 (1,47)	6 (8,82)	–	2 (3,03)	12 (17,64)
Acinetobacter (–)	3 (4,41)	8 (11,76)	1 (1,47)	8 (11,76)	1 (1,47)	1 (1,47)	22 (32,35)
Clebsiella (–)	1 (1,47)	3 (4,41)	2 (3,03)	4 (5,88)	1 (1,47)	1 (1,47)	12 (17,64)
Enterococ (+)	–	4 (5,88)	1(1,47)	3 (4,41)	–	1 (1,47)	9 (13,23)
Candida	–	–	1(1,47)	1 (1,47)	–	–	2 (3,03)
Strep (+)	–	1 (1,47)	–	–	–	–	1 (1,47)
S. aureus (+)	–	1 (1,47)	–	–	1 (1,47)	–	2 (3,03)
Proteus (–)	–	–	1(1,47)	–	–	–	1 (1,47)
Citrobacter (–)	–	1 (1,47)	–	–	–	–	1 (1,47)
Coag. (–) staph (+)	–	–	–	2 (3,03)	–	–	2 (3,03)
Total (n)	5 (7,35)	24 (35,29)	7 (10,29)	24 (35,29)	3 (4,41)	5 (7,35)	68

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infections of our study, gram-negative microorganisms acount for 75% (n = 18) of the cases.

Previous studies high-lighted the tendency and vulnerability to infections of LT patients as a result of technical complexity and immunosuppression [1, 10]. In our study, these conditions led to infections in 30 patients where Acinetobacter was the most frequent pathogen microorganism (Table 2).

Catheter related infections are reported to be the most frequent sites of bacteremia with an incidence of 23 to 30% followed by intra-abdominal/biliary infections with an incidence of 7 to 10% [2, 11]. In our study, catheters were the site for 7,35% of the infections, whereas intra-abdominal (deep-surgical) infections had a relatively high incidence of 37,76%. This relatively high incidence is supposed to be associated with latent contamination in the abdominal cavity rather than failure in intensive care, as similarly stated in previous studies [12]. Although there have been several studies concerning the surveillance and risk factors of infections following liver transplantation, none of them stated a significant risk factor, which can be monitored during follow-up, related with mortality when liver transplant donors are infected.

In a study of Saner F.H., pulmonary infections following liver transplantation are stated to significantly detoriate the outcome [13]. Our study based on patients' positive culture results were mostly from deep

Table 3

Microbiological Disturbance in Patients without Preoperative Hospitalisation History

Microorganism	Bloodstream	Urine	Cath	Total
E. coli	1	1	1	3
Total (n)	1	1	1	3

Table 4

Microbiological Disturbance in Diabetic Patients

Microorganism	Bloodstream	Urine	Surgical Site Infection		Cath	Total
			Deep	Superficial		
Pseudomonas	–	–	1	–	–	1
E. coli	1	1	–	–	–	2
Acinetobacter	–	–	2	–	–	2
Clebsiella	–	–		–	1	1
Enterococ	1	–	–	–	–	1
Candida	1	–	–	–	–	1
Strep	1	–	–	–	–	1
S. aureus	–	–	1	–	–	1
Total (n)	4	1	4		1	10

Table 5

Microbiological Disturbance in Patients with Preoperative Hospitalisation History

Microorganism	Sputum	Bloodstream	Surgical Site Infection		Cath	Total
			Deep	Superficial		
Pseudomonas	–	1	–	–	–	1
E. coli	–	1	1	–	1	3
Acinetobacter	–	3	5	–	–	8
Clebsiella	1	1	1	–	1	4
Enterococ	–	2	–	–	1	3
Candida	–	2	–	–	–	2
Strep	–	1	–	–	–	1
S. aureus	–	–	1	–	–	1
Proteus	–	1	–	–	–	1
Citrobacter	–	1	1	–	–	2
Coag. (–) Staph	–	–	1	–	–	1
Total (n)	1	13	10	–	3	27

Table 6

Microbiological Disturbance in Patients with Living Donor Liver Transplantation

Microorganism	Sputum	Bloodstream	Urine	Surgical Site Infection		Cath	Total
				Deep	Superficial		
E. coli	–	2	1	1	–	1	5
Acinetobacter	–	3	–	3	–	–	6
Clebsiella	1	1	–	1	–	1	4
Enterococ	–	2	–	–	–	–	2
Candida	–	2	–	–	–	–	2
Strep	–	1	–	–	–	–	1
Proteus	–	1	–	–	–	–	1
Citrobacter	–	1	–	1	–	–	2
Coag. (–) Staph	–	–	–	2	–	–	2
Total (n)	1	13	1	8		2	25

Table 7

Microbiological Disturbance in Patients with Cadaveric Liver Transplantation

Microorganism	Bloodstream	Surgical Site Infection		Cath	Total
		Deep	Superficial		
Pseudomonas	1	–	–	–	1
E. coli	–	–	–	1	1
Acinetobacter	–	2	–	–	2
Enterococ	–	–	–	1	1
Total (n)	1	2	–	2	5

Table 8

Comparrison of pre- and post-operative conditions among intected patients contributing to mortality

Condition	Mortality group (n, %)	Surviving group (n, %)	p value
Diabetes mellitus history	5 (31,3%)	6 (42,9%)	0,51
Preoperative hospitalisation history	15 (93,8%)	12 (85,7%)	0,46

Table 9

Comparrison of possible risk factors contributing to mortality among infected patients

Condition	Mortality group	Surviving group	p value
WBC	11 230 ± 10 690	8900 ± 4810	0,45
Plt	51 750 ± 46 393	108 000 ± 92 530	0,04 *
AST	314,06 ± 52,5	290,79 ± 57,00	0,92
ALT	230,63 ± 78,0	200,64 ± 103,0	0,83
T. bil.	11,02 ± 9,64	5,56 ± 4,69	0,064
MELD score	28,44 ± 13,74	25,07 ± 10,16	0,45

surgical site and blood samples collected in case of suspicion for infection. On the other hand, the mentioned study defines pneumonia based on pulmonary infiltrates with clinical symptoms of lower respiratory infection, without positive culture result. Bloodstream infections were the second most frequent site for infection (Table 1), some of which are a result of respiratory tract infection related bacteremia.

In our study, overall Acinetobacter species infections of any site had the highest relation with mortality. Study about bloodstream infections among transplant recipients by Moreno A et al emphasize that bloodstream infections caused by multiple antibiotic-resistant Pseudomonas aeruginosa or Acinetobacter baumanii are associated with significantly higher mortality and increase of stated nosocomial

infections is a worldwide problem resulting in higher mortality and morbidity rates following liver transplantation [11].

Our study reveals a significant relation between thrombocytopenia and mortality (Table 9). We believe that low platelet count would be a remarkable predictor for mortality among infected patients following liver transplantation.

Statement for Conflict of Interest:

Hereby we certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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