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FACTORS FOR DE-SELECTION OF POTENTIAL CANDIDATES FOR LIVE DONOR LIVER TRANSPLANT IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To look for factors responsible for de-selection of patients for live donor liver transplantat tertiary care hospital.

Study Design: Correlational study.

Place and Duration of Study: Study was conducted in Gastroenterology Department of Military Hospital from Nov 2017 to Nov 2018.

Methodology: A study was conducted on patients diagnosed with end stage liver disease (ESLD) and qualifying the criteria for liver transplant at our hospital by a consultant gastroenterologist on the basis of clinical findings, relevant investigations and Model for End Stage Liver Disease (MELD) score.

Results: Out of 145 patients included in the final analysis 69.6% were male and 30.4% were female. Eighty nine (61.3%) patients presented with the chronic liver disease secondary to the hepatitis C virus (HCV). Fifty patients were declared unfit due to some underlying conditions. Advanced stage of hepatocellular carcinoma in 10(20%) patients was the commonest factor leading for rejection of potential recipients for live donor liver transplant followed by spontaneous bacterial peritonitis in 9 (18%) patients.

Conclusion: This study gives a detailed account of the possible factors which could lead to the de-selection of potential candidates for live donor liver transplant. It becomes very important for a third world country like ours where resources are limited to screen the patients thoroughly before administering this highly invasive and expensive treatment so that whole of the effort does not get wasted on a patient who could not get adequate benefit from it due to other medical conditions.

Keywords: Demographic profile, End stage liver disease, Live donor liver transplant, Gastrointestinal.

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INTRODUCTION

Hepatobiliary diseases are one of the commonest gastrointestinal problems prevalent all around the world[1]. Liver diseases stand among the top illnesses affecting the quality of life of the individuals in one way or another[2]. These diseases can be benign or malignant and may lead to temporary or permanent damage to the parenchyma of this vital organ of human body. Chronic or end stage liver disease has been notorious for this act and usually leads to liver failure. In some cases there is an acute phenomenon instead of chronic damage which can lead to liver failure. Once this organ has suffered from cirrhosis or has failed and stopped function then medial remedies are usually of no use[3].

Liver transplant has emerged as a solution to the problem of liver failure. Live and cadaveric both forms of transplant have now been in use for many years[4]. Most of these have been done in the developed countries but developing countries are also trying their level best to introduce this facility in their set ups[5]. Our neighboring country India has been a huge success in this regard and it is not only catering for the local patients but also providing services to the patients of other countries where this facility has been non-existent[6]. Many factors have been involved in this expensive procedure which predicts the success. A multidisciplinary team is required to carry out this huge task and the patient usually requires a lifelong connection with the team after the surgery[7].

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Various factors have been taken into account while evaluating the person for this procedure. Various scales and scores have been designed to prioritize the patients for liver transplant. All the patients with end stage liver disease or liver failure cannot be provided this facility. A study done on 700 patients who were enrolled for the evaluation of liver transplant, 31 percent were rejected or declared unfit for transplantation due to relative or absolute contraindications in the recipients. Advanced stage of tumor was the commonest factor which rendered the patients unfit for this procedure[8]. Another similar study revealed same findings and many factors including sepsis and stage of tumor were involved in de-selection of potential candidates for liver transplant[9]. Another overview on this topic summarized that following the relative and absolute contraindications for this process is beneficial for the recipient, donor and the health care system which has to manage all the resources[10].

In Pakistan these services have been in practice for the past five years at various centers but still under the process of evolution. As ours is a developing country with limited resources which need to manage effectively, so this becomes very important to look for the patients who will get the maximum benefit out of this very expensive and specialized procedure. We therefore designed this study with the rationale to look for the factors responsible for de-selection of patients for live donor liver transplant at Pak Emirates Military Hospital RWP.

METHODOLOGY

This cross-sectional study was conducted at the Gastroenterology unit of Pak Emirates Military Hospital Rawalpindi from November 2017 to November 2018. Sample was gathered by using the non-probability consecutive samp-ling technique. All patients between the age of 12 and 60 years reported in the gastroenterology department with acute or chronic liver failure due to any cause and they were included in the study as potential candidates for liver transplant. Patients who were referred from other military, public sector and private hospitals with the same diagnosis were also included in the analysis in addition to the referrals from the other wards of our hospital. Diagnosis of chronic liver disease or acute liver failure was made on the clinical, laboratory and radiological findings by the consultant gastroenterologist[11,12]. Model for end stage liver disease criteria was used to prioritize the patients for liver transplant.

MELD Formula used was:

0.957 x Loge (Creatinine [mg/dL]) + 0.378 X Loge (Total Bilirubin [mg/mL]) + 1.120 x Loge (INR)+ 0.643

Patients with initial MELD score greater than 15 were included in the analysis as they were considered as potential candidates for the liver transplant[13].

Exclusion criteria were the patients with unclear diagnosis regarding the cause of liver failure. Patients who were pregnant or active alcohol users were also not included from the start and were not considered as potential candidates of liver transplant. Patients with active psychiatric illness or delirium or dementia were also excluded in the beginning and were not enrolled for further steps of evaluation. Patients who were unwilling for the liver transplant due to any reason were also made part of the exclusion criteria.

Ethical approval was taken from the ethical review board committee of Pak Emirates Military Hospital Rawalpindi before the start of this study. After written informed consent from the potential participants, patients presenting with liver diseases in the gastroenterology unit of PEMH Rawalpindi fulfilling the above mentioned criteria of inclusion and exclusion were included in the study. As before including them into the study all work up regarding the nature and extent of liver damage has already been done in addition to the calculation of the MELD score. So after including them into the study and enrolling them as potential candidate for liver transplant further investigations were done to look for medical co-morbids, infections and stage of the

HCC. These included all base line investigations (Blood Complete picture, liver function test, renal function test, C-reactive protein, tumor markers etc) and triphaisc CECT scan of chest and abdomen. Mini mental state examination was also done to look for the signs of hepatic encephalopathy or other causes of delirium in these patients.

Table-I: Characteristics of patients who were potential recipients for live donor liver transplant (n=145).

Age (years)	
Mean ± SD	46.13 ± 2.231
Range (min-max)	12-59 years
Mean MELD score	15.23 ± 1.436
Gender	
Male	101 (69.6%)
Female	44 (30.4%)
Fitness for liver transplant	
Fit	95 (65.5%)
Unfit	50 (34.5%)
Causes of End stage Liver disease	
HCV infection	89 (61.4)
HBV infection	13 (9%)
Hepatocellular carcinoma	12 (8.3%)
Alcoholic liver disease	11 (7.6%)
Autoimmune hepatitis	6 (4.1%)
Wilsons disease	6 (4.1%)
Acute liver failure	3 (2%)
Cryptogenic cirrhosis	4 (2.8%)
Others	1 (0.7%)

All statistical analysis was performed by using the Statistics Package for Social Sciences version 24.0 (SPSS-23.0). Mean and standard deviation for the age and MELD score of study participants was calculated. Frequency and percentages for gender, causes of liver failure and factors causing de-selection of potential candidates were calculated. Binary logistic regression was done to evaluate the relationship of age, gender and duration of cirrhosis with the de-selection of candidates.

RESULTS

A total of 152 patients of liver diseases from non probability consecutive sample requiring liver transplant reported in the department in the given period. Three of them were not fulfilling the age criteria of study, one was active alcohol user and diagnosis of one remained unclear. Two patients did not give consent for the liver transplant, so were not evaluated further. Out of 145 patients included in the final analysis 95 were male and 50 were female. Male to female ratio was 1.9:1. Mean age of patients diagnosed with liver failure in our study was 46.1 (±2) years. Other characteristics of study population have been summarized in table-I.

Table-II: Conditions and factors on which recipients were declared unfit for live donor liver transplant (n=50).

Medical conditions	**n (%)**
Advanced stage of HCC	10 (20)
Spontaneous bacterial peritonitis	9 (18)
Hepatic encephalopathy	8 (16%)
Hepato-renal shut down	6 (12%)
Severe obesity	3 (6%)
Uncontrolled medical condition	6 (12%)
Extra hepatic malignancy	2 (4%)
Sepsis	4 (8%)
others	2 (4%)

Table-III: The correlated factors relating to the de-selection of patients in our study: the binary logistic regression.

	***p*-value**	**OR (95% CI)**
Age (ref. is <35 years)	0.399	1.441 (0.617-3.367)
Gender (ref. is male)	0.009	0.372 (0.177-0.738)
Duration of cirrhosis (ref. is <2 years)	0.928	0.967 (0.465-2.011)

HCV was the commonest cause of liver failure in our setup followed by HBV. Advanced stage of HCC was the commonest factor with which the patients were declared unfit for liver transplant in our study. It was followed by spontaneous bacterial peritonitis (table-II).

Gender had significant association with the de-selection of candidates in our study (table-III).

DISCUSSION

Liver transplant has created a revolution in the lives of patients suffering from end stage liver disease[14]. Previously there was no treatment

option for such patients and they have to wait for the death to rescue them from poor quality of life attributed to the consequences of compromised functioning of this very important organ of the body. It is not just the improvement in life span of the individuals suffering from liver failure but marked improvement in quality of life after this procedure which makes it as treatment of choice among these patients[15]. Like all other medical procedures it has its own merits and demerits. One of the biggest hurdles in carrying out this treatment procedure is its enormous cost and facilities required not only for the surgery but post-surgical management[16] which is the problem with many developing countries including Iran[5]. Issues related to availability of living and deceased donors also pose ethical, cultural and religious problems in many parts of the world[5,17]. Therefore the treating team has to be very vigilant and cater for all these aspects so that there is minimum burden on the individual as well as the health care system.

More than thirty percent of our target population was declared unfit when they underwent detailed evaluation after the initial screening. These figures are in accordance with the existing literature. This finding is very important for the developing country like ours[8] which in comparsion to study by Valentin-gamazo where main cause for deselection from transplantation is donor's factor. If detailed evaluation has not been performed and patient has been transplanted with the liver from live donor, which would have caused wastage of the already limited resources. Patients with absolute and relative contraindications should be segregated in order to find the most suitable candidate for this procedure so that maximum benefit could be obtained from a limited resource setting.

With male to female proportion in our study sample is 69.6:30.4 almost similar to that of a local study of Zubair *et al*[18]. In the study 'Current challenges of liver transplant in Iran' main cause of ESLD is cryptogenic cirrhosis while in our country cryptogenic cirrhosis is increasing but still the leading cause of ESLD is chronic hepatic C. Advance stage of HCC was the commonest factor which led to de-selection of the patient for live donor liver transplant in our study, comparsion is difficult as work is in progress in establishing factors for deselection of recipients But a study conducted by Valentino-Gamazo on 700 patients for liver transplant, the main factor for deselection for liver transplant is advanced stage of HCC[8]. Initial screening was done via ultrasonography and liver biopsy and patient was labeled as candidate for liver transplant but later with the help of triphasic CECT scan when size and extent of tumor was precisely evaluated, it was found in advanced stage in most of the candidates[10]. Out of 12, 11 HCC patients were therefore declared unfit for the liver transplant as they could not benefit from this procedure much due to high mortality linked with the advance stage of this deadly cancer.

Spontaneous bacterial peritonitis is another condition which accounted for most of the unfit patients. It has been clearly mentioned that this condition should be taken as a relative contraindication for liver transplant[10]. It is a highly septic condition which is linked with high mortality especially if surgical procedure is performed during the acute episode. These patients can be given a chance later on when they recover from the acute episode of peritonitis then again their MELD score can be calculated and they could be given another chance to get enrolled in the transplantation program which is also mention in the study of Farkas.

Extra-hepatic malignancy was least reported complication in our patients. One suffered from Hodgkin's lymphoma and other from neuroendocrine tumor of the gut. Studies in past have generated this data that they have not been ideal candidates for the transplant surgeries including liver transplant[8,10]. Resources when limited should be spent on the patients who can get maximum benefit out of them and have no other serious condition in addition to the condition which is under consideration for the transplant surgery[17,18].

We work in the gastroenterology unit of a tertiary care hospital with limited budget and free of cost treatment is provided to the entitled patients. This was the biggest limitation of this analysis as study cannot be generalized due to this problem. Cost is a big issue when we work in a non-welfare state like ours where most of the patients have to bear the treatment cost themselves. Therefore this issue needs to be addressed or patients from public and private sector should have been included. Another limitation is lost to follow up the patients with relative contraindications or temporary medical problems making them unfit at the time of analysis. Long term follow up could have generated different results with patient cooperation. Further studies addressing these limitations and involving multiple centers may generate reasonable results in this regard.

There are additional factors which are responsible for rejection of potential candidates for LDLT involving non-availability/unfit donors and poor socio-economic support system.

CONCLUSION

This study gives a detailed account of the possible factors which could lead to the de-selection of potential candidates for live donor liver transplant. It becomes very important for a third world country like ours where resources are limited to screen the patients thoroughly before administering this highly invasive and expensive treatment so that whole of the effort does not get wasted on a patient who could not get adequate benefit from it due to other medical conditions.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Butt AS. Epidemiology of Viral Hepatitis and Liver Diseases in Pakistan. Eu J Hepato-Gastroenterol 2015;5(1):43-48.
2. Wang FS, Fan JG, Zhang Z. The global burden of liver disease: the major impact of China. Hepatology 2014;60(6):2099-108.
3. Perri GA, Khosravani H. Complications of end-stage liver disease. Can Fam Physician 2016; 62(1): 44-50.
4. Marroni CA, Fleck AM, Fernandes SA, Galant LH, Mucenic M, de Mattos-Meine MH, et al. Liver transplantation and alcoholic liver disease: History, controversies, and considerations. World J Gastroenterol 2018; 24(26): 2785-805.
5. Saidi RF, Kazemaini SM. Current challenges of liver transplantation in Iran. Middle East J Dig Dis 2018; 10(1): 45-49.
6. D'Cruz AL. Pediatric liver transplantation in India: Its time has come. J Indian Assoc Pediatr Surg 2011; 16(1): 1-6.
7. She WH, Chan ACY, Cheung TT, Lo CM, Chok KSH. Survival outcomes of liver transplantation for hepatocellular carcinoma in patients with normal, high and very high preoperative alpha-fetoprotein levels. World J Hepatol 2018; 10(2): 308-18.
8. Valentín-Gamazo C, Malagó M, KarliovaM, Lutz JT, Frilling A, Nadalin S, et al. Experience after the evaluation of 700 potential donors for living donor liver transplantation in a single center. Liver Transpl 2004; 10(9): 1087-96.
9. Lai JC, Feng S, Roberts JP. An examination of liver offers to candidates on the liver transplant wait-list. Gastroenterology 2012; 143(5): 1261-65.
10. Farkas S, Hackl C, Schlitt HJ. Overview of the indications and contraindications for liver transplantation. Cold Spring Harb Perspect Med 2014; 4(5): a015602.
11. Wiegand J, Berg T. The etiology, diagnosis and prevention of liver cirrhosis: part 1 of a series on liver cirrhosis. Dtsch Arztebl Int 2013; 110(6): 85-91.
12. Berzigotti A. Advances and challenges in cirrhosis and portal hypertension. Bio Med Cent Med 2017; 15(1): 200-06.
13. Moraes ACO, Fonseca-Neto OCLD. The use of meld score (model for end-stage liver disease) and derivatives in cardiac transplantation. Arq Bras Cir Dig 2018; 31(2): e1370.
14. Akarsu M. Liver transplantation in Turkey: The importance of experience. Turk J Gastroenterol 2018; 29(6): 629-30.
15. Konidis SV, Hrycko A, Nightingale S. Health-related quality of life in long-term survivors of paediatric liver transplantation. Paediatr Child Health 2015; 20(4): 189-94.
16. Dias FFM, Almeida SS. Assessment and enrol-ment process for liver transplantation: nursing management through quality indicators. Einstein (Sao Paulo) 2018; 16(1): eAO3975.
17. Schiano TD, Rhodes R. The dilemma and reality of transplant tourism: an ethical perspective for liver transplant programs. Liver Transpl 2010; 16(2): 113-17.
18. Zubair UB, Salamat A, Alam MM, Shafqat H, Saeed F. Predictive accuracy of model for end stage liver disease (meld) as a prognostic marker for cirrhosis in comparison with child–pugh score. Pak Armed Forces Med J 2015; 65(1): 22-5.