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HBV/HIV co-infection is associated with poorer outcomes in hospitalized patients with HBV or HIV

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Abstract

We examined the impact of HBV/HIV co-infection on outcomes in hospitalized patients compared to those with HBV or HIV mono-infection. Using the 2011 US Nationwide Inpatient Sample, we identified patients who had been hospitalized with HBV or HIV mono-infection or HBV/HIV co-infection using ICD-9-CM codes. We compared liver-related admissions between the three groups. Multivariable logistic regression was performed to identify independent predictors of in-hospital mortality, length of stay and total charges. A total of 72,584 discharges with HBV mono-infection, 133,880 discharges with HIV mono-infection and 8,156 discharges with HBV/HIV co-infection were included. HBV/HIV co-infection was associated with higher mortality compared to HBV mono-infection (OR 1.67, 95% CI 1.30-2.15) but not when compared to HIV mono-infection (OR 1.22, 95% CI 0.96-1.54). However, the presence of HBV along with cirrhosis or complications of portal hypertension was associated with 3-times greater in-hospital mortality in patients with HIV compared to those without these complications (OR 3.00, 95% CI 1.80-5.02). Length of stay and total hospitalization charges were greater in the HBV/HIV co-infected group compared to the HBV mono-infection group (+1.53 days, $p < 0.001$; \$17595, $p < 0.001$) and the HIV mono-infection

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group (+0.62 days, $p=0.034$; \$8840, $p=0.005$). In conclusion, HBV/HIV co-infection is a risk factor for in-hospital mortality, particularly in liver related admissions, compared to HBV mono-infection. Overall health care utilization from HBV/HIV co-infection is also higher than for either infection alone and higher than the national average for all hospitalizations, thus emphasizing the health care burden from these illnesses.

Keywords

Hepatitis B; mortality; outcomes; hospitalization; HBV-HIV coinfection

INTRODUCTION

There are an estimated 35 million people with HIV and 300 million carriers of hepatitis B virus (HBV) globally[1,2]. Due to a number of shared risk factors, the prevalence of HBV co-infection among HIV-positive individuals varies from about 6% in United States and European cohorts to 10% in African, South American and Asian cohorts[3–10].

Co-infection with HBV and HIV carries important implications long-term for natural history of disease. Several prospective cohorts have shown that HBV/HIV co-infection increases liver-related mortality compared to HIV infection alone[4,5,8,10]. In addition, HIV infection alters the natural history of HBV infection. Among non-HIV infected patients, a majority of those with acute hepatitis B will not progress to chronic infection. In contrast, HIV-positive patients are up to six times more likely to progress to chronic HBV after an acute infection[11]. HBV/HIV co-infected patients also have higher levels of HBV DNA when compared to those with HBV mono-infection[12–14], and progress to cirrhosis faster than those with HBV alone[13].

Despite the considerable literature on overall HBV/HIV co-infection outcomes, there have been few studies about in-hospital outcomes in such patients. Early single-institution studies suggested that chronic viral liver disease was becoming an important cause of hospital admission and mortality in the era of highly active antiretroviral therapy (HAART)[15,16]. HBV/HIV co-infection is associated with an increased risk of all-cause and liver-related hospitalizations[17]. Prior studies have demonstrated that hepatitis C (HCV)/HIV co-infection increases risk of in-hospital liver-related death, especially among patients with cirrhosis and portal hypertension[18]. A study by Puoti et al. previously reported that hepatitis B surface antigen seropositivity was an independent risk factor for in-hospital liver-related death in a small cohort of HIV-positive inpatients. However no studies have examined the outcomes of HBV/HIV co-infection among hospitalized patients. Hospitalized patients often represent those with most advanced disease or related complications and are a group that is particularly vulnerable to poor outcomes in addition to high healthcare utilization. Identifying those at particularly high risk for mortality and morbidity will allow for an exploration of interventions to prevent complications and improve in-hospital outcomes.

Consequently, we performed this study with the following aims: (i) to compare the demographic and clinical characteristics of in-patients with HBV or HIV mono-infection to

those with HBV/HIV co-infection; and (ii) to examine the effect of HBV/HIV co-infection on in-hospital outcomes (mortality, length of stay) in patients with HBV or HIV.

METHODS

Data Source

We used data from the Nationwide Inpatient Sample (NIS) for the most recently available year (2011). This database, maintained by the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality (AHRQ), is the largest all-payer inpatient database in the United States, with data from approximately 8 million hospitalizations, sampled to approximate a 20-percent stratified sample of non-federal, U.S. hospitals[19]. Each discharge is a unique entry and is coded with one primary discharge diagnosis and up to 14 secondary diagnoses as well as 15 associated procedures, coded using the International Classification of Diseases, Clinical Modification, ninth edition (ICD9-CM Codes).

Study Population

Our study population was divided into three groups—1) HBV monoinfection, 2) HIV monoinfection and 3) HBV-HIV coinfection related hospitalizations. The HBV monoinfection group consisted of patients with ICD-9-CM discharge codes for chronic HBV (070.20, 070.21, 070.22, 070.23, 070.30, 070.31, 070.32, 070.33, V026.1) but no associated codes for HIV. Patients with HIV (042, 079.53, and V08) infection alone and no codes for HBV formed the second group of patients (HIV monoinfection group). The HBV/HIV co-infected cohort consisted of patients with discharge codes for both HBV and HIV.

Study variables and outcomes

Age, sex, primary insurance status and race were obtained from the NIS data set. Co-morbidity burden was measured using the Elixhauser index[20], a comprehensive set of 30 co-morbidity measures that has been validated and is a widely used measure of co-morbidity from administrative databases. As liver-related complications were included separately in our analysis, we excluded those variables from calculation of total Elixhauser score. Hospital characteristics were obtained from the NIS hospital data file.

Liver co-morbidities of interest included presence of concurrent hepatitis C virus (HCV) infection, cirrhosis or complications thereof [i.e. portal hypertension, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, variceal bleeding, ascites or hepatorenal syndrome] (Table 2). Of note, due to the nature of ICD-9 coding for HDV where it is usually coded together with HBV, we were not able to assess the true prevalence of hepatitis delta in our cohort. In addition, we examined the frequency of various systemic complications associated with the hospitalization as shown in Table 1. Hospitalizations were considered to be liver-related if the primary or secondary discharge diagnoses for that hospitalization included one of the liver-related co-morbidity measures (Table 2, Supplementary Table 5).

We also examined the presence of various infections during hospitalization including opportunistic [e.g. *Pneumocystis jirovecii* pneumonia (PJP), cytomegalovirus (CMV)

infection,etc] as well as non-opportunistic infections such as pneumonia and urinary tract infection[18,21]. Hospitalizations were considered primary infectious hospitalizations if the primary discharge diagnosis for the hospitalization included one of the ICD-9-CM codes for infectious or parasitic diseases (ICD-9-CM 001–139, excluding codes for primary Hepatitis B infection).

Our primary outcome of interest was in-hospital mortality, which was obtained from the NIS. Cause of death is not provided within the database. We also examined overall length of stay (LOS) and total hospitalization charges. Due to each hospitalization being assigned a unique identifier, it is not possible to identify repeat hospitalizations for the same patients from the NIS.

Statistical analysis

Data were analyzed with the appropriate survey estimation (`-svy-`) commands using STATA MP/13.1 (StataCorp, College Station, TX, USA). The raw numbers from the NIS were converted into national estimates after applying the corresponding strata weights provided. Continuous variables were expressed as means with standard deviations while categorical variables were summarized with proportions. The t-test was used to compare continuous variables while the chi-square test was used to perform between-group comparisons for categorical variables. Univariable and multivariable logistic regression was performed to identify independent factors associated with in-hospital mortality. A P-value <0.1 was used for inclusion of variables in the final multivariable model where a P-value <0.05 was considered to indicate statistical significance. Similarly, multivariable linear regression was used to analyze continuous outcomes of LOS and hospitalization charges. This study was exempt from IRB approval as the data source is a publically available de-identified dataset.

RESULTS

Study population

There were 72,584 discharges with HBV mono-infection, 133,880 discharges with HIV mono-infection and 8,156 discharges with HBV/HIV co-infection included in our study. There were several demographic differences between the three groups (Table 1). Patients with HBV mono-infection tended to be older than those with HIV mono-infection or HBV/HIV co-infection (age 51-65: HBV mono-infection 42%, HIV mono-infection 34% and HBV/HIV co-infection 31%, $P<0.001$). Males were over-represented in the HBV/HIV co-infection group (77%) compared to the mono-infected groups (HBV mono-infection 57%, HIV mono-infection 67%). Patients with HBV mono-infection were more likely to be white (42%) than those with HIV mono-infection (26%) or HBV/HIV co-infection (27%). Patients on Medicaid comprised the largest insurance subgroup for HIV mono-infected (41%) and HBV/HIV (44%) co-infected groups. Socioeconomic status as determined by zip code level income quartile was highest in the HBV mono-infected cohort (19% in quartile 4) compared to the HIV mono-infected (11% in quartile 4) and HBV/HIV co-infected (11% in quartile 4) cohorts ($P<0.001$). The comorbidity burden was lowest in the HBV mono-infected cohort and highest in the HBV/HIV co-infected cohort.

The distribution of systemic complications showed a greater frequency of acute renal failure (19% vs 13%), hypovolemia (11% vs 6%), acute respiratory failure (9% vs 5%), acidosis (8% vs 5%), malnutrition (9% vs 5%) and cachexia (8% vs 1%) in the HBV/HIV co-infected cohort compared to the HBV mono-infected cohort (Table 1). Differences between HIV mono-infection and HBV/HIV co-infection were not as pronounced. For example, frequency of acute renal failure was 13.2% in HBV mono-infection, 15.9% in HIV mono-infection and 19.1% in HBV/HIV co-infection ($P<0.001$).

Comparison of the HBV/HIV co-infected group to those with HBV virus mono-infection

Hospitalization patterns—There were significant differences in the clinical presentation in hospitalized patients with isolated HBV compared to co-infected patients. Liver-related admissions formed a larger proportion of hospitalizations among the HBV mono-infection cohort (33%) compared to co-infected patients (23%, $P<0.001$) (Table 2). The presence of cirrhosis (20% vs 11%, $P<0.001$) or complications of cirrhosis such as ascites (10% vs 7%, $P<0.001$) were more common in the HBV mono-infection cohort. While co-existing alcoholic liver disease was more common in the HBV mono-infected cohort (8% vs 2%, $P<0.0001$), hepatitis C infection was more common in the HBV/HIV co-infected cohort (32% vs 28%, $P<0.001$), likely reflecting shared risk behaviors.

HBV/HIV co-infection as a risk factor for adverse outcomes—On multivariate logistic regression, HBV/HIV co-infection was associated with significantly higher adjusted in-hospital mortality when compared to patients with HBV mono-infection [adjusted odds ratio (OR) 1.67, 95% CI 1.30-2.15] (Table 3). Interestingly, this increase in risk of mortality was primarily observed in liver-related admissions (OR 1.83, 95% CI 1.27-2.62) and not infectious-related hospitalizations (OR 1.13, 95% CI 0.81-1.57). The overall adjusted LOS (1.53 days, 95% CI 0.93–2.13, $p<0.001$) and total hospitalization charges (\$17595, 95% CI 11120-24069, $p<0.0001$) was higher in the co-infected group compared to the HBV mono-infection group even after adjusting for comorbidity and disease related complications. (Supplementary Tables 1 and 3).

To examine if HIV had different impact on patients with HBV depending on severity of underlying liver disease, we repeated the multivariable analysis stratifying by the presence of cirrhosis or complications suggesting decompensation. Among those with such decompensation, the mortality with HBV-HIV coinfection was 10.7% compared to 7.3% with HBV alone (multivariate OR 1.72, 95% CI 1.11–2.67). In those without cirrhosis or complications or cirrhosis, the mortality was 3.7% compared to 1.9% (multivariate OR 2.09, 95% CI 1.53–2.86). Thus, there is increased mortality in the HBV/HIV co-infection group as compared to the HBV mono-infection group regardless of the severity of liver disease.

Comparison of the HBV/HIV co-infected group to those with HIV mono-infection

Hospitalization patterns—Infectious complications were equally common in patients with HIV (48%) compared to HBV/HIV co-infected patients (47%) ($P=0.40$) (Table 2). Pneumonia was the most common infection in both groups at a frequency of 18% and 20% ($P=0.104$). Skin infections and septicemia were more common in the co-infected group compared to the HIV mono-infection group (8% vs 7%, $P=0.02$ and 13% vs 10%, $P=0.001$

respectively). However, opportunistic infections such as *Pneumocystis pneumonia* (PCP) (7% vs 6%, $P=0.08$) and cryptococcal meningitis (1.2% vs 0.7%, $P=0.06$) were more common in the isolated HIV group compared to the HBV/HIV co-infected group. By contrast, liver-related admissions were twice as common in the HBV/HIV co-infected group compared to the HIV mono-infection group (23% vs. 11%, $P<0.001$). The etiology of these liver related admissions in HBV/HIV co-infected group consisted of Hepatitis C (44.8%), NASH (26.9%), alcoholic liver disease (12.9%) and DILI (1%). In contrast, the etiology of liver related admissions in the HIV mono-infected cohort consisted of NASH (43.6%), Hepatitis C (40.7%), alcoholic liver disease (9.1%) and DILI (0%).

HBV/HIV co-infection as a risk factor for adverse outcomes—On multivariate analysis, adjusting for age, comorbidity, insurance and concurrent complications, we found that HBV/HIV co-infection by itself was not associated with higher in-hospital mortality (OR 1.22, 95% CI 0.96-1.54) than HIV mono-infection alone (Table 4). This was true for both liver-related admissions (OR 1.05, 95% CI 0.73-1.50) and primary infectious admissions (OR 1.08, 95% CI 0.79-1.47). However, the presence of HBV along with cirrhosis or complications of portal hypertension was associated with 3-times greater in-hospital mortality in patients with HIV compared to those without these complications (OR 3.00, 95% CI 1.80-5.02). In addition, length of stay (0.62 days, 95% CI 0.05-1.20, $p=0.034$) and cost of hospitalization (\$8840, 95% CI 2604-15077, $p=0.005$) were increased in patients with HBV/HIV co-infection compared to HIV mono-infection. (Supplementary Tables 2 and 4)

HBV/HIV/HCV Triple Infection

We also assessed whether triple infection—that is, infection with HBV, HIV and HCV—was a risk factor for adverse outcomes during hospitalization. We found that in the HBV/HIV dual infected population, HCV was not a risk factor for increased mortality (OR 1.07, 95% CI 0.65-1.76). In addition, in the HBV/HIV dual infected population, HCV was not a risk factor for increased length of stay (−1.02 days, 95% CI −2.46-0.41, $p=0.162$) or total charges (−\$11926, 95% CI −\$29625-\$5773, $p=0.186$).

Sensitivity analysis

We carried out a sensitivity analysis to ensure that our findings were not driven simply by HCV as a high percentage of our cohort was coinfecting with HCV: 28% of HBV mono-infected, 19.5% of HIV mono-infected and 32.3% of HBV/HIV coinfecting (Table 2). We thus carried out the multivariable logistic regressions above excluding HCV from the cohort. We found that HBV/HIV coinfection continued to be associated with increased mortality when compared to HBV mono-infection (OR 1.60, 95% CI 1.17-2.19). Similarly HBV/HIV coinfection was not associated with increased mortality when compared to HIV mono-infection (OR 1.11, 95% CI 0.83-1.49).

Nationwide rates of hospitalization in the three cohorts

Using previously published population estimates of the prevalence of HBV[22], HIV [23] and HBV/HIV co-infection[5,6,10], we calculated crude hospitalization rates in the three groups. Among an estimated 72,000 individuals in the US with HBV/HIV co-infection, our

hospitalization estimate of 8,156 suggests a hospitalization rate of 11.3% which is higher than the 9.9% estimated for HBV mono-infection (among 730,000 US residents with HBV and our hospitalization estimate of 72,584). The rate of hospitalization in patients with co-infection (11.3%) was significantly higher than patients with HBV mono-infection (9.9%, $P<0.0001$) but not higher than patients with HIV mono-infection (11.2%, $P=0.80$) (Table 5).

DISCUSSION

An estimated 700,000 to 2.2 million people are chronically infected with hepatitis B (HBV) in the United States [24]. While recent therapeutic advances for Hepatitis C are estimated to significantly reduce the burden from this disease, the burden of HBV in the United States is expected to grow because of immigration into the US from highly endemic countries. Furthermore, the rate of hospitalization for HBV-related diagnoses increased from 5 to 20 per 100,000 person years over a span of a decade [25]. Hospitalizations for liver disease are associated with significant morbidity and mortality, and account for a large proportion of healthcare costs. Thus it is important to study those who are at a particularly high risk for poor outcomes. One such group is the HIV/HBV coinfecting population. Recent studies in cohorts of people living with HIV have shown that hospitalization rates are higher among patients with HBV and/or HCV coinfection [17].

Infection with HIV alters the natural history of HBV. Published literature has established that HBV/HIV co-infection progresses to cirrhosis faster than HBV alone, and is associated with higher liver-related mortality than HIV alone [4,5,8,10,13]. However, most studies have been in ambulatory, HIV-positive populations. In a large nation-wide study of hospitalized patients, we demonstrate that HBV/HIV co-infection is associated with higher in-hospital mortality, length of stay, and hospitalization costs than those with HBV alone. Interestingly, this difference was more striking for liver-related hospitalizations. Despite the smaller proportion of liver-related admissions and liver-related complications, liver-related mortality was actually higher in the HBV/HIV co-infected group than the HBV-only group (OR 1.83, 1.27-2.62) suggesting an incremental or compounding effect of HIV on liver-related mortality in HBV/HIV co-infected patients. In contrast, mortality in primary infectious admissions was not higher in the HBV/HIV co-infected group compared to the HBV mono-infection group. These data demonstrate that HBV/HIV co-infection leads to greater mortality through liver-related deaths and not infectious processes when compared to HBV mono-infection alone.

These data support prior studies demonstrating excess hepatic mortality among persons with HBV/HIV vs HBV alone. For example in the Multicenter AIDS Cohort study, individuals coinfecting with HIV and HBV, especially those with low CD4+ nadir counts, were shown to be at increased risk for liver-related mortality with a rate of 14.2/1000 versus only 1.7/1000 ($p<0.001$) in the HIV mono-infection group and only 0.8/1000 ($p<0.001$) in the HBV mono-infection group [10]. In addition, our data could also support an accelerated natural history of liver disease which has been documented in prior studies of coinfection versus mono-infection [13]. In one study comparing the survival of HIV-infected and HIV-uninfected patients with decompensated cirrhosis due to HCV, HIV coinfection considerably reduced the survival of patients with HCV-related end stage liver disease independent of other

markers of poor prognosis [26]. A similar aggressive decompensation could be postulated for HBV-related cirrhosis in combination with HIV infection. An additional explanation for the increased mortality seen in our HBV/HIV coinfecting group compared to HBV monoinfection, particularly in the subgroup with cirrhosis or complications of portal hypertension is Hepatitis delta (HDV) co-infection. The addition of HDV to HIV/HBV coinfection is associated with a particularly aggressive course of liver disease, frequently leading to cirrhosis, decompensation, and death [27]. Due to the nature of ICD-9 coding for HDV where it is usually coded together with HBV, we were not able to assess the true prevalence of hepatitis delta in our cohort. Future research should tease out the specifics of whether HDV plays an important role in hospitalization and mortality in HBV/HIV coinfecting populations.

Prospective cohort studies in outpatient settings have reported that HBV/HIV co-infection is associated with an increased risk of both all-cause and liver-specific mortality compared to HIV alone [6,8]. We did not find a significant difference in overall in-hospital mortality between the co-infected and HIV-only groups (OR 1.22, 95% CI 0.96-1.54). This was true for both liver-related admissions (OR 1.05, 95% CI 0.73-1.50) and primary infectious admissions (OR 1.08, 95% CI 0.79-1.47). However, the presence of HBV along with cirrhosis or complications of portal hypertension was associated with 3-times greater in-hospital mortality in patients with HIV compared to those without these complications (OR 3.00, 95% CI 1.80-5.02). This suggests that there may be a subgroup of patients with HBV/HIV coinfection with complicated liver disease who are at a substantially higher mortality risk compared to those with HIV monoinfection. Similar findings have been shown with HCV/HIV infection [18,21]. Because the excess mortality in HBV/HIV coinfection seems to be attributable to chronic liver disease, especially cirrhosis and its complications, our data support the notion that cirrhosis is a strong risk factor for mortality in patients with HIV. Our data thus emphasize the importance of prevention, identification, and comprehensive management of hepatitis B in individuals infected with HIV in order to prevent advancement to cirrhosis.

Consistent with prior studies on the financial implications of coinfection[17], we found that both length of stay and total hospitalization charges were increased in the HBV/HIV co-infected group compared to the HBV mono-infection group (+1.53 days and \$17595) and the HIV mono-infection group (+0.62 days and \$8840). In addition, using outcomes data for all cause hospitalizations, we find that in-hospital mortality for HBV/HIV co-infection is much higher at 11.3% compared to the all cause in-hospital mortality of 1.9%. Similarly, length of stay and average hospitalization charges for HBV/HIV co-infection are significantly higher than that for all cause hospitalizations (7.87 versus 4.5 days, \$62652 vs \$35,213). The same results hold for both HBV mono-infection and HIV mono-infection when compared to all-cause hospitalization. This suggests that the overall health care utilization and costs associated with either HBV or HIV infection are higher than the national average for all hospitalizations. Policy-makers should be aware of the financial implications of coinfection as they allocate scarce health care resources and establish capitated costs for accountable care organizations.

Our study has several strengths. To our knowledge, it is the first study using a nationwide representative sample to perform a three-way comparison of outcomes between groups with HBV or HIV monoinfection and HBV/HIV co-infection. Using previously validated or utilized ICD-9-CM codes improves our ability to capture patients of interest and preserves replicability and comparability between studies. A national representative sample such as the NIS provides estimates that are generalizable to the entire US population and not subject to biases from single center or tertiary referral hospital studies.

There are a few limitations to our study. As in other studies from administrative databases, use of ICD-9-CM discharge codes is subject to errors of miscoding. Some inaccuracy of data, particularly for the demographic category of race, is evident based on the fact that only 15% of our HBV cohort was Asian, compared to 59-72% seen in other studies [28,29]. We also did not have information on individual laboratory data (such as CD4 counts, HBV DNA or liver function tests) or history of treatment (e.g. ART) to examine their effect on outcomes. The NIS design does not permit longitudinal tracking of patients to examine rates of repeat hospitalization. It is possible, that a higher overall rate of hospitalization may be a reflection of a small cohort of patients with frequent readmissions.

In conclusion, HBV/HIV co-infection is a risk factor for in-hospital mortality, particularly in liver related admissions, compared to HBV mono-infection. Overall health care utilization from HBV/HIV co-infection is also higher than for either infection alone and higher than the national average for all hospitalizations, emphasizing the health care burden from these illnesses.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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List of Abbreviations

HBV	Hepatitis B virus
HIV	Human immunodeficiency virus
ICD-9-CM	International Classification of Diseases, Clinical Modification, 9th edition
NIH	National Institutes of Health

NIS	Nationwide Inpatient Sample
HCUP	Healthcare Cost and Utilization Project
AHRQ	Agency for Healthcare Research and Quality
SBP	Spontaneous bacterial peritonitis
LOS	Length of stay
HCC	Hepatocellular cancer
AASLD	American Association for the Study of Liver Diseases
LFTs	Liver function tests

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KEY POINTS BOX

- No studies have examined outcomes of HBV/HIV co-infection among hospitalized patients, a group that represents those with advanced disease and vulnerable to poor outcomes and high healthcare utilization.
- HBV/HIV co-infection was associated with higher in-hospital mortality compared to HBV mono-infection.
- The presence of HBV along with cirrhosis or complications of portal hypertension was associated with 3-times greater in-hospital mortality in patients with HIV compared to those without these complications.
- Overall health care utilization from HBV/HIV co-infection is higher than for either infection alone and higher than the national average for all hospitalizations, emphasizing the health care burden from these illnesses.

Table 1

Demographic characteristics and systemic complications in patients with Hepatitis B virus (HBV) or Human immunodeficiency virus (HIV) mono-infection and HBV/HIV co-infection

Variable	HBV monoinfection (n= 72,584)%	HIV monoinfection (n= 133,880) %	HBV/HIV co-infection (n= 8,156) %
Age group (in years)			
0-18	0.3	0.3	0
18-35	15.8	19.6	17.4
36-50	25.4	41.8	48.4
51-65	41.5	33.7	31.2
66+	17.0	4.6	3.0
Sex			
Male	57.4	66.6	77.3
Female	42.6	33.4	22.8
Race			
White	42.2	25.5	26.5
Black	23.3	52.9	53.5
Hispanic	7.9	11.3	10.6
Asian or Pacific Islander	15.0	0.5	0.4
Other/missing	11.2	9.7	8.8
Insurance			
Medicare	33.7	32.2	33.9
Medicaid	30.5	40.9	44.4
Private	23.2	15	11.6
Self-pay	7.3	7.7	6.6
No charge	1.1	0.8	0.5
Other/Missing	4.2	3.4	3
Zip code level income quartile			
Quartile 1	36.3	48.1	47.4
Quartile 2	23.4	24.1	22.9
Quartile 3	21.4	17.3	19.0
Quartile 4	19.0	10.6	10.8
Elixhauser co-morbidity burden			
0	16.6	10.2	8.1
1	17.7	19.9	19.1
2	20.5	24.7	24.8
3 or more	45.2	45.2	50.0

Variable	HBV monoinfection (n= 72,584)%	HIV monoinfection (n= 133,880) %	HBV/HIV co-infection (n= 8,156) %
Hospital teaching status			
Teaching	64.1	70.7	80.1
Non teaching	35.9	29.3	19.9
Hospital bed size			
Small	7.9	6.2	3.7
Medium	22.7	21.3	20.8
Large	69.5	72.5	75.5
Hospital region			
Northeast	27.4	31.1	39.0
Midwest	16.1	12.7	10.4
South	34.7	44.1	40.1
West	21.9	12.2	10.6
Systemic complications			
Acute renal failure	13.2	15.9	19.1
Hypovolemia	6.3	9.3	11.0
Acute respiratory failure	5.4	7.7	8.9
Acidosis	5.2	7.0	7.6
Hypo-osmolality	9.0	10.7	12.2
Malnutrition	4.7	6.9	8.8
Anemia	20.1	19.8	18.4
Cachexia	1.4	6.0	7.9
Noncompliance	5.9	16.5	19.0

Table 2

Frequency of liver-related and infection-related hospitalizations in patients with Hepatitis C virus (HBV) or Human immunodeficiency virus (HIV) mono-infection or HBV/HIV co-infection

Variable	HBV mono-infection (n= 72,584)%	HIV mono-infection (n= 133,880) %	HBV/HIV co-infection (n= 8,156) %
Liver Specific Complications			
All liver related admissions	33.4	11.4	22.6
Hepatitis C	28.0	19.5	32.3
Cirrhosis	20.4	4.0	11.4
Portal hypertension	6.3	1.0	3.8
Spontaneous bacterial peritonitis	1.0	0.1	0.2
Encephalopathy	1.0	0.5	0.5
Variceal bleeding	1.4	0.1	0.8
Ascites	10.0	2.2	6.7
Hepatorenal syndrome	1.1	0.1	0.3
Alcoholic liver disease	7.7	1.5	2.1
Alcoholism	11.7	5.1	6.2
Other sequela of chronic liver disease	2.0	0.4	1.0
Coagulopathy	3.8	1.4	3.6
Hepatocellular carcinoma	5.0	0.3	1.5
Acute liver failure	1.5	0.7	1.7
Infection specific complications			
Primary infection-related admissions	27.2	48.4	47.4
Pneumonia	8.2	18.1	19.7
Skin infections	5.5	6.7	8.2
Urinary tract infections	7.8	8.3	8.9
Septicemia	6.2	10.3	12.8
PCP	0.01	6.9	5.7
MAC	0.1	3.0	2.6
CMV	0.2	2.7	3.1
Pulmonary TB	0	0	0
Diarrheal illness	1.7	3.5	6.0
Cryptococcal meningitis	0.01	1.2	0.7
Progressive multifocal leukoencephalopathy	0	0.7	0.6

Table 3

Comparison of in-hospital mortality between HBV/HIV co-infected patients and HBV-monoinfected patients

Subgroup	% among HBV/HIV co-infection	% among HBV mono-infection	Univariate Odds Ratio	95% CI	Multivariate Odds Ratio *	95% CI
All patients	4.7	3.2	1.50	1.18-1.91	1.67	1.30-2.15
Liver-related admissions	10.2	6.9	1.53	1.08-2.17	1.83	1.27-2.62
Primary infectious admissions	5.9	5.7	1.03	0.75-1.42	1.13	0.81-1.57

Adjusted for age, sex, insurance, Elixhauser co-morbidity burden and hospital region which were significant on univariate analysis.

Table 4

Comparison of in-hospital mortality between HBV/HIV co-infected patients and HIV-monoinfected patients

Subgroup	% among HBV/HIV co-infection	% among HIV mono-infection	Univariate Odds Ratio	95% CI	Multi-variate Odds Ratio*	95% CI
All patients	4.7	3.7	1.28	1.01-1.62	1.22	0.96-1.54
Liver related admissions	10.2	9.5	1.08	0.76-1.54	1.05	0.73-1.50
Primary infectious admissions	5.9	5.2	1.15	0.85-1.55	1.08	0.79-1.47

* Adjusted for age, sex, insurance, Elixhauser co-morbidity burden and hospital region which were significant on univariate analysis.

Table 5

Hospitalization rates among Hepatitis B virus (HBV), Human immunodeficiency virus (HIV) and HBV/HIV co-infected patients

Cohort	Prevalence estimate in the United States [*]	Number of hospitalizations [#]	Hospitalization rate (per 100 individuals)
HBV	730,000	72,584	9.9
HIV	1,200,000	133,880	11.2
	72,000	8,156	11.3

^{*} From previously published data[5,6,10,22,23].

[#] From current study.