INELIGIBILITY FOR LIVER TRANSPLANTATION IN HEPATOCELLULAR CARCINOMA.

Abdul Aziz Sahito[1], Muhammad Sibtain Shah[2], Bharat Lal[3], Zafarullah[4], Waseem Raja[5], Aamir Shahzad.[6]

ABSTRACT

Introduction: HCC is common problem in pakistan. **Objective:** to assess the Ineligibility For Liver Transplantation In Hepatocellular Carcinoma. **Methods:** This descriptive case series study was conducted in the Department of Medicine Peoples University Of Medical & Health Sciences For Women Nawabshah from 1st May 2017 to 30th April 2019.One ninety eight patients were enrolled in this study.All consecutive patients diagnosed as Hepatitis B, Hepatitis C with or without cirrhosis were included.Exclusion criteria was biopsy proven secondary metastatic deposits in liver, metabolic storage disease, Wilsons Disease, Haemochromatosis. All baseline and clinical variables recorded in a structured questionnaire and the data were evaluated in Statistical Package for the Social Sciences (SPSS) version 21.0. A p value of <0.05 is considered to be statistically significant. **Results:** A total of 198 patients, 58.58% (n= 116) were HCV and 41.41% (n= 82) were HBV positives were included. The mean age of HBV positive patients was 39.21 ± 13.77 years while HCV positive patients were comparatively elder 47.74 ± 9.78 years. Non-eligible patients were higher in HCV group (49.13%) as compared to HBV group (32.92%). Only two parameters had shown significant association with non-eligibility of liver transplant. HBV patients with right lobe of liver involvement while HCV patients with both lobes involved and OKUDA score in both HBV and HCV groups were significantly associated with non-eligibility of liver transplantation (p <0.05). **Conclusion:** We have observed higher percentage of HCV patients non-eligible for liver transplantation based on the clinical grounds than HBV patients. HBV patients with right lobe of liver involvement & HCV patients with both lobes involved, and higher the OKUDA score in both HBV and HCV groups were significantly associated with non-eligibility of liver transplant (p - <0.05).
Key words: Liver transplantation, HBV,HCV,HCC

1. Associate Professor & Chairman Department Of Medicine PUMHSW Nawabshah.
2. Assistant Professor Oncology Medical unit I PUMHSW Nawabshah.
3. Associate Professor & Incharge Medical unit III PUMHSW Nawabshah.
4. Assistant Professor Medical unit II PUMHSW Nawabshah.
5. Assistant Professor Medical Unit II PUMHSW Nawabshah.
6. Assistant Professor Medical Unit II PUMHSW Nawabshah.

Coressponing author; Muhammad Sibtain Shah, Assistant Professor Oncology Medical unit I PUMHSW Nawabshah. Email: drmsibtain@hotmail.com

How to cite this article: Sahito A A[1], Shah M S[2], Lal B[3], Zafarullah[4], Raja W[5], Shahzad A[6]. **INELIGIBILITY FOR LIVER TRANSPLANTATION IN HEPATOCELLULAR CARCINOMA. JPUMHS;2020;10(03)84-88.**
http://doi.org/10.46536/jpumhs/2020/10.02.231

INTRODUCTION

Viral hepatitis particularly Hepatitis C virus (HCV) and Hepatitis B virus (HBV) infections are the two most common leading causes of viral infections affect liver and are associated with high disease burden particularly in low to middle income countries particularly Pakistan. Great discrepancy has been observed in epidemiological distribution curve but data estimates the burden of viral hepatitis C infection is around 130 to 170 million people.[1] while the burden of hepatitis B infection is more than HCV and estimated to be more than 350 million people carrying the HBV infection.[2]

Patients with HBV and HCV infection if left untreated are more prone to develop and present with end stage liver disease called liver cirrhosis. The burden of conversion to end stage liver disease is different in different regions but as the viral hepatitis is more common in developing countries due to multiple factors such as lack of awareness, lack of screening program and lack of financial support to treat the disease hence the disease burden higher in such countries. Patients with compensated liver cirrhosis have a median survival of 6 – 12 years and in decompensated liver cirrhosis the median survival decreases to 2 years[3,4]. Due to lack of awareness and late diagnosis of underlying disease these patients are more prone to the development of end stage liver disease and become candidates for liver transplant or may end up in supportive care[5,6].

We have evaluated in this study the comparative burden of HCV and HBV infected patients who end up with supportive care and are not candidates for liver transplant due to various comorbid & socioeconomic issues in a tertiary care hospital of Nawabshah.

METHODS

This descriptive case series study was conducted in the Department of Medicine Peoples

University of Medical & Health Sciences For Women Nawabshah from 1st May 2017 to 30th April 2019. One ninety eight patients were enrolled in this study.All patients were underwent a brief medical history and physical examination.biochemical and radiological imaging studies included CBC,Urea creatinine, electrolytes, serum prothrombin time, serum partial activated prothrombin time, serum albumin, viral profile for hepatitis B,C & D, serum ferritin, total iron binding capacity, serum caeruloplasmin, fibro scan & multiphasic CT scan abdomen were performed.Okuda score Child Pugh Trucotte class and King College Hospital criteria for liver transplantation were calculated. A structured questionnaire was used to collect the relevant data such as age, gender, area of residence, marital status, type of viral liver infection HBV, HCV and outcome patients who needs liver transplant or supportive care. Supportive care includes improvement in the quality of life in which patients will be managed symptomatically such as relief of pain, treatment of concomitant infection, and management of end stage liver disease associated clinical signs & symptoms such as pedal edema, ascites, dyspnea, and vomiting. Quantitative data numerical parameters i.e. age in years was calculated as mean ± SD. Qualitative data such as marital status, education status, area of residence, type of liver infection, and outcome patients who needs liver transplant or supportive care were calculated as number and percentage. The data were evaluated in Statistical Package for the Social Sciences (SPSS) version 21.0 and a p value of <0.05 is considered to be statistically significant.

RESULTS

A total of 198 patients with hepatitis B and hepatitis C virus infection were included in this study. Among them, 58.58% (n= 116) were HCV and 41.41% (n= 82) were HBV positives. The mean age of HBV positive patients was 39.21 ± 13.77 years while HCV positive patients were comparatively elder 47.74 ± 9.78 years. In both groups more than 60% were males. While surprisingly, higher burden of HCV and HBV cases were from rural areas shown in table number: 01. Non-eligible patients were higher in HCV group 49.13% as compared to HBV group 32.92% shown in figure number 01. The association of clinical and radiologic characteristics of patients suffering from hepatitis B & C eligible & not eligible for liver transplantation revealed that HBV patients with right lobe of liver involvement while HCV patients with both lobes involved were significantly not eligible for liver transplantation. The higher Okuda score in both HBV and HCV groups were significantly associated with non-eligible for liver transplantation shown in table no: 02 & 03.

Table 1: Descriptive statistics of patients (n=198)

Characteristics	HBV (n = 82) N (%)	HCV (n= 116) N (%)
Mean age ± SD	46.21 ± 13.77	51.74 ± 9.78
Gender		
Male	53 (64.63)	70 (60.34)
Female	29 (35.36)	46 (39.65)
Marital Status		
Married	58 (70.73)	88 (75.86)
Single	24 (29.26)	28 (24.13)
Area of residence		
Urban	39 (47.56)	39 (33.62)
Rural	43 (52.43)	77 (66.37)
Comorbid		
DM	17 (20.73)	39 (33.62)
HTN	29 (35.36)	44 (37.93)

Table No. 02: Clinical & radiological characteristics of patients eligible for liver transplantation(n = 114)

Characteristics	HBV (n = 55) N (%)	HCV (n = 59) N (%)	p value
CT Scan Findings			
Single	37 (67.27)	28 (49.12)	**0.01***
Multicentric	12 (21.81)	16 (28.07)	
Diffuse	6 (10.90)	13 (22.80)	
Lobe of Liver			
Right	35 (63.63)	30 (52.63)	0.15
Left	16 (29.09)	21 (36.84)	
Both	4 (7.27)	6 (10.52)	
Liver Cirrhosis			
Yes	18 (32.72)	22 (38.59)	0.18
No	37 (67.27)	35 (61.40)	
CTP Class			
A	29 (52.72)	34 (59.64)	**0.03***
B	20 (36.36)	13 (22.80)	
C	6 (10.90)	10 (17.54)	
OKUDA Stage			
I	33 (60)	31 (54.38)	0.11
II	22 (40)	28 (26.31)	
III	0 (0)	0 (0)	

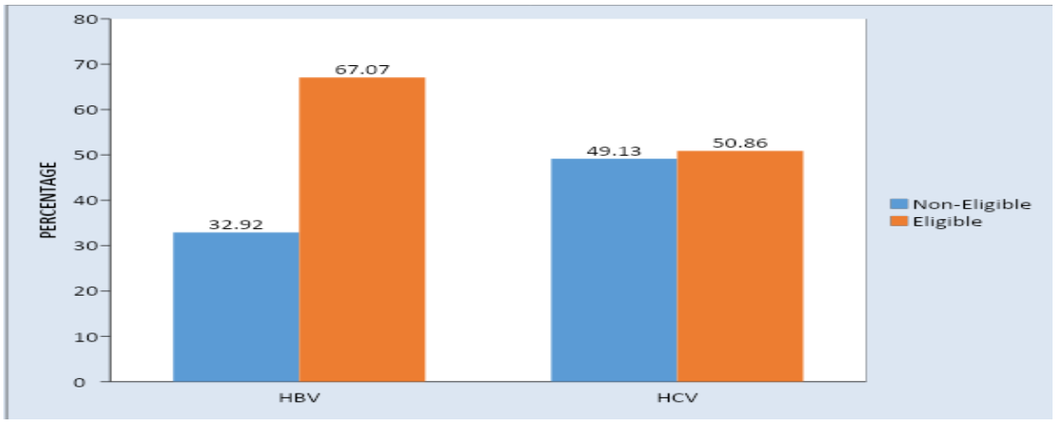
*P value <0.05 is considered to be statistically significant, m CTP: Child-Turcotte-Pugh

Table No: 03.Clinical & radiological characteristics of patients not eligible for liver transplantation (n = 84)

Characteristics	HBV (n = 27) N (%)	HCV (n = 57) N (%)	p value
CT Scan Findings			
Single	7 (25.92)	23 (40.35)	0.07
Multicentric	9 (33.33)	12 (21.05)	
Diffuse	11 (40.74)	22 (38.59)	
Lobe of Liver			
Right	19 (70.37)	15 (26.31)	**0.03***
Left	6 (22.22)	10 (17.54)	
Both	1 (3.70)	32 (56.14)	
Liver Cirrhosis			
Yes	9 (33.33)	21 (36.84)	0.48
No	18 (66.66)	36 (63.15)	
CTP Class			
A	15 (55.55)	22 (38.59)	0.31
B	8 (29.62)	19 (33.33)	
C	4 (14.81)	16 (28.07)	
Okuda Stage			
I	16 (59.25)	31 (54.38)	**0.01***
II	7 (25.92)	15 (26.31)	
III	4 (14.81)	11 (19.29)	

*P value <0.05 is considered to be statistically significant CTP: Child-Turcotte-Pugh

Figure NO: 01. Frequency of patients non eligible for liver transplantation (n=198)



DISCUSSION

Chronic HCV and HBV are the two most common viral causes of hepatitis in Pakistan. Recent data has shown more than eight million people in Pakistan are infected with HCV infection and statistically Pakistan is the second most common country with highest burden of HCV infection globally while burden of HBV infection in Pakistan is more or less similar to HCV and estimated there are 7-9 million carriers of HBV infection in Pakistan. This huge burden of liver disease may transform to end stage if untreated and causing high rates of morbidity and mortality. Patients with end stage liver disease may end up with a choice to go for liver transplant due to financial and clinical & radiologic characteristics not meeting the criteria of liver transplant such as metastatic hepatocellular carcinoma such clinical characteristics and burden of patients those who are agree for liver transplant but their clinical criteria doesn't meet and they end up having supportive care due possibility to late presentation of such patients.[7,8,9]

To date, HCV and HBV related liver disease remains the single most common diagnosis at the time of liver transplant. Pretransplant attempts to eradicate HCV and HBV have traditionally been unsuccessful and poorly tolerated, particularly in patients with decompensated cirrhosis. Thus, HCV and HBV recurrence has been universal and known to also negatively impact the outcome, with up to 30% of patients progressing to graft cirrhosis[10,11,12,13]. In our study, a total of 84 patients (42.42%) were non eligible for liver transplant out of 198 HBV and HCV patients. Among them, non-eligible patients were higher in HCV group 49.13% as compared to HBV group 32.92%. Unfortunately, there is no data available in Pakistan and that is why our study has filled the major statistical gap present in our region but data from internationally is sparse and studies are more focused on the factors why liver transplant is refused by the family or patient.[14,15] In our study we have observed that two clinical factors were significantly associated with ineligibility of liver transplantation, involvement of right lobe of liver in HBV & both lobes in HCV and high Okuda score, ($p < 0.05$). Although the prevalence of non-eligible candidates for liver transplant is less than 33% and 50% in HBV and HCV population, respectively but this shows quite late presentation of such patients or possibly they have ignored their disease due to lack of awareness regarding the disease or either outcome of the disease. That is why cumulative steps should be taken collectively by the doctors, decisions makers, and government personnel so that by providing the awareness regarding the disease and its outcome the incidence of such disease would be decrease and if patients came to hospital they more likely to clinically eligible for liver transplant rather than debilitating state.

CONCLUSION

Our study has shown higher percentage of HCV patients those who are in-eligible for liver transplant based on the clinical grounds than HBV patients. Based on the data provided by our study, future studies can be conducted in Pakistan on larger scale so that other clinical and non-clinical factors which contribute in the in-eligibility of liver transplantation can be ascertained hence disease burden can be reduced.

References:

1. Averhoff FM, Glass N, Holtzman D. Global burden of hepatitis C: considerations for healthcare providers in the United States. Clin Infect Dis 2012 Jul;55 Suppl 1:S10-S15.
2. Wright TL. Introduction to chronic hepatitis B infection. Am J Gastroenterol 2006;101 Suppl 1:S1-S6.
3. Sun YT, Zhang YX, Tang H, Mao Q, Wang XZ, Zhang LY, et al. Clinical characteristics and current management of hepatitis B and C in China. World J Gastroenterol 2014 Oct 7;20(37):13582-90.

4. Tu T, Block JM, Wang S, Cohen C, Douglas MW. The Lived Experience of Chronic Hepatitis B: A Broader View of Its Impacts and Why We Need a Cure. Viruses 2020 May 7;12(5).
5. Muller PC, Kabacam G, Vibert E, Germani G, Petrowsky H. Current status of liver transplantation in Europe. Int J Surg 2020 May 23.
6. Norton BC, Srivastava A, Ramos K, Vine L, Taylor R, Aluvihare V, et al. Risk-adjusted survival in liver transplant patients assessed and managed by a non-transplanting centre: South West Liver Unit experience. Frontline Gastroenterol 2020;11(3):202-8.
7. Ruiz-Extremera A, Diaz-Alcazar MDM, Munoz-Gamez JA, Cabrera-Lafuente M, Martin E, Arias-Llorente RP, et al. Seroprevalence and epidemiology of hepatitis B and C viruses in pregnant women in Spain. Risk factors for vertical transmission. PLoS One 2020;15(5):e0233528.
8. Razavi H. Global Epidemiology of Viral Hepatitis. Gastroenterol Clin North Am 2020 Jun;49(2):179-89.
9. Russell S, Sturua L, Li C, Morgan J, Topuridze M, Blanton C, et al. The burden of non-communicable diseases and their related risk factors in the country of Georgia, 2015. BMC Public Health 2019 May 10;19(Suppl 3):479.
10. Shao ZH, Shi J, Yao T, Feng D, Dong S, Shi S, et al. [Characteristics of methadone maintenance treatment clinic patients and influencing factors for HBsAg positivity based on Bayesian network model]. Zhonghua Liu Xing Bing Xue Za Zhi 2020 Mar 10;41(3):331-6.
11. Okada M, Oeda S, Katsuki N, Iwane S, Kawaguchi Y, Kawamoto S, et al. Recommendations from primary care physicians, family, friends and work colleagues influence patients' decisions related to hepatitis screening, medical examinations and antiviral treatment. Exp Ther Med 2020 Apr;19(4):2973-82.
12. Yang WS, Zeng XF, Liu ZN, Zhao QH, Tan YT, Gao J, et al. Diet and liver cancer risk: a narrative review of epidemiological evidence. Br J Nutr 2020 Apr 1;1-11.
13. Liu Z, Suo C, Mao X, Jiang Y, Jin L, Zhang T, et al. Global incidence trends in primary liver cancer by age at diagnosis, sex, region, and etiology, 1990-2017. Cancer 2020 May 15;126(10):2267-78.
14. Karman JF, Sileri P, Kamuda D, Cicalese L, Rastellini C, Wiley TE, et al. Risk factors for failure to meet listing requirements in liver transplant candidates with alcoholic cirrhosis. Transplantation 2001 May 15;71(9):1210-3.
15. Lai JC. Defining the threshold for too sick for transplant. Curr Opin Organ Transplant 2016 Apr;21(2):127-32.