

ORIGINAL ARTICLE

Frequency of Hepatic Encephalopathy in Post liver Transplant Patients

HASSAN NADEEM¹, MUHAMMAD OMER FAROOQ², NIAZ MUHAMMAD³, KASHIF RAFI⁴, ASMAT ULLAH⁵, SADIA JABBAR⁶

¹Senior Registrar Transplant Hepatology, Pakistan Kidney and Liver Institute and Research Centre, Lahore

²Senior Registrar Department of Gastroenterology & Hepatology, Sheikh Zayed Medical College/ Hospital Rahim Yar Khan

³Consultant Gastroenterologist and Hepatologist, Department of Gastroenterology and Hepatology, Bolan Medical Complex Hospital, Quetta

⁴Senior Registrar, Pakistan Kidney and Liver Institute & Research Centre, Lahore

⁵Assistant Professor, Pir Abdul Qadir Shah Jilani Institute of Medical Sciences, Gambat Khairpur Mirs Sindh

⁶Senior Registrar, Department of Gastroenterology and Hepatology PGMI/General Hospital, Lahore

Corresponding author: Hassan Nadeem, Email: hassan_nadeem151@yahoo.com, Cell: +92 333 4800103

ABSTRACT

Objective: The objective of this study was to determine the frequency of hepatic encephalopathy in post liver transplant patients at a tertiary care hospital in Punjab.

Study Design: It was a descriptive case series.

Setting: Research was conducted at Department of Gastroenterology, Shaikh Zayed Hospital Lahore.

Duration: Duration of study was 6 months after the approval of synopsis from 05/08/2017 to 04/02/2018.

Material and Methods: This study involved 139 patients of both genders aged between 30-70 years diagnosed of chronic liver disease and undergoing liver transplantation. Patients were followed in the post-transplant period and hepatic encephalopathy was diagnosed using West Haven Criteria \geq Stage I during 4 weeks period after transplant. A written informed consent was obtained from every patient.

Results: The mean age of the patients was 48.1 ± 8.6 years. Most of the patients were aged between 51-65 years (59.0%) followed by 35-50 years (41.0%). There were 90 (64.7%) male and 49 (35.3%) female patients in the study group with a male to female ratio of 1.8:1. Chronic hepatitis C was the most frequent underlying cause and was observed in 105 (75.5%) patients followed by chronic hepatitis B (12.9%) and autoimmune hepatitis (11.6%). Post-transplant hepatic encephalopathy was diagnosed in 17 (12.2%) patients. 10 (7.2%) patients had stage-I, 5 (3.6%) patients had stage-II and 2 (1.4%) patients had stage-III encephalopathy. There was no significant difference in the frequency of post-transplant hepatic encephalopathy across age (p -value=0.988), gender (p -value=0.997) and underlying cause (p -value=0.714).

Conclusion: Hepatic encephalopathy was observed in a substantial proportion of patients undergoing liver transplantation for chronic liver disease which warrants routine monitoring of such patients in the post-operative period so that timely identification and management can improve the outcome among such cases.

Keywords: Chronic Liver Disease, Liver Transplant, Hepatic Encephalopathy

INTRODUCTION

Living donor and cadaveric allograft liver transplants are the most often performed surgical procedures in patients with end-stage liver disease. Liver transplantation has made significant and dramatic development since Dr. Starzl's first successful operation in 1963, with 1-year and 5-year post-transplant survival rates of 88% and 74%, respectively [1].

The recovery of transplant patients is complicated by a range of post-transplant problems that may or may not be related to allograft function. CNS infections, seizures, cerebrovascular problems and abnormalities in encephalopathy are among the most common neurologic consequences [2]. Complications like this may be the first signs of a malfunctioning transplanted liver and necessitate immediate medical intervention. These complications and the quality of life of these patients improve as a result of an increase in liver function. Consequently, these side effects should be aggressively sought out and treated when discovered [1,3].

In Egypt, Osman et al. (2016) found that 10% of post-liver transplant patients had encephalopathy [4]. In Egypt, Gad et al. (2015) found that 12.6 percent of such individuals had a similar frequency [5].

The incidence of encephalopathy in German post-liver transplant patients was reported by Saner et al. (2010) to be 47.6 percent. Previously, Saner et al. (2006) found that 72.1 percent of the population had this condition [7].

An encephalopathy was found to be present in 12.9% of Italian patients by Rompianesi and coworkers in 2015, while Vizzini and coworkers reported the same in 2011 [8,9].

Variable rates of post-liver transplant encephalopathy have been recorded in Spain (53.85%) in 2011, the United States (27.72%, respectively), and Korea (2%, respectively) in 2007 by Garcia-Martinez et al., Dhar et al., and Korea's Kim et al.

According to this research, encephalopathy is a common side effect in patients having liver transplantation that has a negative impact on their quality of life and their prognosis [1]. Although the reported prevalence ranges from 2.0 percent in Korean to 72.1 percent in German population [7,12], there is considerable variation. In addition, there is a wide range of estimates from the same population ranging from 47.6 percent to 72.1% in German [6, 7] to 5.3 percent to 12.9% in Italian [8, 9]. Patients undergoing transplantation for various reasons may be the root of this discrepancy, according to some researchers. Hepatitis C is the most common cause of liver failure in

Asians, while alcoholic cirrhosis is the most common among Westerners [13]. There is a need to replicate this study in the local population because of this debate in the existing literature and the different aetiology that necessitates transplanting. The findings of this investigation will provide a clearer picture of the problem's scope. There is no such published information available in the local area that the candidate is aware of.

MATERIALS AND METHODS

This descriptive study was conducted at Department of Gastroenterology, ShaikhZayed Hospital Lahore. Duration of study was 6 months after the approval of synopsis from 05/08/2017 to 04/02/2018. Total 139 patients of both genders aged between 30-70 years undergoing liver transplant were included in this study. Detailed demographics were recorded after taking written informed consent. Patients with cerebrovascular accident and patients who developed renal dysfunction in post-operative period were excluded.

All operations were carried out using standard techniques, and postoperative care was the same for all of the patients included. All of the patients underwent immunosuppressive therapy, which included corticosteroids, mycophenolatemofetile (MMF, 1 g/12h), cyclosporine (CsA, 5mg/kg/12h orally), and tacrolimus (TAC, 0.05mg/kg/12h orally) among other medications.

Patients were observed for four weeks following transplantation, at which time hepatic encephalopathy was diagnosed in accordance with the operational definition. The candidate completed the attached proforma, which contained the patient's demographic information as well as the aetiology of the need for a transplant, the occurrence of encephalopathy, and the stage of encephalopathy. Every patient was evaluated clinically by a single resident (who was also a candidate himself) under supervision, and every surgery was conducted by a single surgical team in order to avoid any potential bias. Exclusion has been used to keep confounding variables under control.

SPSS version 21 was used to enter and evaluate all of the data that had been gathered. The mean standard deviation (mean±SD) of numerical variables, such as age, has been presented. Frequency and percentage data have been reported for categorical variables, such as gender, underlying cause, stage of hepatic encephalopathy, and other factors. Age, gender, and underlying aetiology have all been stratified in order to address effect modifiers in the data. The post-stratification chi-square test was used, with a p-value of less than 0.05 considered significant.

RESULTS

The age of the patients ranged from 35 years to 65 years with a mean of 48.1±8.6 years. Most of the patients were aged between 51-65 years (59.0%) followed by 35-50 years (41.0%). There were 90 (64.7%) male and 49 (35.3%) female patients in the study group with a male to female ratio of 1.8:1. Chronic hepatitis C was the most frequent underlying cause and was observed in 105 (75.5%) patients followed by chronic hepatitis B (12.9%) and autoimmune hepatitis (11.6%) as shown in Table 1.

Post-transplant hepatic encephalopathy was diagnosed in 17 (12.2%) patients as shown in figure 1.

Table 1: Baseline Characteristics of Study Population

Characteristics	Participants n=139
Age (years)	48.1±8.6
• 35-50 years	57 (41.0%)
• 51-65 years	82 (59.0%)
Gender	
• Male	90 (64.7%)
• Female	49 (35.3%)
Etiology	
• Chronic Hepatitis C	105 (75.5%)
• Chronic Hepatitis B	18 (12.9%)
• Autoimmune Hepatitis	16 (11.6%)

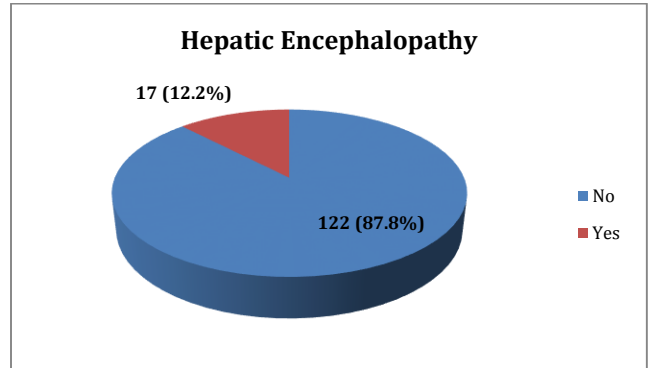


Figure 1: Frequency of Post-Transplant Hepatic Encephalopathy

10 (7.2%) patients had stage-I, 5 (3.6%) patients had stage-II and 2 (1.4%) patients had stage-III encephalopathy as shown in Table 2.

Table 2: Frequency of Various Stages of Post-Transplant Hepatic Encephalopathy (n=17)

Post-Transplant Hepatic Encephalopathy	Frequency (n)	Percent (%)	Valid Percent (%)
Stage-I	10	7.2	58.8
Stage-II	5	3.6	29.4
Stage-III	2	1.4	11.8
Stage-IV	0	0	0
Total	17	12.2	100.0

There was no significant difference in the frequency of post-transplant hepatic encephalopathy across age (p-value=0.988), gender (p-value=0.997) and underlying cause (p-value=0.714) as shown in Table 3.

Table 3: Stratification of Post-Transplant Hepatic Encephalopathy

Characteristics	n	Hepatic Encephalopathy n (%)	P-value
Age			
• 35-50 years	57	7 (12.3%)	0.98
• 51-65 years	82	10 (12.2%)	
Gender			
• Male	90	11 (12.2%)	0.99
• Female	49	6 (12.2%)	
Etiology			
• Chronic Hepatitis C	105	14 (13.3%)	0.71
• Chronic Hepatitis B	18	2 (11.1%)	
• Autoimmun e Hepatitis	16	1 (6.3%)	

DISCUSSION

Surgical and postoperative protocols have advanced tremendously and rapidly since Dr Starzl performed the world's first successful liver transplantation in 1963. Survival rates at one and five years after a successful liver transplantation are now 88% and 74%, respectively [1]. The incidence of neurologic difficulties after orthotopic liver transplantation (LT) ranges from 13 to 47 percent of patients, with a much lower incidence in patients who receive a living donor liver transplantation compared to patients who receive cadaveric grafts. The majority of neurological problems occur early after surgery and are associated with increased morbidity, mortality, and length of hospitalisation [1,5]. The aetiology is frequently associated with immunosuppressive drug neurotoxicity as well as opportunistic infections. For liver transplant recipients, the most common problems include seizures and encephalopathy, with the incidence of central pontine myelinolysis being a rather unique condition. Hepatic encephalopathy can occur as a result of delayed allograft function, and the neurotoxicity of calcineurin inhibitors is often seen as tremor, headaches, and encephalopathy in patients. Clinical improvement is typically observed with the reduction of neurotoxic immunosuppressants or the conversion to an alternate treatment [1].

The reported frequency of post-transplant hepatic encephalopathy varied not only among populations but among difference reports from same population (Table 4) while there was no such local published material which necessitated the present study.

Table 4: Review of Existing Literature on Post-Transplant Hepatic Encephalopathy

Author	Year	Population	Post-Transplant Encephalopathy (%)
Saner et al. [7]	2006	Germany	72.1
Garcia-Martinez et al. [10]	2011	Spain	53.85
Saner et al. [6]	2010	Germany	47.6
Dhar et al. [11]	2007	USA	27.72
Saner et al. [14]	2009	Germany	17.8
Rompianesi et al. [8]	2015	Italy	12.9
Gad et al. [5]	2015	Egypt	12.6
Bronster et al. [15]	2000	USA	11.8
Lewis et al. [16]	2003	UK	11.0
Wijdicks et al. [17]	1995	USA	11.0
Osman et al. [4]	2016	Egypt	10.0
Vizzini et al. [9]	2011	Italy	5.3
Kim et al. [12]	2007	Korea	2.0
Present Study	2018	Pakistan	12.2

It was the goal of this study to investigate the prevalence of hepatic encephalopathy in post liver transplant patients at a tertiary care hospital in Punjab.

The patients in this study were on average 48.1 years old. Italy has the same mean age of 48.9 34.7 years for liver transplant recipients as Rompianesi et al. (2015), but

Saner et al. (2010) found it to be 48 14 years in German liver transplant recipients [6]. On the other hand, Kim et al. found that the median age of Korean liver transplant recipients was 49 years old [12].

We found a male to female ratio of 1.8:1 in our study group, which included 90 men (64.7%) and 49 women (35.3%). Otan et al. (2015) found a male-to-female ratio of 1.8:1 among liver transplant recipients in Turkey, which is in line with other studies [18]. Among liver transplant patients, males outnumber females (1.6:1), Dhar et al. (1.7:1), Oliver et al. (1.9:1), and Gad et al. (2.2:1) similarly showed comparable male preponderance [5, 11, 19–20].

Most patients in the current study had chronic hepatitis C (75.5%) as the primary aetiology, followed by chronic hepatitis B (12.9%) and autoimmune hepatitis (11.9%). (11.6 percent). By Saner et al. [6, 77.5 percent of German patients with chronic liver disease had chronic hepatitis C, 9.9 percent had chronic hepatitis B, and 12.1 percent had autoimmune liver disease]. Chronic hepatitis C (72.3%) and chronic hepatitis B (10.9%) were found in similar proportions in these patients at Shifa International Hospital Islamabad [21]. [

In the current investigation, hepatic encephalopathy was found in 17 (12.2 percent) of the patients who received a liver transplant. Stage-I encephalopathy affected 10 patients (7.2%), stage-II encephalopathy affected 5 patients (3.6%), and stage-III encephalopathy affected 2 individuals (1.4%). In Egyptian post-liver transplant patients, Gad et al. (2015) found a comparable incidence of 12.6% of encephalopathy [5]. Rompianesi et al. (2015) found a comparable incidence of 12.9% in Italian individuals with this condition [8]. Moreover, our findings are in line with those of Bronster et al. from the United States in 2000 (11.8 percent), Lewis et al. from the United Kingdom in 2003 (11.0 percent), Wijdicks et al. from the United States in 1995 (11.0 percent) and Egyptian researchers Osman et al. from 2016 (10.0 percent).

Hepatic encephalopathy occurred in a significant number of patients undergoing liver transplantation for chronic liver disease regardless of the patient's age, gender, or the underlying aetiology, which necessitates routine monitoring of such patients in the post-operative period so that timely identification and management can improve the outcomes among such cases.

An essential flaw in the current investigation was the fact that we didn't compare the incidence of encephalopathy among the immunosuppressive regimens utilised nor the long-term consequences of these regimens on patient outcomes. Such a study should be carried out in the future.

CONCLUSION

A significant number of patients with chronic liver disease who underwent liver transplantation showed signs of hepatic encephalopathy, indicating the need for post-operative routine surveillance of these patients in order to detect and treat them sooner rather than later.

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