# Liver Transplantation in Patients With Hepatitis B Virus Infection: Outcome in Asian Versus White Patients

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**Previous studies have found that Asian patients transplanted for hepatitis B virus (HBV) infection had worse outcomes than white patients. The aim of this study was to compare outcomes in Asian and white patients listed for liver transplantation for HBV infection. Data of all patients with HBV infection listed for liver transplantation between January 1996 and June 1998 from 20 centers in North America were collected using a survey. Total patients enrolled were 325 (171 whites, 126 Asians, 28 other races). There was no difference in demographics, liver biochemistry, and HBV replicative status between Asians and whites at the time of listing. More Asians had hepatocellular carcinoma and fewer Asians had hepatitis C or D virus coinfection. At the time of this survey, 70 Asians (55%) and 99 whites (58%) had been transplanted. Actuarial 2-year survival posttransplantation for Asians (88%) and whites (92%) was similar. Recurrent HBV infection occurred in 8 (11%) Asians and 12 (12%) whites. Five patients with recurrent HBV infection died, 4 of whom were Asian. Actuarial 2-year survival for Asians versus whites with recurrent HBV infection was 60% versus 90% ($P = .04$). In this large cohort of patients, overall survival and recurrent HBV infection posttransplantation were comparable between Asians and whites. However, Asians with recurrent HBV infection posttransplantation had significantly higher mortality. (HEPATOLOGY 2001;34:126-132.)**

Early studies of liver transplantation (LT) for hepatitis B reported rates of recurrent hepatitis B virus (HBV) infection of 75% and survival of 50% 2 years post-LT.[1,2] The use of hepatitis B immune globulin (HBIG) and/or lamivudine prophylaxis led to a significant reduction in recurrent HBV infection and improved survival in these patients. A study from Europe reported a recurrent HBV infection rate of 36% at 3 years with long-term use of HBIG.[1] Studies in the United States using higher doses of HBIG reported recurrent HBV infection rates of 11% to 19% at 2 years.[3,4] Lamivudine monotherapy decreased recurrent HBV infection rate to 10% to 29% at 1 year post-LT,[5,6] but recurrent HBV infection increased to 50% at 2 years because of selection of lamivudine resistant mutants.[7] Preliminary results suggest that a combination of lamivudine and HBIG may be more effective in preventing recurrent HBV infection.[8-10]

Previous studies have found that recurrent HBV infection was related to HBV replication pre-LT and coinfection with hepatitis D (HDV).[2,11] Three early reports suggested that Asians who had LT for hepatitis B have impaired outcomes. The first study reported on 3 Asians who developed recurrent HBV infection within 2 months post-LT: all 3 died within 6 months.[12] A second report on 45 patients (16 Asians vs. 29 non-Asians) found that Asians had higher rates of recurrent HBV infection (72% vs. 32%, $P < .05$) and higher mortality rate post-LT (87% vs. 22%, $P < .05$).[13] A third study on 35 patients (15 Asians vs. 20 non-Asians) found that Asians had lower 1-year survival rate post-LT (59% vs. 94%, $P < .05$) but 5-year survival rates were similar (59% vs. 54%).[14] Poor 1-year survival rates among Asians were attributed to late referral and more advanced liver disease at transplantation. There were no differences in recurrent HBV infection rate (64% Asians vs. 50% non-Asians) or deaths related to recurrent HBV infection.

A high percentage of patients with HBV infection listed for LT in North America are Asian. It is important to ascertain if Asians transplanted for hepatitis B have a worse outcome. We conducted a retrospective analysis of a large cohort of patients listed for LT for hepatitis B to compare the rates of pre- and post-LT survival rates and recurrent HBV infection in Asians and whites, and to identify factors that may account for any difference in their outcome.

## PATIENTS AND METHODS

A retrospective survey was conducted in 20 LT centers across North America. Patients with hepatitis B listed for LT between January 1996 and June 1998 were included. Patients were categorized into whites (Hispanic and non-Hispanic) and Asians (Chinese, Indians, Japanese, Koreans, Pacific Islanders, and individuals born in Southeast Asian countries) and other races (American Indians including Alaskans, African Americans, etc). Baseline demographics; indications for LT; liver biochemistries; hepatitis B, C, and D serology; and the use of antiviral therapy pre-LT were recorded. Indications for LT were categorized as fulminant hepatitis, end-stage cirrhosis, or hepatocellular carcinoma by investigators at each center. Hepatitis serology was tested using commercial enzyme immunoassays (Abbott Laboratories, North Chicago, IL). Serum HBV DNA was

Abbreviations: LT, liver transplantation; HBV, hepatitis B virus; HBIG, hepatitis B immune globulin; HDV, hepatitis D virus; mCTP, modified Child-Turcotte-Pugh; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NS, not significant.

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TABLE 1. Factors Considered for Univariate and Cox Regression Analyses

| | Factors for Univariate Analysis | | Factors for Cox Regression Analysis |
|---|---|---|---|
| Post-LT survival | Age | Gender | Age |
| | Ethnicity | Indications for LT | Ethnicity |
| | AST at listing and LT | ALT at listing and LT | Indication for LT |
| | Albumin at listing and LT | Total bilirubin at listing and LT | AST at listing |
| | PT at listing and LT | mCTP at listing and LT | mCP at listing and LT |
| | Anti-HCV | Anti-HDV | Recurrent HBV post-LT |
| | Antiviral treatment pre-LT | HBeAg/HBV DNA at listing and LT | |
| | Recurrent HBV post-LT | Post-LT immune prophylaxis | |
| Post-LT recurrent HBV | Age | Gender | Age |
| | Ethnicity | Indications for LT | Gender |
| | AST at listing and LT | ALT at listing and LT | Ethnicity |
| | Albumin at listing and LT | Total bilirubin at listing and LT | Indications for LT |
| | PT at listing and LT | HBeAg/HBV DNA at listing and LT | HBeAg/HBV DNA at LT |
| | Anti-HCV | Anti-HDV | Post-LT immune prophylaxis |
| | Post-LT immune prophylaxis | | |
| Pre-LT survival | Age | Gender | Age |
| | Ethnicity | Indications for LT | Gender |
| | AST at listing | ALT at listing | Ethnicity |
| | Albumin at listing | Total bilirubin at listing | Indications for LT |
| | HBeAg/HBV DNA at listing | Antiviral treatment | HBeAg/HBV DNA at listing |
| | Breakthrough infection | mCTP at listing | Antiviral treatment |
| | Anti-HCV | Anti-HDV | mCTP at listing |

tested at each center, using liquid hybridization (Abbott Laboratories), branched DNA (Chiron/Bayer, Emeryville, CA), or hybrid capture assays (Digene, Gaithersburg, MD). In patients who were not transplanted at the time of survey, liver biochemistries and HBV serology at last visit, the duration of follow-up, and deaths while waiting for LT were documented. For the transplanted patients, data recorded included liver biochemistries and HBV serology at transplantation and last visit, duration of follow-up, and prophylactic therapies post-LT. The end points were pre- and post-LT mortality and recurrent HBV infection. Recurrent HBV infection was defined as detection of serum HBV DNA (by unamplified assays) and/or hepatitis B surface antigen greater than 1 month post-LT. In 7 patients, HBV markers were not tested regularly and the time to recurrent HBV infection was estimated as the midpoint between LT and when the HBV marker first tested positive. There was significant heterogeneity in the post-LT prophylactic regimens, which can be categorized into 3 groups: HBIG only, lamivudine only, and a combination of HBIG and lamivudine. Of the 94 patients in the combination prophylaxis group, 63 received lamivudine and high-dose intravenous HBIG throughout their post-LT course, and 31 received combination therapy for the first 3 to 20 months and then lamivudine only. The Child-Turcotte-Pugh (CTP) score was not in the United Network for Organ Sharing criteria for listing patients until June 1998. Because the degree of ascites and encephalopathy at listing were not recorded in most patients, a modified CTP score (mCTP) was used to assess severity of liver disease. This score was derived by adding the points for serum albumin, bilirubin, and prothrombin time or international normalized ratio.

Data were entered into an Excel (Microsoft, Redmond, WA) database and analyzed using SPSS version 9.0 (SPSS Inc., Chicago, IL). Statistical tests were performed using $\chi^2$ or Fisher's exact test for categorical, and Student's $t$ test for continuous variables. Comparisons of survival and recurrent HBV infection were performed using the Kaplan-Meier method and log rank test. Cox regression analyses were performed to identify independent factors associated with recurrent HBV infection and mortality pre- and post-LT (Table 1).

## RESULTS

### *Characteristics of the Patients Studied*

A total of 325 patients with HBV infection were listed for LT in the 20 centers between January 1996 and June 1998. Twenty-eight patients being neither Asian nor white were excluded from this study. Of the remaining 297 patients, 171 (57.6%) were white and 126 (42.4%) were Asian. At the time of listing, the two groups were comparable in gender, age, liver biochemistries, mCTP score, and HBV replicative status (Table 2). Compared with whites, Asians were more likely to be listed for hepatocellular carcinoma (HCC) (26% vs. 6%, $P < .0001$) and less likely to have hepatitis C virus (HCV) (1% vs. 18%, $P < .0001$) or HDV coinfection (6% vs. 26%, $P =$

TABLE 2. Characteristics of the Patients Studied

| | Asian | White | P |
|---|---|---|---|
| No. of patients | 126 (42) | 171 (58) | |
| Sex | | | |
| Male | 98 (77) | 146 (85) | .09 |
| Female | 28 (23) | 25 (15) | |
| Age* (years) | 49.5 ± 1.0 | 50.4 ± 0.8 | .43 |
| Indications for listing | | | |
| Cirrhosis | 92 (73) | 154 (90) | <.001 |
| Fulminant hepatitis B | 5 (4) | 8 (4) | |
| HCC | 29 (23) | 9 (6) | |
| At listing | | | |
| Viral serology: | | | |
| HBeAg+ | 33/83 (40) | 51/120 (43) | .36 |
| HBV DNA+ | 42/90 (47) | 58/127 (46) | .53 |
| Anti-HCV+ | 1/104 (1) | 24/134 (18)† | <.0001 |
| Anti-HDV+ | 2/34 (6) | 14/54 (26)† | .02 |
| Liver biochemistries* | | | |
| ALT (IU/L) | 193 ± 36 | 283 ± 92 | .43 |
| Albumin (g/dL) | 3.1 ± 0.1 | 3.0 ± 0.1 | .32 |
| Bilirubin (mg/dL) | 7.1 ± 0.9 | 5.2 ± 0.6 | .09 |
| PT (sec) | 17.3 ± 0.8 | 16.6 ± 0.6 | .47 |
| mCTP score | 6.6 ± 0.2 | 5.9 ± 0.2 | .67 |
| Antiviral therapy prior to transplantation | 63 (50) | 91 (53) | .58 |

NOTE. Data expressed as no. (%).
*Mean ± SEM.
†Three patients had triple infection.

.018). Of the patients with HCC, two thirds had biochemical evidence of hepatic decompensation, and none had vascular invasion or extrahepatic metastasis. About 50% of patients in each group received antiviral pre-LT, with all except one receiving lamivudine.

### *Transplanted Patients*

At the time of the survey, 169 (57%) patients, including 99 (58%) white and 70 (55%) Asian patients had been transplanted (Table 3). The proportions of patients transplanted, waiting time to LT, duration of follow-up post-LT, use of antiviral therapy, and occurrence of breakthrough infection (reappearance of serum HBV DNA after initial response to antiviral) pre-LT were comparable in both groups. The proportions of Asian and white patients receiving each prophylactic regimen were also similar: 26% versus 19% received HBIG only, 14% versus 16% received lamivudine only, and 56% versus 55% received a combination of lamivudine and HBIG (Table 4).

Six patients (4 whites and 2 Asians) with breakthrough infection caused by lamivudine resistance were transplanted. Post-LT, 4 received a combination of HBIG and lamivudine, 1 received HBIG alone, and 1 received lamivudine monotherapy. Recurrent HBV infection was observed in only 1 patient at 9 months post-LT (a white patient who received combination prophylaxis for 3 months followed by lamivudine monotherapy).

TABLE 3. Characteristics of the Transplanted Patients

| | Asian | White | *P* |
|---|---|---|---|
| No. of patients | 70 (56) | 99 (58) | |
| Sex | | | |
| Male | 55 (79) | 84 (85) | .29 |
| Female | 15 (21) | 15 (15) | |
| Age* (years) | 50.4 ± 1.3 | 50.1 ± 1.1 | .86 |
| Indications for listing | | | |
| Cirrhosis | 45 (64) | 84 (85) | .002 |
| Fulminant hepatitis B | 5 (7) | 7 (7) | |
| HCC | 20 (29) | 8 (8) | |
| At listing | | | |
| Viral serology | | | |
| HBeAg+ | 19/50 (38) | 27/74 (37) | .61 |
| HBV DNA+ | 21/53 (40) | 31/75 (41) | .89 |
| Anti-HCV+ | 0/57 (0) | 15/82 (18) | .003 |
| Anti-HDV+ | 0/25 (0) | 11/38 (29) | .01 |
| Liver biochemistries* | | | |
| ALT (IU/L) | 263 ± 60 | 394 ± 154 | .49 |
| Albumin (g/dL) | 2.9 ± 0.1 | 2.9 ± 0.1 | .82 |
| Total bilirubin (mg/dL) | 9.4 ± 1.5 | 6.4 ± 1.0 | .08 |
| PT (sec) | 18.2 ± 1.3 | 17.1 ± 0.8 | .47 |
| mCTP score | 6.5 ± 0.3 | 6.2 ± 0.2 | .34 |
| At transplantation | | | |
| Viral serology | | | |
| HBeAg+ | 7/37 (19) | 20/56 (36) | .10 |
| HBV DNA+ | 12/44 (27) | 13/67 (19) | .32 |
| Liver biochemistries* | | | |
| ALT (IU/L) | 131 ± 35 | 261 ± 79 | .20 |
| Albumin (g/dL) | 3.1 ± 0.1 | 2.9 ± 0.1 | .06 |
| Total bilirubin (mg/dL) | 9.9 ± 1.6 | 7.3 ± 1.1 | .16 |
| PT (sec) | 18.1 ± 1.1 | 16.9 ± 0.7 | .35 |
| mCTP score | 6.1 ± 0.3 | 6.1 ± 0.2 | .89 |

NOTE. Data are expressed as no. (%).
*Mean ± SEM.

TABLE 4. Outcome of Transplanted Patients

| | Asian | White | *P* |
|---|---|---|---|
| No. of patients | 70 (56) | 99 (58) | |
| Pre-LT | | | |
| Use of antiviral therapy | 35 (50) | 50 (51) | .98 |
| Breakthrough infection | 2/35 (5.7) | 4/50 (8) | |
| Interval from listing to LT (mo) | 6.0 ± 0.9 | 6.9 ± 0.8 | .46 |
| Post-LT | | | |
| Duration of follow-up (mo) | 19.8 ± 1.5 | 21.0 ± 1.3 | .71 |
| Recurrent HBV infection (total) | 8 (11) | 12 (12) | .89 |
| Prophylactic regimen | | | |
| HBIG | 0/19 (0) | 1/19 (5) | .54 |
| Lamivudine | 5/10 (50) | 4/16 (25) | |
| HBIG + lamivudine | 3/39 (8) | 7/55 (13) | |
| Unknown | 0/2 (0) | 0/9 (0) | |
| Mortality | | | |
| All causes | 8 (11) | 7 (7) | .33 |
| Liver related | 7 (10) | 6 (6) | .34 |

NOTE. Data are expressed as no. (%).
*Mean ± SEM.

***Recurrent HBV Infection.*** Recurrent HBV infection was reported in 20 (11.8%) patients, including 8 (11%) Asians and 12 (12%) whites (not significant [NS]), all of whom were men. Cumulative 1- and 3-year recurrent HBV infection rates were 12% and 17%, respectively for both groups (Fig. 1). The proportions of Asian and white patients with recurrent HBV infection post-LT and time to recurrent HBV infection were similar. Recurrent HBV infection occurred in similar proportions of Asian and white patients receiving the same prophylactic therapies: 0% versus 5% of those who received HBIG only, 50% versus 25% who received lamivudine only, and 8% versus 13% who received combination therapy (Table 4). Of the 20 patients with recurrent HBV infection, only 1, a white patient, received additional treatment with adefovir. Despite similar management, Asian patients with recurrent HBV infection had significantly higher mortality. Four (50%) Asian patients and 1 (8%) white patient with recurrent HBV infec-

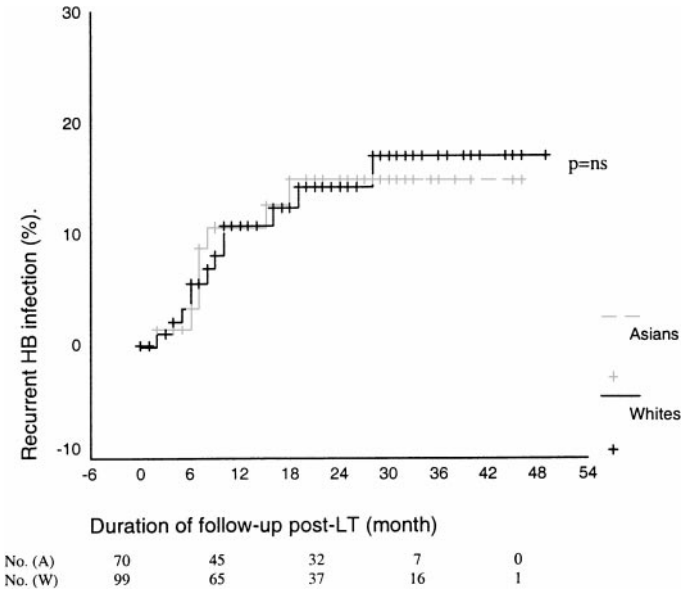


FIG. 1. Cumulative rates of recurrent HBV infection post-LT in Asian and white patients.

tion died. Actuarial survival rates at 1 and 2 years were 60% for Asians and 90% for whites who developed recurrent HBV infection ($P = .04$) (Fig. 2). Causes of death for the 4 Asian patients were liver failure secondary to recurrent HBV infection in 3 patients and metastatic HCC in 1 patient. The cause of death for the white patient was liver failure caused by recurrent hepatitis B. Of the 15 surviving patients with recurrent HBV infection, 12 had stable liver disease after a mean follow-up of 12 months (2 to 27 months) postrecurrent HBV infection. The other 3 patients had hepatic decompensation. Using univariate analysis, the factors associated with recurrent HBV infection were male sex ($P = .03$) and post-LT prophylactic regimen ($P = .001$). Overall, neither HBV replication status (HBeAg/HBV DNA) at listing or at transplantation, nor indication for LT was associated with the rate of recurrent HBV infection post-LT. When the 2 races were analyzed separately, a significantly higher rate of recurrent HBV infection was observed among white patients with replicative infection at listing, 20% versus 3% at 2 years ($P = .03$), but not among Asian patients, 22% versus 14% ($P = .51$). There was no correlation between the rate of recurrent HBV infection and HBV replicative status at transplant in both white and Asian patients. Regardless of race, the rates of recurrent HBV infection were similar among patients transplanted for cirrhosis, fulminant hepatitis B, and HCC ($P = .94$). On Cox regression analysis, the only independent risk factor for recurrent HBV infection was post-LT prophylactic regimen ($P = .03$).

***Mortality Post-LT.*** Eight (11%) Asian and 7 (7%) white patients died post-LT. Actuarial 1-, 2-, and 3-year survival rates were 88%, 88%, and 82% in Asian patients and 94%, 92%, and 92% in white patients, respectively (NS) (Fig. 3). Of the 10 patients who died with no evidence of recurrent HBV infection, the causes of death in the 4 Asian patients were recurrent HCC (1), primary nonfunction of liver graft (1), respiratory failure (1), and liver failure (1); whereas the causes of death in the 6 white patients were liver failure (3), sepsis (2), and cardiomyopathy (1). Factors associated with decreased survival post-LT on univariate analysis were recurrent HBV infection ($P = .02$) and high aspartate aminotransferase at listing ($P = .02$). Because no female patients had recurrent HBV infection, Cox regression analysis was performed only for men. The only independent risk factor associated with decreased survival post-LT in men was recurrent HBV infection ($P = .004$). Cox analysis was not performed for women because there were only 4 deaths among the 30 women transplanted.

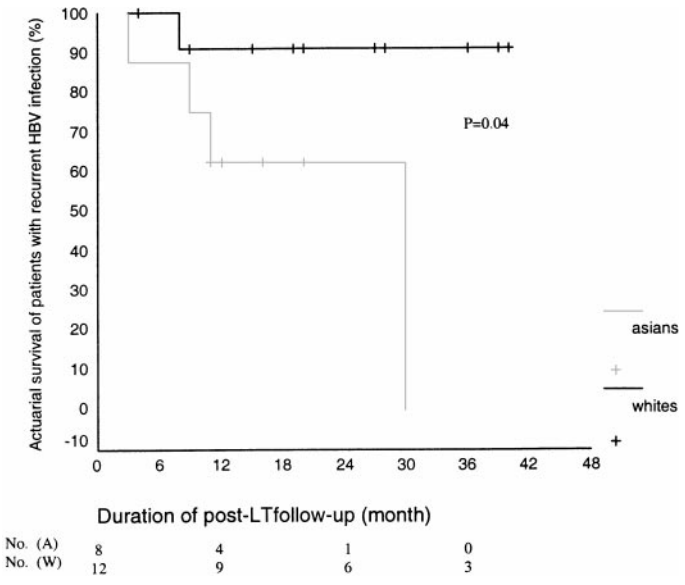


FIG. 2. Actuarial rates of survival in Asian and white patients with recurrent HBV infection.

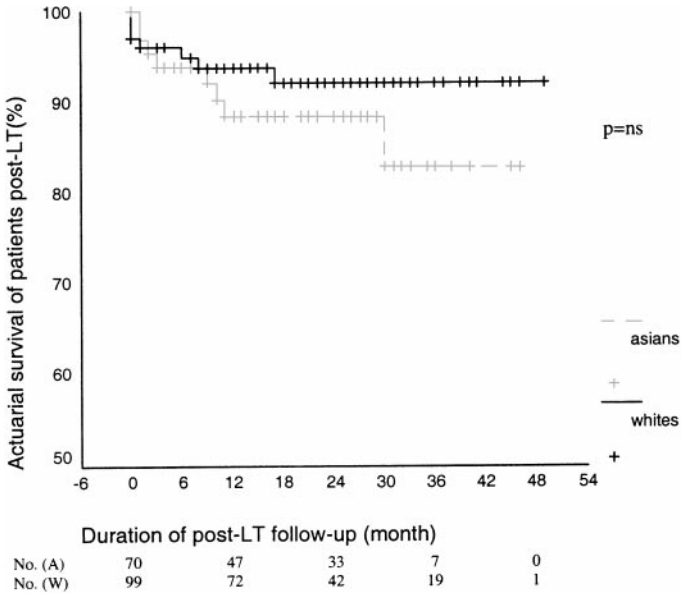


FIG. 3. Actuarial rates of post-LT survival in Asian and white patients.

Of the 28 patients transplanted for HCC (20 Asian and 8 white), 3 (2 Asian and 1 white) had recurrent tumor, 1 Asian patient died from recurrent HCC. Patients transplanted for HCC had similar post-LT survival as patients transplanted for cirrhosis or fulminant hepatitis B ($P = .6$).

### *Nontransplanted Patients*

Fifty-six (44%) Asian and 72 (42%) white patients were not transplanted at the time of survey (Table 5). Seven (12.5%) Asian and 20 (28%) white patients died while awaiting LT (Table 6). Actuarial 1- and 2-year survival rates in patients awaiting LT were 87% and 83% in Asian and 72% and 65% in white patients ($P = .043$) (Fig. 4). Better survival among Asian patients was related to a higher proportion of Asians with HCC as the indication for LT. Patients listed for HCC had more preserved liver function (mCTP score $4.0 \pm 0.5$ vs $5.5 \pm 1.8$, $P = .04$) than patients listed for cirrhosis. None of the patients with HCC died while awaiting LT. When only patients listed for cirrhosis were analyzed, the difference in survival between the 2 groups was not significant ($P = .12$). On Cox regression analysis, the only independent risk factor for decreased survival pre-LT was mCTP score ($P = .002$). Seven (13%) Asian and 11 (15%) white patients were removed from the LT waiting list (NS). Six Asian patients were removed for non–liver-related causes and 1 for extensive HCC. Eleven white patients were removed from the list for non–liver-related causes (6), deterioration in general condition (3), extensive HCC (1), and improvement in liver disease (1). Breakthrough infection was seen in 4 Asian (15%) and 8 white patients (20%). One Asian patient died because of worsening liver failure 3 months after breakthrough infection. The re-

TABLE 5. Characteristics of Nontransplanted Patients

| | Asian | White | P |
|---|---|---|---|
| No. of patients | 56 (44) | 72 (56) | |
| Sex | | | |
| Male | 3 (77) | 62 (86) | .17 |
| Female | 13 (23) | 10 (14) | |
| Age* (years) | 48.3 ± 1.4 | 50.9 ± 1.0 | .13 |
| Indications for listing | | | |
| Cirrhosis | 47 (84) | 70 (97) | .006 |
| Fulminant hepatitis B | 0 (0) | 1 (1.5) | |
| HCC | 9 (16) | 1 (1.5) | |
| At listing | | | |
| Viral serology | | | |
| HBeAg+ | 14/33 (42) | 24/46 (52) | .39 |
| HBV DNA+ | 21/37 (57) | 29 (54) | .77 |
| Anti-HCV+ | 1/47 (2) | 9/52 (17) | .02 |
| Anti-HDV+ | 2/9 (22) | 3/15 (20) | 1.00 |
| Liver biochemistries* | | | |
| ALT (IU/L) | 98 ± 15 | 123 ± 22 | .38 |
| Albumin (g/dL) | 3.2 ± 0.1 | 3.1 ± 0.1 | .24 |
| Bilirubin (mg/dL) | 3.9 ± 0.8 | 3.5 ± 0.6 | .69 |
| PT (sec) | 16.1 ± 0.6 | 15.7 ± 0.9 | .79 |
| mCTP score | 5.4 ± 0.3 | 5.5 ± 0.2 | .74 |
| At last visit | | | |
| Viral serology | | | |
| HBeAg+ | 3/7 (43) | 8/15 (53) | .65 |
| HBV DNA+ | 6/15 (40) | 5/25 (20) | .17 |
| Liver biochemistries* | | | |
| ALT (IU/L) | 58 ± 11 | 65 ± 7 | .57 |
| Albumin (g/L) | 3.6 ± 0.1 | 3.2 ± 0.1 | .02 |
| Bilirubin (mg/dL) | 1.7 ± 0.2 | 2.4 ± 0.5 | .21 |
| PT (sec) | 15.3 ± 0.8 | 15.4 ± 0.6 | .95 |
| mCTP score | 5.3 ± 0.4 | 5.7 ± 0.3 | .47 |

NOTE. Data are expressed as no. (%).
*Mean ± SEM.

maining 11 patients were alive after a mean follow-up of 7 months post-breakthrough infection (0 to 26 months).

### *Impact of HCV and HDV Coinfection*

A significantly lower percent of Asian patients had HCV or HDV coinfection. However, there was no correlation between recurrent HBV infection, pre- and post-LT survival, and HCV or HDV coinfection. Recurrent HBV infection occurred in 2 of 15 (13%) patients with and in 17 of 124 (13%) patients without HCV coinfection (NS). Actuarial 1- and 3-year survival rates post-LT were 92% and 84%, and 92% and 88% for patients with and without HCV coinfection, respectively (NS).

TABLE 6. Outcome of Nontransplanted Patients

| | Asian | White | P |
|---|---|---|---|
| No. of patients | 56 (44) | 72 (42) | |
| Antiviral therapy pre-LT | 27/56 (48) | 41/84 (49) | .33 |
| Duration of follow-up* (mo) | 12.8 ± 1.4 | 10.5 ± 1.0 | .20 |
| Breakthrough HBV infection prior to LT | 4/27 (15) | 8/41 (20) | .62 |
| Mortality while awaiting LT | | | |
| All causes | 7 (13) | 20 (28) | .04 |
| Liver related | 7 (13) | 16 (22) | .12 |
| Removal from transplant waiting list | | | |
| All causes | 7 (13) | 11 (15) | .80 |
| Liver related | 1 (2) | 5 (7) | .40 |

NOTE. Data are expressed as no. (%).
*Mean ± SEM.

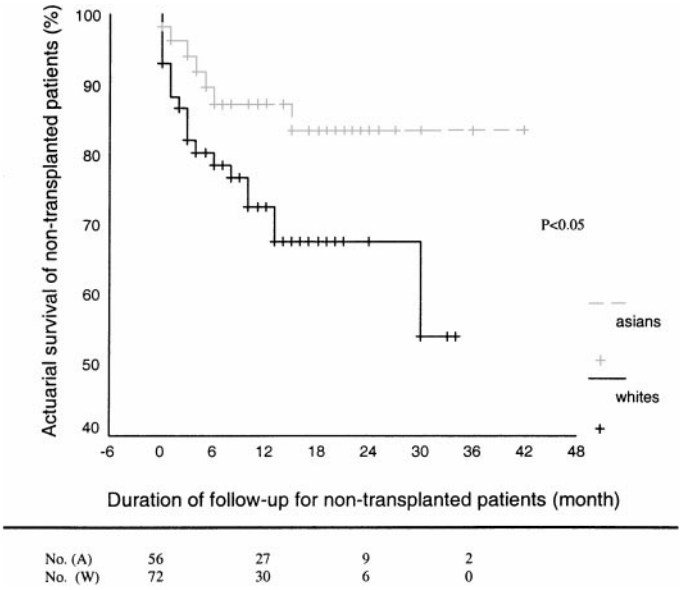


FIG. 4. Actuarial rates of survival in nontransplanted Asian and white patients.

For nontransplanted patients, actuarial 1- and 2-year survival were 70% regardless of the HCV status. Of the 63 transplanted patients with known HDV status, recurrent HBV infection occurred in 1 of 10 (10%) patients with and 10 of 53 (19%) patients without HDV coinfection (NS). Actuarial 1- and 3-year survival rates post-LT were 100% and 100% for patients with and 86% and 86% for patients without HDV coinfection (NS). The impact of HDV coinfection on pre-LT survival was not analyzed as HDV status was available in 25 (20%) patients only.

## DISCUSSION

In this large study involving 297 patients, Asian and white patients with HBV infection listed for LT had similar outcomes. Although our data were based on retrospective surveys with inherent limitations caused by incomplete data collection and heterogeneity in patient management, this is the largest study on LT for hepatitis B in North America. Our study included transplant centers distributed across the United States and Canada thus providing a good representation of hepatitis B patients in North America. We found that Asians constitute a high percent (40%) of patients who require LT for hepatitis B in North America.

The age at infection is in general earlier in Asian than white patients (perinatal vs. adult acquired). A longer duration of HBV infection in Asian patients may have contributed to the higher rate of HCC at listing. Contrary to the study of Ho et al.,[14] we found that the severity of liver disease at the time of listing and at transplantation was similar in Asian and white patients. This may be related to the heightened awareness of hepatitis B and improvement in access to LT in the Asian community in the last decade.

In contrast to previous reports,[12-14] our study showed that Asian patients who had LT for hepatitis B had similar 1- and 3-year survival rates post-LT to white patients. The basis for the difference in outcome between our study and earlier studies may be related to the lower rate of recurrent HBV infection as a result of the use of effective prophylactic therapies. In our

study, the only independent risk factor for mortality post-LT was recurrent HBV infection. Unlike the study of Jurim et al.,[13] we found that Asians and Whites had identical rates of recurrent HBV infection post-LT. Our findings may be related to the fact that HBV replication markers were detected in similar proportions of Asian and white patients at listing and at transplantation. In addition, the use of antiviral therapy pre-LT and prophylactic therapy post-LT were comparable in the two groups. We found that post-LT prophylactic therapy was the only independent factor associated with recurrent HBV infection ($P = .03$) and that Asian and white patients receiving the same prophylactic therapy had similar rates of recurrent HBV infection. Our study confirmed an association between the rate of recurrent HBV infection post-LT and HBV replicative status at listing among white patients. The lack of correlation between recurrent HBV infection and HBV replicative status at transplantation may be related to the high proportion (>40%) of patients with missing data and the alteration of replicative status by pre-LT lamivudine therapy. The explanation for the lack of association between recurrent HBV infection post-LT and HBV replicative status at listing among Asians is not obvious. Both groups had similar proportions of patients with missing data on HBeAg or serum HBV DNA, and received similar prophylactic therapies post-LT.

Despite a similar rate of recurrent HBV infection, Asian patients with recurrent HBV infection had higher mortality than white patients. This difference was not related to differences in the use of salvage therapy because only 1 white patient received adefovir treatment. Because of the small number of patients who died from recurrent HBV infection, we were not able to ascertain the significance of the difference in mortality between Asian and white patients or to determine if factors other than race may have contributed to the higher mortality in the Asian patients. It is possible that differences in prevalence of HBV genotypes, precore or core promoter variants between Asian and white patients may contribute to the lack of correlation between recurrent HBV infection post-LT and HBeAg/serum HBV DNA status at listing and the higher mortality rate among Asian patients with recurrent HBV infection post-LT.

An unexpected finding in this study was that Asian patients awaiting LT for hepatitis B had significantly better survival than white patients. This apparent difference in survival can be explained by the higher percentage of Asian patients with HCC. As a group, patients listed for HCC had more preserved hepatic function compared with patients listed for liver failure. None of the patients with HCC but 22% of patients with end-stage cirrhosis died while waiting for LT. In this study, the higher proportion of Asian patients with HCC did not contribute to higher mortality post-LT. This may be related to the short duration of post-LT follow-up (mean $19.8 \pm 1.5$ and $21.0 \pm 1.3$ months in Asian and white patients, respectively) and the stringent selection of patients with early HCC for LT.

A major difference between Asian and white patients listed for LT for hepatitis B was a lower prevalence of HCV and HDV coinfection among the Asian patients. This is most likely related to the different modes of HBV infection in Asian and white patients. Asian patients were most likely to be infected perinatally from carrier mothers whereas most white patients likely acquired HBV infection in adult life through injection drug use or sexual exposure. The latter routes are also risk factors for HCV and HDV infection. HCV and HDV coinfection have been reported to be associated with lower rates of recurrent HBV infection post-LT possibly through suppression of HBV replication.[2,15] We did not find an association between recurrent HBV infection and HCV coinfection and a weak correlation with HDV coinfection. The lack of association may be related to the low rate of recurrent HBV infection and the high percentage of patients with missing data for HDV. Coinfection with HCV may result in higher mortality pre- and post-LT caused by more severe hepatic decompensation pre-LT and recurrent hepatitis C post-LT. In this study, HCV coinfection had no effect on the survival of patients pre- or post-LT. However, we acknowledge that the duration of post-LT follow-up was short and the impact of recurrent hepatitis C on survival may not be apparent at this early stage.

In summary, in this study involving a large number of patients with HBV infection listed for LT in North America, we found that the outcome of Asian and white patients was not different. Asian patients had similar rates of recurrent HBV infection post-LT and comparable rates of pre- and post-LT survival with white patients. Asian patients did not have more advanced liver failure but were more likely to have HCC at listing. Coinfection with HCV or HDV was less common in Asian patients but did not have an impact on outcome. In light of our findings, we recommend that Asian patients with hepatitis B requiring LT be managed similarly to white patients. More studies are needed to confirm if Asian patients with recurrent HBV infection post-LT have higher mortality rates than white patients and to identify the factors that account for the difference.

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## APPENDIX

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