# Acute Hepatitis B in an Urban Tertiary Care Hospital in the United States

## *A Cohort Evaluation*

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**Background:** The incidence of acute hepatitis B virus (HBV) infection in the United States is declining, and precise epidemiology for newly acquired infection remains obscure.

**Goals:** We sought to clarify the clinical presentation and management of acute symptomatic HBV infection at a hepatology referral center.

**Study:** We prospectively evaluated the demographic, epidemiological, clinical, and treatment data of 32 patients with acute symptomatic HBV who were referred to a single urban tertiary care hospital in the United States.

**Results:** Slightly more than half of the patients were male (53%) or belonged to the black race (53%) and slightly fewer than half of the patients (47%) were unemployed. The median patient age was 41.9 years, and 20 (63%) patients were unmarried. The most common HBV risk factor was a new sexual partner over the previous months (34%). Fifteen percent of the patients reported no known risk factors. Four (13%) patients were diabetic. Presenting symptoms included jaundice (75%), abdominal pain (63%), and marked fatigue (59%). The mean peak for aspartate aminotransferase/alanine aminotransferase was 1822/2109 IU/L, for total bilirubin was 12.6 mg/dL, and for International Normalized Ratio was 1.53. Eight patients (25%) were started on oral nucleot(s)ide therapy. One diabetic patient underwent liver transplantation.

**Conclusions:** In a sample of patients from a US urban tertiary hepatology center, common epidemiological features of acute symptomatic hepatitis B were being middle aged and unmarried and having acquired the infection through a new sexual contact. Antiviral therapy was sometimes but not commonly started. These data reinforce the need for HBV vaccination of individuals at risk, including those not traditionally targeted.

**Key Words:** acute hepatitis B, nosocomial infection, hepatitis B, treatment, epidemiology

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Hepatitis B virus (HBV) infection is a global public health problem affecting more than 350 million people worldwide, and an estimated 1 million deaths occur annually from HBV-related liver disease.[1] Estimates from the Centers for Disease Control and Prevention (CDC) suggest that the incidence of acute HBV infection in the United States declined from 8.5 cases per 100,000 in 1990 to 1.5 per 100,000 in 2007.[2] Probable causes for the decline are widespread vaccination efforts and adoption of safer sex practices after the start of the AIDS epidemic. The CDC estimate is limited by several factors, including inaccuracies of voluntary reporting, potential underreporting, incomplete risk factor data, and absence of treatment data.[2] Thus, the current epidemiology of this condition remains incomplete.

Approximately 70% of the patients with acute hepatitis B have subclinical or anicteric hepatitis, whereas 30% develop icteric hepatitis.[3] The disease may be more severe in patients coinfected with other hepatitis viruses or with underlying liver disease.[3] In addition, it is unclear whether oral hepatitis B antiviral therapy is now being utilized in the acute setting. We sought to clarify the clinical presentation and management of acute symptomatic HBV infection by analyzing a population of patients who presented to a large urban hepatology referral center.

## MATERIALS AND METHODS

The present study is a secondary analysis of a prospective study on the prevalence of HBV mutational variants in the case of acute HBV infection.[4] We evaluated a cohort that consisted of all patients who presented with acute symptomatic hepatitis B to the Henry Ford Health System in Detroit, MI, from January 2008 to September 2010. We defined acute symptomatic hepatitis B infection as having a discrete onset of symptoms and jaundice or elevated serum aminotransferase levels along with IgM anti-HBc/HBsAg positivity and compatible clinical history.[5]

We assessed the demographic, epidemiological, and clinical data by chart review. Demographic data included age, gender, and race. Epidemiological data included occupation, risk factors for acquisition of hepatitis B, alcohol use, marital status, and drug use, both prescription and illicit. Clinical data included biochemical variables, symptomatology, length of hospital stay, and whether or not antiviral treatment was initiated.

The study was approved by the Institutional Review Board of Henry Ford Hospital.

## RESULTS

### Demographics

Between January 2008 and September 2010, 32 patients fulfilled the definition of being infected with acute

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symptomatic hepatitis B at our institution and were thus included in the study. The patients' ages ranged from 22 to 79 years (median, 41.9 y; Table 1). Eleven (34%) patients were aged between 41 and 50 years. Seventeen (53%) patients were men, 17 (53%) were black, 11 (34%) were white, and 4 (13%) were Hispanic.

## Social History

Heavy drinking, defined as consuming >2 drinks/d (a standard drink is one 12-ounce bottle of beer or wine cooler, one 5-ounce glass of wine, or 1.5 ounces of 80-proof distilled spirits), was reported by 13 (41%) patients. Seven (22%) patients reported moderate/occasional drinking, and 12 (38%) had no drinking history. Five (16%) patients reported a history of intravenous drug abuse, 4 (13%) reported a remote history of illicit drug use, and 23 (72%) reported no illicit drug use.

For marital status, 20 (63%) patients were single, 8 (25%) were married, and 4 (13%) were divorced. Fifteen (47%) patients were unemployed. Among the 17 patients who were employed, 5 reported working as truck or bus drivers or curriers, 3 worked as cooks, and 9 had other occupations.

## Medical History

Eleven (34%) patients did not have any significant past medical history. Four (13%) had diabetes and 7 (22%) had hypertension. One (3%) patient had HIV and 4 (13%) had hepatitis C.

The 4 patients with diabetes were older than the overall cohort (age, 47 to 79 y), and of them all but one, who was 79 years old, reported a recent new sexual encounter as being the potential source of the acute hepatitis B infection. The 79-year-old man reported having a household member infected with hepatitis B as his potential source of acute infection. Only 1 patient in our series developed acute liver failure and underwent liver transplantation; this patient had underlying diabetes.

**TABLE 1.** Baseline Characteristics

| Characteristics | Study Population (N = 32) |
|---|---|
| Age [median (range)] (y) | 41.9 (22-79) |
| Age [n (%)] (y) | |
| 21-30 | 7 (22) |
| 31-40 | 8 (25) |
| 41-50 | 11 (34) |
| 51-60 | 4 (13) |
| > 60 | 2 (6) |
| Gender [n (%)] | |
| Male | 17 (53) |
| Female | 15 (47) |
| Race [n (%)] | |
| Black | 17 (53) |
| White | 11 (34) |
| Hispanic | 4 (13) |
| Marital status [n (%)] | |
| Single | 20 (63) |
| Married | 8 (25) |
| Divorced | 4 (13) |
| Occupation [n (%)] | |
| Unemployed | 15 (47) |
| Truck or bus driver | 5 (16) |
| Cook | 3 (9) |
| Others | 9 (28) |
| Alcohol consumption [n (%)] | |
| Heavy | 13 (41) |
| Moderate | 7 (22) |
| None | 12 (38) |

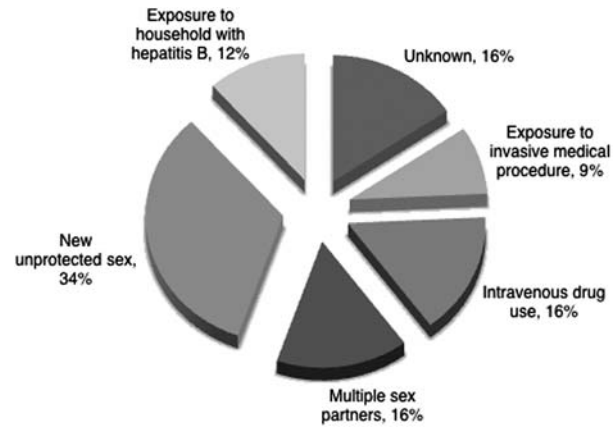


**FIGURE 1.** Reported risk factors for hepatitis B transmission.

## Hepatitis Risk Factors

Eleven (34%) patients reported an unprotected sexual encounter with a new partner within the 6 months preceding their infection (Fig. 1). Five (16%) reported having multiple sexual partners and high-risk sexual behaviors. Five (16%) reported intravenous drug use. Three (9%) had a potential nosocomial exposure, including 1 with a recent surgical procedure, 1 with a recent dental procedure, and 1 nursing student with an accidental needle stick. All 3 reported that the exposures occurred within 4 to 6 weeks before their acute hepatitis infection. Four (12%) had exposure to a household contact with hepatitis B. We could not identify a risk factor in 5 (16%) patients.

## Symptomatology

The most common presenting symptom was jaundice, reported in 24 (75%) patients. Abdominal discomfort was reported in 20 (63%) patients. Nineteen (59%) patients reported fatigue and 11 (34%) reported severe nausea and vomiting.

## Clinical/Laboratory Data

Among the patients, the mean hospital stay was 4.54 days (Table 2). For total bilirubin, the mean peak was 12.6 mg/dL and the highest reported value was 33.3 mg/dL. For alanine aminotransferase (ALT), the mean peak was 2109 IU/L and the highest peak was 5223 IU/L. For aspartate aminotransferase (AST), the mean peak was 1822 IU/L and the highest reported value was 3816 IU/L. The mean peak alkaline phosphatase level was 257 IU/L and the highest reported value was 758 IU/L. The peak mean International Normalized Ratio (INR) was 1.53 and the highest reported value was 3.2.

## Outcome

Only 8 (25%) patients were started on oral nucleot-(s)ide therapy (4 on lamivudine and 4 on tenofovir). The decision to start therapy was made by the admitting hepatology team on the basis of preference and clinical judgment. Five of the treated patients were female (63%), and 4

**TABLE 2.** Biochemical and Clinical Variables

| | Study Population (N = 32) | |
|---|---|---|
| **Variables** | **Mean (SD)** | **Median (Range)** |
| Hospital stay (d) | 4.54 (1.72) | 4 (2-9) |
| Peak total bilirubin (mg/dL) | 12.6 (7.6) | 13 (1.3-33.3) |
| Peak AST (IU/L) | 1822 (787.3) | 1621 (701-3816) |
| Peak ALT (IU/L) | 2109 (1125.1) | 1606 (761-5223) |
| Peak ALP (IU/L) | 257 (132.1) | 242 (100-758) |
| Peak INR | 1.53 (0.51) | 1.18 (0.98-3.2) |

ALP indicates alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, International Normalized Ratio.

were black (50%). As judged on the basis of biochemical indicators, the 8 treated patients seemed to have more severe disease compared with untreated patients (n = 24): mean peak INR was 2.53 and 1.53, mean peak ALT was 2343 and 2109 IU/L, mean peak AST was 2675 and 1822 IU/L, and mean peak bilirubin was 17.2 and 12.6 mg/dL for treated and untreated patients, respectively. Only one of the treated patients had acute liver failure requiring liver transplantation. A transplant evaluation was started on another patient but subsequently canceled because of complete resolution.

A total of 23 (72%) patients had documented follow-up. One diabetic patient developed acute liver failure and underwent successful liver transplantation. The remaining patients had complete normalization of liver biochemistries within 120 days, with resolution within 20 days in 4 (13%) cases. Documentation of hepatitis B surface antigen loss was available in 11 (34%) cases, with seroconversion to anti-HBs as early as 20 days in 1 case and as late as 8 months in another. The remaining cases had no seroconversion follow-up data or were lost to follow-up. To our knowledge, there were no readmissions. Two patients developed subsequent chronic hepatitis B: 1 presented with acute HBV/HIV coinfection, and the other had alcoholic liver disease.

## DISCUSSION

We prospectively observed severe acute hepatitis B cases referred to our tertiary liver center, which is one of 2 liver transplant centers in the state of Michigan. Between January 2008 and September 2010, we observed 32 cases of acute icteric hepatitis B. The majority of these cases (75%) represented our local population from Wayne County, which is predominantly urban and in which blacks represent 40.5% of the population.[6] However, the cases also included a referral population from southeastern Michigan, which is predominantly nonurban and white.

At our institution, the epidemiology of acute symptomatic hepatitis B is mainly represented by adults who are middle aged and unmarried. Slightly more than half of the patients were black, and half reported a sexual risk factor as the probable cause of acquiring the disease. Our results are consistent with a 2009 report from the CDC, which indicated that sexual transmission and percutaneous drug injection were the most common modes of transmission of hepatitis B acute icteric presentation.[2] The 32 patients in our cohort were among 264 cases of acute hepatitis B that were reported to the CDC for the years 2008 through 2010 for the Detroit area of southeast Michigan including Wayne, Macomb, and Oakland counties (Dr Scott Holmberg, CDC, personal written communication). Among the 264 patients in the tricounty area, 138 (52%) were male, which is similar to the proportion of male patients in our cohort (53%), and 91 (34%) were black.

The present study included a comprehensive clinical data set. In this study population, the predominant symptoms necessitating hospitalization were jaundice and abdominal pain. The pattern of liver injury was mainly hepatic, with a rapid rise of aminotransferases and significant biochemical and clinical resolution by the time of hospital discharge. Bilirubin elevation was often very high and occasionally exceedingly elevated. The demographics and route of viral acquisition confirmed by this study suggest that, in an urban setting, acute hepatitis B remains a lifestyle disease risk among, in particular, unmarried middle-aged adults.

All of the cases reported herein required admission to the hospital. One of the cases developed acute liver failure requiring liver transplantation. In general, hepatic failure occurs only in approximately 0.1% to 0.5% of patients with acute hepatitis B infection cases and likely results from a vigorous immunologic response to infected hepatocytes.[7] In this study, the patient who developed acute liver failure had diabetes, as did 3 other patients, constituting a total of 13% of the patient population. This observation reinforces the recent recommendation by the Advisory Committee on Immunization Practices that hepatitis B vaccination should be administered to unvaccinated adults with diabetes mellitus aged 19 through 59 years (recommendation category A).[8] Persons aged 23 through 59 years with diabetes have 2.1 (95% confidence interval, 1.6-2.8) times the odds of developing acute hepatitis B as those without diabetes.[9] Data from 2009 to 2010 have indicated that acute HBV-infected patients with diagnosed diabetes have a higher case-fatality rate compared with those without diabetes, although the difference is not statistically significant (5% vs. 2%, $P = 0.127$).[9] Acute HBV infection progresses to chronic infection in approximately 5% of otherwise healthy adults.[10]

Eight patients (25%) were started on oral nucleot(s)ide therapy, and the decision to treat was made by the rounding hepatology service team. The treated group seemed to have a more severe clinical course, with higher AST, ALT, bilirubin, and INR values. Two patients had disease severe enough to undergo a transplant evaluation, and one of them received a transplant. There remains controversy on the wisdom of treating patients with acute hepatitis B infection. Antiviral therapy is generally not necessary in patients with symptomatic acute hepatitis B because up to 95% of immunocompetent adults with acute hepatitis B recover spontaneously. The current American Association for the Study of Liver Diseases practice guidelines[11] provide a "Category 3" recommendation that treatment is only indicated for patients with acute hepatitis B and those with protracted, severe acute hepatitis B. Small and not actively controlled case series, with or without comparisons to historical untreated controls, have suggested that oral lamivudine improves survival in patients with severe or acute hepatitis B.[12–16]

In this study, 3 (9%) cases had potential nosocomial exposure to hepatitis B. A recent report from the CDC confirms the observation that a variety of health care settings may inadvertently serve as the route of HBV

acquisition.[17] Mechanisms of transmission may include patient-to-patient transmission caused by failure of health care personnel to adhere to fundamental principles of infection control and aseptic technique (eg, reuse of syringes or lancing devices) and lapses in adherence to standard precautions, safe injection practices, and phlebotomy practices.[18] Surgeon-to-patient HBV transmission may also occur despite apparent compliance with recommended infection-control practices.[19]

Our study lacks long-term follow-up to document the time to complete resolution of acute infection; this limitation is derived both from patient noncompliance and subsequent return to the primary referring team because of rapid inpatient clinical improvement. Nevertheless, we are not aware of any patients who were readmitted or who subsequently developed chronic hepatitis B infection, other than 2 patients, 1 with HBV/HIV coinfection and the other with alcoholic liver disease.

Some of our data were obtained by chart review, which limited the collection of some demographic information, including sexual orientation. Previous CDC data have suggested that 10.5% of cases of acute hepatitis B reported male homosexual activity,[2] but we were unable to corroborate this estimate. Finally, the data may be subject to selection bias for more severe disease because the patients in this study either presented to or were referred to a liver transplant center.

The data presented in the current analysis reflect a more detailed clinical and epidemiological observation than that which has been previously reported in the literature by surveillance centers[2]; such data are limited mainly by underreporting and voluntary reporting, incomplete risk factor information, and the absence of treatment data. Additional limitations of individual state databases include misclassification of cases as acute versus chronic and underreporting of cases, often because of a lack of resources to follow-up reported laboratory data.

The present descriptive cohort study confirms in a real-world setting the ongoing transmission of hepatitis B among American adults. State and national surveillance systems to detect and report acute cases could benefit from additional details. Finally, our data reinforce the need for HBV vaccination of individuals at risk, including those not traditionally targeted.

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