ORIGINAL ARTICLE

Retrospective Study

Liver transplantation for hepatitis B virus: Decreasing indication and changing trends

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Abstract

AIM: To evaluate the indication and outcome of hepatitis B virus (HBV)-related liver transplantation (LT) in the era of newer antiviral agents.

METHODS: We collected data on all patients who underwent transplantation at King Faisal Specialist Hospital and Research Center. These data included demographic, perioperative and long-term postoperative follow-up data including viral serological markers, HBV DNA, and repeated liver imaging. Between January 1990 and January 2012, 133 patients (106 males and 27 females) underwent LT for HBV-related cirrhosis at our center. All patients were followed up frequently during the first year following transplantation, according to our standard protocol; follow-up visits occurred every 3-6 mo thereafter. Breakthrough infection was defined

as re-emergence of HBV-DNA or hepatitis B surface antigen (HBsAg) while on treatment. Five patients transplanted prior to 1992 did not receive immediate posttransplant anti-HBV prophylaxis; all other patients were treated with HBIG and at least one nucleos(t)ide analog.

RESULTS: One hundred and thirty-three patients underwent LT for HBV and were followed for a median of 82 mo (range: 1-274). The rates of post-LT survival and HBV recurrence during the follow-up period were 89% and 11%, respectively. The following factors were associated with disease recurrence: younger age (44.3 ± 16.2 years *vs* 51.4 ± 9.9 years, $P = 0.02$), positive pretransplant hepatitis B e antigen (HBeAg) (60% *vs* 14%, $P < 0.0001$), detectable pretransplant HBV DNA (60% *vs* 27%, $P = 0.03$), positive posttransplant HBsAg (80% *vs* 4%, $P < 0.0001$) and positive posttransplant HBeAg (27% *vs* 1%, $P < 0.0001$). Forty-four (33%) patients had hepatocellular carcinoma (HCC). In the first (pre-2007) group, HBV was the second leading indication for LT after hepatitis C virus infection. A total of 64 transplants were performed, including 46 (72%) for decompensated HBV cirrhosis, 12 (19%) for decompensated cirrhosis complicated by HCC and 6 (10%) for compensated cirrhosis complicated by HCC. In the second group, nonalcoholic steatohepatitis surpassed HBV as the second leading indication for LT. A total of 69 HBV related transplants were performed, including 43 (62%) for decompensated HBV cirrhosis, 7 (10%) for decompensated cirrhosis complicated by HCC and 19 (27.5%) for compensated cirrhosis complicated by HCC. There was a significant ($P = 0.007$) increase in the number of transplants for compensated cirrhosis complicated by HCC.

CONCLUSION: The use of potent anti-HBV agents has led to a changing trend in the indications for LT. HBV is currently the third leading indication for LT in this hyperendemic area.

Key words: Hepatitis B; Hepatitis C; Non-alcoholic steatohepatitis; Liver transplantation; Hepatocellular carcinoma

Core tip: Hepatitis B virus (HBV) is considered hyperendemic in the Middle East. In the 1980s, the overall prevalence of HBV infection in Saudi Arabia was 8.3%, making it one of the most highly endemic areas in the world. This high prevalence made HBV-related disease a leading indication for liver transplantation (LT). The use of potent anti-HBV agents has led to a changing trend in the indications for LT. HBV is currently the third leading indication for LT in this hyperendemic area. Additionally, there has been a shift in the indication for transplantation from hepatic decompensation to hepatocellular carcinoma.

INTRODUCTION

The World Health Organization (WHO) estimates that approximately 2 billion people worldwide have been infected with hepatitis B virus (HBV), and approximately 350 million people live with chronic infection[1,2]. HBV is considered hyperendemic in Saudi Arabia. In the 1980s, the overall prevalence of HBV infection in Saudi Arabia was 8.3%, making it one of the most highly endemic areas in the world. In 1989, the HBV vaccine was integrated into the expanded program of immunization, through which all newborn children have been vaccinated for HBV in Saudi Arabia ever since. This effort significantly decreased the prevalence of HBV in younger Saudi Arabians. However, the prevalence remains high for people older than 25 years, which is expected to increase the health care system burden for the next several decades[3,4].

Liver transplantation (LT) is the ultimate therapy for patients with hepatic failure and/or hepatocellular carcinoma (HCC) related to HBV. In the past, patient outcome was suboptimal because of severe disease recurrence resulting in graft loss. Therefore, HBV-related liver disease was previously considered a contraindication for LT[5,6]. Advances in HBV antiviral prophylaxis following LT have dramatically improved transplant outcomes, resulting in increased patient and graft survival. The use of hepatitis B immune globulin (HBIG) in combination with lamivudine has dramatically improved the outcome of HBV-related transplantation[7-11]. The availability of newer antivirals, such as adefovir, tenofovir and entecavir, alone or in combination, offers alternative treatment options, especially in patients with lamivudine resistance[12-14]. Additionally, overall patient survival has improved due to the prevention of disease progression to cirrhosis.

Here, we report the rates and indications of HBV-related LT at our center over the last 10 years. We also evaluated predictors of disease recurrence. In addition, we studied the effects of hepatitis delta virus (HDV) coinfection and HCC on transplant outcome.

MATERIALS AND METHODS

Patient population

In this retrospective study we collected data on all patients who underwent transplantation at King Faisal Specialist Hospital and Research Center. These data included demographic, perioperative and long-term

postoperative follow-up data. Between January 1990 and January 2012, 133 patients (106 males and 27 females) underwent LT for HBV-related cirrhosis at our center. All the patients were followed up frequently during the first year following transplantation, according to our standard protocol; follow-up visits occurred every 3-6 mo thereafter. Breakthrough infection was defined as re-emergence of HBV-DNA or hepatitis B surface antigen (HBsAg) while on treatment.

Transplant listing criteria

For all patients in our institution the criteria for medical urgency and patient waiting list ranking are based on the Model for End Stage Liver Disease (MELD). Patients with HCC typically have low calculated MELD scores because of compensated liver disease. Therefore, patients with HCC that are within the Milan criteria receive exceptional MELD points when their lesions exceed 2 cm in diameter. Additionally, HCC management with various ablation techniques is also discussed in the tumor board and treatment is offered to suitable patients. All patients will have their MELD score assessed regularly while they are on the waiting list.

Posttransplant protocol

Five patients transplanted prior to 1992 did not receive immediate posttransplant anti-HBV prophylaxis, all other patients were treated with HBIG and at least one nucleos(t)ide analog. HBIG was administered intravenously at a dose of 10000 units during the anhepatic phase and then at a dose of 5000 units daily during the first week; the goal was a hepatitis B surface antibody (HBsAb) titer of > 500 IU/mL. Subsequently, the antibody titer was monitored every 1-2 wk for the first 3 mo to maintain a titer of > 250 IU/mL. The HBsAb titer was then monitored every 1-2 mo to maintain the level at > 100 IU/mL during the first year following transplantation. Beginning in 2009, the majority of our patients received HBIG for 1 year after LT. Prior to 2009, the duration of HBIG was variable, and it was extended in many patients at the discretion of the treating physician. In addition to HBIG, the majority of our patients were administered lamivudine. Adefovir, entecavir and tenofovir were used in the more recent transplants after these agents became available in Saudi Arabia.

The standard immunosuppression protocol in our institution includes calcineurin inhibitors and myco-phenolate mofetil during the first 6-12 mo after transplantation and oral prednisone for the first 3 mo. The doses of immunosuppressive medications were adjusted according to their serum levels and were modified in patients with renal impairment.

A complete blood count, liver function and serum levels of liver enzymes and immunosuppressive drugs were assessed at each visit. The levels of HBV DNA and HBsAg were tested monthly for the first 3 mo and every 6 mo thereafter. HBV viral load was performed using real time PCR technology. The assay provides a detection limit from 15 to 100000000 IU/mL. Results from earlier transplants utilizing older assays measuring viral loads in copies/mL were converted to IU/mL for standardization of results. Breakthrough infection was defined as the reemergence of HBV DNA and HBsAg while a patient was undergoing treatment.

Pretransplant follow-up

While on the transplant waiting list, all patients were closely followed up every 1-3 mo. Standard biochemical liver function assays were performed at each visit. Each patient on the list underwent Doppler ultrasound of the liver every 3 mo. Forty-four patients were diagnosed with HCC (33%) and all patients achieved viral suppression before transplant. After an examination of explants from these patients, five patients were confirmed to have HCC beyond the Milan criteria. Nine patients received surgical or ablative therapy while they were on the waiting list.

Statistical analysis

All variables were checked for normality. Descriptive statistics were summarized as the mean (standard deviation), median (range) or frequency (percentage), as appropriate. A χ^2 test was used to assess group differences for categorical variables, and a t-test was used to assess differences between continuous variables. ORs were calculated to determine associations between the variables of interest and recurrence. All the tests were two-sided with a 5% level of significance. All the analyses were performed using Stata version 10 (StataCorp, Texas, United States). The statistical methods of this study were reviewed by Safiyya Ali and Majid Almadi who are trained biostatisticians with extensive biomedical research experience from the Gastroenterology research unit, King Saud University. This study was approved by the research ethics committee of our hospital.

RESULTS

General characteristics of the study population

The mean ± SD age of all the patients was 50.6 ± 11.0 years and 106 (80%) was males. Ninety-seven (73%) patients underwent deceased donor LT and 36 (23%) patients underwent living donor LT. The median post-LT follow-up was 82 mo (range: 1-274) and HBV recurrence occurred in 15 patients (11%). The median time between LT and HBV recurrence was 42 mo. Pretransplant HBsAg and hepatitis B e antigen (HBeAg) were positive in 126 (95%) and 24 patients (19%), respectively. Thirty-six patients (27%) had detectable HBV DNA levels at the time of LT. Pretransplant lamivudine was taken by 81 (61%) patients; 5 (4%) took adefovir; 2 (2%) began with lamivudine and were then switched to adefovir; 20 (15%) took a

Table 1 Characteristics of the study population, both overall and grouped by recurrence *n* (%)

Characteristics				
Age (yr)	50.6 ± 11.0	44.3 ± 16.2	51.4 ± 9.9	0.02[2]
Gender				
Male	106 (80)	14 (13)	92 (87)	0.16
Female	27 (20)	1 (3.7)	26 (96)	
Posttransplantation follow-up (mo)	82 (1-274)[1]	206 (74-274)	53 (1-254)	< 0.0001
Pretransplantation HBsAg				
Negative	6 (5)	0	6 (5)	0.37
Positive	126 (95)	15 (100)	111 (95)	
Pretransplantation HBeAg				
Negative	108 (81)	6 (40)	102 (87)	< 0.0001[2]
Positive	24 (19)	9 (60)	15 (134)	
Pretransplant HBV DNA				
Negative	86 (73)	4 (60)	82 (73)	0.03
Positive	36 (27)	6 (60)	30 (26)	
HBIG duration (mo)[1]	14 (1-140)	14 (1-140)	14 (1-132)	0.83
MELD score	20.8 ± 7.6	19.2 ± 7.7	21.0 ± 7.6	0.39
Posttransplantation HBsAg				
Negative	114 (88)	3 (20)	111 (97)	< 0.0001[2]
Positive	16 (12)	12 (80)	4 (3)	
Posttransplant HBeAg				
Negative	122 (96)	11 (73)	111 (99)	< 0.0001[2]
Positive	5 (4)	4 (5)	1 (1)	
HDV coinfection				
Negative	70 (69)	8 (80)	62 (67)	0.41
Positive	32 (31)	2 (20)	30 (33)	

[1]The results are expressed as the median (range); [2]Significant at *P* < 0.05. HDV: Hepatitis delta virus; HBsAg: Hepatitis B surface antigen; HBeAg: Hepatitis B e antigen; HBV: Hepatitis B virus.

combination of lamivudine and adefovir; 4 (3%) took entecavir; 7 (5%) took tenofovir; and 6 (5%) took interferon. HCC was diagnosed in 44 (33%) patients. The median duration of treatment with HBIG in 102 patients was 14 (range 1-140) mo, and 24 (19%) patients were still undergoing active HBIG treatment at the time of data collection. The average MELD score was 20.8 ± 7.6. HDV coinfection was present in 32 (24%) patients.

Recurrence
The 15 patients who developed breakthrough HBV infection were on monotherapy, and switching to or adding a different oral agent helped control their infection. After transplantation, 16 (12.3%) patients were positive for HBsAg. Patients who experienced recurrence had a significantly greater median duration of posttransplant follow-up compared with patients without recurrence (median 206, range 74-274 and median 53, range 1-254, respectively, *P* < 0.0001). The following factors were associated with disease recurrence: younger age (44.3 ± 16.2 years *vs* 51.4 ± 9.9 years, *P* = 0.02), positive pretransplant HBeAg (60% *vs* 14%, *P* < 0.0001), detectable pretransplant HBV DNA (60% *vs* 27%, *P* = 0.03), positive posttransplant HBsAg (80% *vs* 4%, *P* < 0.0001) and positive posttransplant HBeAg (27%

vs 1%, *P* < 0.0001). Patients who were positive for HBeAg before transplantation were more likely to experience recurrence compared with those who were negative (OR = 9.6, 95%CI: 2.99-30.85; *P* < 0.0001). Patients who had positive HBV DNA levels before transplantation were almost four times more likely to have recurrence compared with those who did not (OR = 4.1, 95%CI: 1.08-15.5; *P* = 0.04). Similarly, patients who were positive for HBsAg or HBeAg after transplantation were more likely to experience recurrence than those who did not (OR = 111, 95%CI: 22.2-555.9; *P* < 0.0001 and OR = 40.4, 95%CI: 4.1-393.5; *P* = 0.001, respectively). There were no significant associations between the patient's gender or MELD score and recurrence (Table 1).

Hepatitis delta virus coinfection
Patients with HBV and hepatitis delta virus (HDV) coinfection were similar to the HBV-monoinfected patients in terms of their age at the time of transplantation (47.7 years *vs* 51.2 years, *P* = 0.15), pretransplant MELD score (22.1 *vs* 20.2, *P* = 0.28) and post-LT disease recurrence (6% *vs* 11%, *P* = 0.41). HDV infection was not a significant predictor of death: none of the patients who had HDV died.

HCC status
HCC was present prior to LT in 44 (33%) patients. A single lesion was present in 37 patients with an average size of 3.9 cm. Seven patients had multifocal HCC that was within the Milan criteria. Despite strict adhesion to Milan criteria when listing patients for LT, five patients were confirmed to have HCC beyond the Milan criteria after examination of explants. Prior to transplantation all patients underwent a chest CT and a bone scan to rule out distant metastasis. The patients with HCC were significantly younger than those without HCC (48.4 ± 11.3 years *vs* 55.2 ± 8.6 years, *P* = 0.0007). HBV recurrence was not significantly associated with the presence of HCC, the duration of survival or HBV markers. The patients who had HCC had significantly lower MELD scores than those who did not (18 ± 8.2 *vs* 22.2 ± 6.9, respectively, *P* = 0.0024) (Table 2). Our data revealed that an increasing number of the more recent transplants (2007-2012) were for well-compensated cirrhosis complicated by HCC compared with the pre-2007 transplants (*P* = 0.007) (Table 3).

Indications for LT
Between January 2001 and January 2012, 500 patients received transplants and were followed up at our center. All the transplant indications recorded in our database were reviewed. During the first study period, January 2001-December 2006, 50% of the patients received transplants for hepatitis C virus (HCV)-induced cirrhosis, 17% for HBV-induced cirrhosis and 12% for nonalcoholic steatohepatitis (NASH)-related cirrhosis.

Table 2 Characteristics of the study population grouped by the presence of hepatocellular carcinoma *n* (%)

Variable	No HCC	HCC	*P* value
	n = 89 (67)	*n* = 44 (33)	
Age (yr)	48.4 ± 11.3	55.2 ± 8.6	0.0007[1]
Gender			
Male	69 (78)	37 (84)	0.38
Female	20 (22)	7 (16)	
Pretransplant HBsAg			
Negative	4 (5)	2 (5)	1.00
Positive	84 (95)	42 (95)	
Pretransplant HBeAg			
Negative	69 (82)	33 (79)	0.63
Positive	15 (18)	15 (21)	
Pretransplant HBV DNA			
Negative	57 (72)	29 (67)	0.59
Positive	22 (28)	14 (33)	
MELD score	22.2 ± 6.9	18.0 ± 8.2	0.002[1]
Posttransplant HBsAg			
Negative	75 (86)	39 (91)	0.46
Positive	12 (14)	4 (9)	
Posttransplant HBeAg			
Negative	81 (95)	41 (98)	0.53
Positive	4 (5)	1 (2)	
HDV coinfection			
Negative	50 (68)	20 (71)	0.71
Positive	24 (32)	8 (29)	

[1]Significant at $P < 0.05$. HDV: Hepatitis delta virus; HBsAg: Hepatitis B surface antigen; HBeAg: Hepatitis B e antigen; HBV: Hepatitis B virus.

Table 3 Comparison of indications for transplantation before and after January 2007

	Before January 2007	After January 2007	*P* value
	(*n* = 64)	(*n* = 69)	
Transplantations for well-compensated HCC	6	19	0.007
Transplantations for liver decompensation without HCC	46	43	Not significant

HCC: Hepatocellular carcinoma.

During the second study period (January 2007-January 2012), 35%, 20%, and 16% of the patients received transplants for HCV-, NASH-, and HBV-induced cirrhosis, respectively. During the second study period, NASH-related cirrhosis surpassed HBV as an indication for LT, whereas the rates of transplantation for all other indications remained the same throughout the study.

DISCUSSION

The development of potent HBV drugs with high genetic barriers to resistance has resulted in significant suppression of viral replication. As a result, overall patient survival has improved due to the prevention of disease progression to cirrhosis. Recent data showed the regression of cirrhosis in 71 out of 96 (74%) cirrhotic patients treated with tenofovir, which was confirmed by paired biopsies at baseline and after 5 years. However, the preventive effect of these agents against HCC development is less clear. Furthermore, the outcome of LT for HBV-related liver disease has dramatically changed since the introduction of oral antiviral agents and HBIG[15-18].

Here, we reported the rates and indications of HBV-related LT in a Saudi population. We also reported the long term outcomes of HBV-related LT in our country. According to the WHO classification, HBV is considered hyperendemic in Saudi Arabia, where the overall prevalence is 8.3%[3,4]. Saudi Arabia is among the most highly endemic areas for HBV infection in the world.

However, a comparison of the data from the earlier and later periods of this study has clearly demonstrated that HBV-related transplantation has decreased from being the second leading indication for LT, following HCV-related liver disease, to being the third indication, with a corresponding increase in the proportion of LTs due to NASH-related liver disease. The decline in HBV-related liver disease as an indication for LT is likely related both to the various mass screening programs in the Kingdom, which have enabled the detection of chronically infected HBV patients at various disease stages, and to the introduction of effective antiviral treatment[19-24]. Interestingly, similar observations have been noted in various studies from Europe, the United States, Australia, and New Zealand, where massive reductions in HBV-related disease as an indication for LT have been reported[25,26]. For example, Burra *et al*[27] showed that HBV-related cirrhosis had dropped from 24% to 16% in patients transplanted for solely virus-related liver disease in Europe.

NASH-related liver disease is a rising global concern due to the obesity epidemic. Major risk factors for NASH-related liver disease, including diabetes mellitus, obesity, and hyperlipidemia, are extremely common in Saudi Arabia. Recent data have suggested overall prevalence rates of these risk factors of 23.7%, 35.5% and 54%, respectively[28,29].

Our results demonstrated a change in the indications for HBV-related LT from hepatic decompensation to HCC. European and American studies have also reported this trend, noting that the occurrence of HCC in patients with viral-related liver disease doubled from 2006-2010 compared with 1988-1994[23]. This finding could be related to improvements in the control of viral replication with potent medications (entecavir and tenofovir), which has prevented the progression of liver disease to more advanced stages of fibrosis and has prevented decompensation in already cirrhotic patients. HBV-related carcinogenesis develops independently of the onset of cirrhosis; therefore, antiviral treatments such as nucleo(t)side analogs, which may result in the regression of fibrosis or prevent clinical decompensation, often fail to prevent HCC, especially in Asian and African countries[30]. A randomized study conducted by Liaw *et al*[31] demon-

strated that lamivudine therapy for a median of 32 mo resulted in a decrease in the incidence of HCC in patients with advanced fibrosis, but not in patients with decompensated liver disease. Other studies have similarly failed to show any protective effect of lamivudine against the development of HCC in patients with decompensated liver disease[32,33]. The limitations of these studies include their relatively short follow-up periods and small sample sizes.

In our study population, 15 patients (11%) developed HBV reinfection during the follow-up period, which is in agreement with the rates described in other studies[34-36]. Most of the patients in our study who developed resistance underwent transplantation early during the study period, which explains their significantly longer posttransplant follow-up. The most important predictor of disease recurrence is viral replication at the time of transplantation. Patients who were positive for HBeAg or had detectable HBV DNA pretransplantation were more likely to develop recurrence than patients with negative pretransplantation results. This observation has also been reported in several other studies. Yasunaka *et al*[37] evaluated disease recurrence following LT for HBV-related liver disease and concluded that serum HBV DNA before LT correlated with the HBV reinfection rate even with the successful administration of low-dose HBIG prophylaxis.

Thirty-two (24%) of our patients experienced HBV/HDV coinfection. Of the 15 patients with post-transplantation recurrence, only two had HBV/HDV coinfection. This rate was lower than for the HBV-infected patients (6% *vs* 11%); however, this difference was not statistically significant. Furthermore, HDV infection was not a significant predictor of graft loss or posttransplant mortality; none of the patients with HDV died. This observation is similar to other reports on the outcome of transplantation for HBV/HDV coinfection. Caccamo *et al*[38] reported no recurrence of HBV infection following LT in HBV/HDV-infected patients, whereas others have reported lower rates of HBV recurrence in patients with HBV/HDV coinfection compared with HBV monoinfection[38-40]. Burra *et al*[27] reported that HDV coinfection was associated with better survival outcomes compared to HBV monoinfection which is thought to be related to the inhibitory effect of HDV on the HBV replication cycle. Despite the aggressive course of HBV and HDV coinfection in immunocompetent patients, the LT outcomes in HDV-coinfected patients are similar to those in HBV-monoinfected patients.

Forty-four patients in our study were diagnosed with HCC prior to LT. With the exception of 5 patients, all the patients were within the Milan criteria (a single tumor $\leqslant$ 5 cm or a maximum of 3 tumors < 3 cm each). Patients within the Milan criteria who receive transplants due to HCC have a survival rate similar to that of HCC-negative patients[41,42]. The risk factors for tumor recurrence include a larger pretransplantation tumor size, lymphovascular invasion, and post-LT

systemic chemotherapy. Saab *et al*[36] evaluated the effects of both HCC recurrence and HBV reinfection on the long-term survival of patients after LT. They concluded that pre-OLT HCC and the recurrence of HCC after transplantation were associated with HBV reinfection and decreased patient survival. However, in their cohort, 50 out of 88 transplant patients with HCC were beyond the Milan criteria based on pathological examinations. This finding likely explains the inferior outcome of patients transplanted for HBV-HCC compared with the HCC-negative patients in their study. In contrast, Wong *et al*[43] compared the clinical outcomes of LT candidates with chronic hepatitis B who did or did not have HCC. In their study, the patients with HCC had a higher rate of LT and a shorter interval from wait list assignment to transplant compared with the HCC-negative patients; however, the two groups had similar post-OLT survival and HBV recurrence rates. This finding may be explained by the observation that 72% of the HCC patients were within the Milan criteria, and 23 of the 25 patients who exceeded the Milan criteria underwent some form of HCC treatment to downstage their disease.

Although the present study has many strengths, it also has several limitations, including its retrospective design. HBV immunoprophylaxis during the posttransplant follow-up period was not consistent for all the patients. Data on pretransplantation HBV DNA status, pretransplantation HBV serological markers, and HDV coinfection were not available for some of the study individuals. However, posttransplantation HBV DNA and HBV serological data were available and complete. Furthermore, this is the largest study originating from our region, an area that is considered endemic for HBV infection.

In conclusion, the use of highly potent anti-HBV agents has led to adequate control of viral replication, significant biochemical remission, histological improvement, and the prevention of hepatic decompensation. These effects are expected to subsequently result in a reduction in the rate of HBV-related LT and a shift in the indication for transplantation from HBV-related hepatic decompensation to HBV-related HCC. The availability of a newer generation of nucleos(t)ide analogs has also resulted in a significant improvement in the outcome of LT for HBV-related liver disease. Controlling viral replication and adhering to the Milan criteria when performing transplants in patients with HBV-related HCC will improve transplantation outcomes.

COMMENTS

Background

The indications for liver transplantation (LT) for hepatitis B (HBV) infected patients are hepatic de-compensation, fulminant liver failure or development of hepatocellular carcinoma. Currently, adequate control of viral replication can be achieved with potent antiviral therapy. The authors believe that with better control of viral replication using potent medication will result in a drop in HBV related transplantation associated with a change in the indication for LT from

hepatic-decompensation to hepatocellular carcinoma.

Research frontiers

Nonalcoholic steatohepatitis (NASH) related cirrhosis surpassed HBV as an indication for LT while the rates of transplantation for all other indications remained the same. With the increasing prevalence of DM and obesity and the progress in the treatment of hepatitis C virus (HCV) and HBV infection NASH related cirrhosis may replace HCV and HBV as the leading indication for transplantation in the future.

Innovations and breakthroughs

LT for HBV decreased dramatically in our region. And the outcome of LT for HBV-related liver disease has dramatically changed since the introduction of oral antiviral agents resulting in better graft and patient survival. Similar observations have been noted in various studies from Europe, the United States, Australia, and New Zealand, where massive reductions in HBV-related disease as an indication for LT have been reported.

Applications

The advances in treating viral hepatitis resulted in a better outcome and resulted in a decrease in viral related transplantation. NASH related cirrhosis is becoming the leading indication for LT. Therefore, there is a dire need for governmental efforts to control the growing obesity epidemic that is impacting the increasing need for liver transplant due to NASH-related cirrhosis.

Peer-review

In this study, the authors clearly demonstrate a decreasing indication for HBV related transplantation associated with a changing trend in the indication from hepatic de-compensation to hepatocellular carcinoma. Additionally, NASH related cirrhosis surpassed HBV as an indication for LT.

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