European Review for Medical and Pharmacological Sciences 2012; 16(Suppl 1): 3-7

A descriptive analysis of 188 liver transplant patient visits to an Emergency Department

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Abstract. – *Background:* **The aim of the study is to seek the causes of application, the demographic and clinical characteristics of liver transplant patients and to share the experiences of our Emergency Department.**

Materials and Methods: **One hundred eighty-eight Emergency Department visits of ninety patients who underwent liver transplant operations between 2002 and 2009 were evaluated retrospectively.**

Results: **The patients applied to the Emergency Department with the complaints of fever 28.2% and abdominal pain 30.9%. It was detected that the final diagnosis of 52.4% of the patient visits was associated with the gastrointestinal system. It was observed that the most common treatment was drug therapy by 45.2% and that antibiotics treatment was the most applied method in drug treatment. Alanine aminotransferase (ALT) median value of hospitalized patients (45.5 U/L) is significantly higher than that of discharged patients (35 U/L) ($p = 0.04$). From the records of the patients, positive correlations between the length of hospitalization and levels of total bilirubin, direct bilirubin, ALT and fever during the visit were detected ($p = 0.001$, $p < 0.001$, $p = 0.01$, $p = 0.01$, respectively).**

Conclusions: **Most frequently liver transplant recipients visited the Emergency Departments with the complaints of fever and abdominal pain. The diagnosis was generally associated with gastrointestinal system disorders. The percentage of hospitalization was high and the length of stay at the hospital was long. The treatment of these patients required a multidisciplinary approach and antibiotics constituted the most used drug treatment. Also, fever and liver function tests examined at the time of admittance to the Emergency Department affected the length of hospitalization.**

Key Words:

Liver transplantation; Emergency; Liver function tests; Fever.

Introduction

Liver transplantation is a treatment method for end-stage liver disease patients. The number of transplantations is increasing and reported to be about 19,850 worldwide[1]. Our hospital is a transplantation centre in which an average of 145 liver transplantations a year is carried out (based on the last three years). In parallel with the increase in the number of the cases, for Emergency physicians the possibility of facing with liver transplanted patient is increasing.

Transplantation unrelated and/or related complex problems such as adverse effects of the treatments administered to transplant patients and post operative complaints are present in Emergency services[2,3]. The effects and side effects of immunosuppressive agents used in solid organ transplant in order to prevent allograft rejection are known[4]. Immunosuppression increases the risk of infection. The most common infection types of bacterial infections after liver transplantation consist of intraabdominal infections (abscess, peritonitis, and cholangitis) and bacteremia[5]. There are also surgical complications for adult recipients such as biliary stricture, hernia, bowel obstruction[6]. As a consequence liver transplant patients are a group applying to the Emergency Department for various reasons in the post operative period.

The aim of the study is to seek the causes of application, the demographic and clinical characteristics of liver transplant patients and to share the experiences of our Emergency Department.

Methods

In this study, 188 Emergency Department visits of 90 patients who underwent liver transplant operations between 2002 and 2009 were evaluated retrospectively.

Computer-based patient records of liver transplant patients who applied to our Emergency Department were obtained. The information of age and gender of the patients at the visits was record-

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ed. Number of visits, complaints, the cause of the transplantation, and their age at transplantation were noted. The type of liver transplantation was determined (from living donor/cadaveric donor). The time between liver transplantation and Emergency Department visit was calculated. The levels of fever, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, direct bilirubin during the visit and the final diagnosis were recorded. Hospitalization, discharge from Emergency service, if hospitalized their length of hospitalization were noted. The treatment applied and medications were recorded. Our research protocol was approved by Inonu University School of Medicine Local Research Ethics Committee Malatya, Turkey.

Statistical Analysis

The data were given as Mean±SD, Median (Min-Max), number and percentage. The assumption of normality was tested by Kolmogorov Smirnov Z. Mann-Whitney U test and Spearman's rank correlation coefficients were used in statistical analyses. $p < 0.05$ was considered as statistically significant.

Results

Transplantation age of the 90 patients who underwent transplantation was between 16 and 66 years (44.9±13.0) and the number of visits was 1-9 (2.1±1.4). Sixty seven of the patients (74.4%) were male and twenty three of the patients (25.6%) were female. In terms of the source of the transplantations, 18 (20%) from cadaver and 72 (80%) from live donors were observed. HBV was the most common reason for liver transplantation with 64.4% (Table I). There were no significant differences between sex, organ source, liver transplantation age and visit frequency to the Emergency Department ($p > 0.05$).

Table I. The causes of liver transplantation of liver transplant recipients visiting Emergency Department.

Cause of liver transplantation	n	%
Hepatitis B	58	64.4
Hepatocellular carcinoma	12	13.3
Cryptogenic cirrhosis	7	7.8
Hepatitis C	6	6.7
Alcoholic cirrhosis	5	5.6
Hepatitis D	4	4.4
Wilson disease	4	4.4
Primary biliary cirrhosis	2	2.2
Neuroendocrine tumors	1	1.1
Crohn's disease	1	1.1
Celiac disease	1	1.1
Secondary biliary cirrhosis	1	1.1
Echinococcus alveolaris	1	1.1
Alpha-1 anti trypsin deficiency	1	1.1
Budd Chiari syndrome	1	1.1
Cholestatic hepatic fibrosis	1	1.1
Kalaazar	1	1.1
Cytomegalovirus	1	1.1

When the records of 188 emergency visits of 90 transplant recipient patients were checked, we observed that their ages at the time of visits were between 17 and 67 years (45.5±12.1). The duration between transplantation date and the visit to the Emergency Department was 8-1125 days (214.1±201.0). 18.1% of the patients were discharged from Emergency Department and 81.9% of them were hospitalized as inpatient. Hospitalization length of stay was 0-90 days (9.5±12.7). Levels of total bilirubin, direct bilirubin, AST, ALT and fever which were examined in the Emergency Department are shown on Table II. The patients applied to the Emergency Department with the complaints of fever 28.2% and abdominal pain 30.9% (Table III). It was detected that the final diagnosis of 52.4% of the patients was associated with gastrointestinal system disorders (Table IV). It was observed that the most common treatment was drug therapy by 45.2% (Table V) and that an-

Table II. Liver function tests† and fever were obtained at the time of initial Emergency Department visit.

Laboratory tests and Fever	n	Mean	Std. deviation
Total bilirubin (mg/dL)	188	2.4	4.1
Direct bilirubin (mg/dL)	188	1.5	3.0
AST (U/L)*	188	55.9	62.6
ALT (U/L)#	188	80.6	111.6
Fever (°C)	188	37.0	0.7

†Liver function tests consisted of ALT, AST, total and direct bilirubin levels; *AST: Aspartate aminotransferase; #ALT: Alanine aminotransferase.

Table III. The complaints of liver transplant recipients visiting Emergency Department.

Complaint	n	%
Gastrointestinal		
Abdominal pain	58	30.9
Diarrhea	19	10.1
Nausea-vomiting	11	5.9
Icterus	6	3.2
Melena	6	3.2
Hematemesis	5	2.7
Constipation	3	1.6
Side pain	2	1.1
Respiratory system		
Cough	7	3.7
Dyspnea	1	0.5
Neurologic		
Headache	4	2.1
Somnolence	1	0.5
Dizziness	1	0.5
Head and Neck		
Throat ache	2	1.1
Hearing loss	1	0.5
Cardiovascular		
Chest pain	2	1.1
Genitourinary		
Hematuria	1	0.5
Swelling in the inguinal region	1	0.5
Dermatological		
Pruritus	10	5.3
Musculoskeletal		
Leg pain	3	1.6
Lumbar pain	2	1.1
Back pain	1	0.5
Foot pain	1	0.5
Other		
Fever	53	28.2
Weakness	9	4.8
Problems on incision point	8	4.3

tibiotics treatment was the most applied method in drug treatment (Table VI).

ALT median value of hospitalized patients 45.5 U/L (5-902) is significantly higher than that of discharged patients 35 U/L (7-162) ($p = 0.04$).

From the records of the patients, positive correlations between the length of hospitalization and levels of total bilirubin, direct bilirubin, ALT and fever during the visit were detected (Spearman's rho = 0.23, $p = 0.001$; Spearman's rho = 0.25, $p < 0.001$; Spearman's rho = 0.18, $p = 0.01$; Spearman's rho = 0.18, $p = 0.01$, respectively).

The median duration between the transplantation time and visit for the discharge from Emergency Department was higher than that for hospitalization ($p = 0.004$). Similarly, the median visit for discharge from Emergency Department was significantly higher than that for hospitalization ($p = 0.006$).

Also a positively significant correlation was detected between AST levels measured and the frequency of the visits (Spearman's rho = 0.21, $p = 0.005$). We detected a positively significant correlation between the length of time passed after liver transplantation to visit Emergency De-

Table IV. The diagnoses of the liver transplant recipients visiting Emergency Department.

Diagnosis	n	%
Gastrointestinal		
Biliary stricture	17	9.0
Gastroenteritis	17	9.0
Bilioma	15	7.9
GIS hemorrhage	12	6.3
Cholangitis	11	5.8
Infection in paracentesis fluid	7	3.7
Intraabdominal abscess	5	2.6
Ileus	4	2.1
Cholestasis	3	1.5
Acute pancreatitis	2	1.0
Biliary peritonitis	2	1.0
Intraabdominal hematoma	2	1.0
Splenomegaly	1	0.5
Peptic ulcus	1	0.5
Biliary fistula	1	0.5
Genitourinary		
Urinary system infection	4	2.1
Renal colic	1	0.5
Inguinal hernia	1	0.5
Neurologic		
Meningitis	1	0.5
Encephalopathy	1	0.5
Pulmonary		
Pneumonia	4	2.1
Pleural effusion	2	1.0
Empyema	1	0.5
Cardiovascular		
Deep vein thrombosis	3	1.5
Hypertension	2	1.0
Hypotension	1	0.5
Haematological		
Anemia	1	0.5
Leucopenia	1	0.5
Head and Neck		
Upper respiratory infection	3	1.5
Sinusitis	2	1.0
Hearing loss	1	0.5
Endocrine		
Hyperglycemia	3	1.5
Dermatological		
Urticaria	5	2.6
Others		
Non specific	38	20.2
Fever of unknown origin	9	4.7
Surgery point problems	7	3.7
Malposition of T tube	1	0.5
Rejection	1	0.5

Table V. The treatments applied to the liver transplant recipients visiting Emergency Department.

Treatment	n	%
Drug	85	45.2
Only observation	68	36.1
Surgery	20	10.6
Percutaneous drainage	19	10.0
ERCP*	16	8.5
Blood and blood product support	15	7.9
Regulating the dosage of the drugs	8	4.2
Catheter thoracostomy	5	2.6
Tube thoracostomy	2	1.0
Embolization	2	1.0
Sclerotherapy	1	0.5

*ERCP: Endoscopic retrograde cholangiopancreatography.

partment and AST levels (Spearman's rho = 0.17, $p = 0.01$).

A positive correlation was detected between the length of passed time after liver transplantation and the age of the patient (Spearman's rho = 0.17, $p = 0.01$).

Table VI. Drugs administered to the liver transplant recipients visiting Emergency Department.

Drug	n	%
Antibiotics		
Imipenem	25	13.2
Cefoperazone	17	9.0
Meropenem	14	7.4
Teicoplanin	13	6.9
Piperacillin-tazobactam	12	6.3
Ciprofloxacin	11	5.8
Sulbactam ampicillin	7	3.7
Amikacin	5	2.6
Metronidazole	5	2.6
Tigecycline	5	2.6
Moxifloxacin	4	2.1
Netilmicin	2	1.0
Levofloxacin	2	1.0
Vancomycin	2	1.0
Linezolid	2	1.0
Ceftriaxone	2	1.0
Clarithromycin	1	0.5
Anti tuberculosis(isoniazid, rifampicin, ethambutol, pyrazinamide)	1	0.5
Trimethoprim sulfamethoxazole	1	0.5
Cefamezine	1	0.5
Proton pump inhibitors	17	9.0
Antiviral		
Acyclovir	1	0.5
Oseltamivir	1	0.5
Antifungal		
Fluconazole	10	5.3
Antihistaminic	6	3.1
Insulin	6	3.1
Heparin	4	2.1

Discussion

In this study, the most frequently liver transplant recipients visited the Emergency Departments with the complaints of fever and abdominal pain. The diagnosis was generally associated with gastrointestinal system disorders. The percentage of hospitalization was high and the length of stay at the hospital was long. These patients required a multidisciplinary approach and antibiotics constituted the most used drug treatment. Also, fever and liver function tests examined at the time of admittance to the Emergency Department affected the length of hospitalization.

In the literature it has been stated that liver transplant recipients admitted to the Emergency Department with any complaint have a high ratio of hospitalization (68.1%)[2]. The ratio in our hospital is detected as 81.9%. High percentage of hospitalisation of these patients is significant. Moreover, it has been detected that the length of the inpatients was high (9.5±12.7).

It has been determined that as the patients aged, the duration between liver transplantation and Emergency Department visits increased. This cause may be associated with the patients' decrease of sensitivity against the complaints as they get older.

The most common complaints of Emergency Department visits are consist of fever or abdominal pain. Also it is known that the most common complaints of liver transplant recipients are abdominal pain and gastrointestinal symptoms at their visits to the Emergency Department[2]. We think that fever and abdominal pain complaints following the post operative complications and the side effects of medical treatment used can constitute the most common reason of visits in liver transplanted patients.

It was stated that the underlying cause of the visits of the patient and the final diagnosis were associated with hepatic, biliary, and intestinal disorders[7]. The diagnosis of our patients was generally associated with gastrointestinal system disorders such as biliary stricture, bilioma, cholangitis and gastroenteritis.

Due to the immunosuppression needed in transplant patients, they are sensitive to infections with opportunistic organisms and infections are frequently observed[8,9]. While excessive immunosuppression increases the risk of infection, insufficient immunosuppression may lead to graft rejection[10]. Bacteria are the microorganisms causing the most frequent infections[9,11,12]. In our

study it was observed that antibiotic treatment was the most applied treatment by taking bacterial infection into consideration.

Although liver function tests such as alkaline phosphatase, AST, ALT, bilirubin, PT are considered as sensitive indicators for important graft dysfunction, their specificity is poor[7]. Due to rejection before or after retransplantation, continuous monitoring of liver function is crucial for long term survival and when the liver function tests become abnormal, closer follow-up is required[13]. In our study we observed that as the AST levels detected during visits increased, visit numbers, the length of duration between transplantation time and admittance to Emergency Department increased. ALT level of hospitalized patients was significantly higher than the discharged patients of the ED. It was observed that as the levels of total bilirubin, direct bilirubin, ALT and fever increased the length of hospitalisation of these patients increased. These findings indicated the importance of examining the levels of fever, total bilirubin, direct bilirubin, ALT and AST when liver transplant recipients visited the Emergency Department with any complaint.

In our study, we observed that as the duration between the transplantation time and Emergency Department visit and the frequency of visits increased, the discharge from Emergency Department increased. Liver transplantation is known to have various complications[13,14]. As the length of time increased between the liver transplantation time and the visit to the Emergency Department, the possibility of having early stage surgical complications decreased and this might have increased the discharge of the patients. It might also result from the more familiarization of the patient because of the frequency of the visits.

Conclusion

Most frequently liver transplant recipients visited the Emergency Department with the complaints of fever and abdominal pain. The diagnosis was generally associated with gastrointestinal system disorders such as biliary stricture, bilioma, cholangitis and gastroenteritis. The percentage of hospitalization was high and the length of stay at the hospital was long. These patients required a multidisciplinary approach and antibiotics constituted the most used drug treatment. Also, fever and liver function tests examined at the time of admittance to the Emergency Department affected the length of hospitalization.

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