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INCREASED RISK OF ACUTE HEPATITIS B IN ADULTS DIAGNOSED WITH DIABETES

[1]Dr Muhammad Adeel, [2]Dr Alina Sayyed, [3]Dr Saira Nasir

[1]Central Park Medical College, Lahore, [2]Multan Medical and Dental College, Multan, [3]Multan Medical and Dental College, Multan.

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Abstract:

Background: *The risk of acute hepatitis B in adult diabetic patients is unknown. We examined the link between diagnosed diabetes and acute hepatitis B.*

Methods: *This study was held in the Medicine Unit-II of Jinnah Hospital Lahore for one-year duration from August 2019 to August 2020. Confirmed cases of acute hepatitis B were diagnosed with diabetes included in the study. Odds ratios (ORs) comparing acute hepatitis B among adults diagnosed with diabetes mellitus versus those without known diabetes were determined by multivariate logistic regression by age, sex, and race / ethnicity, and stratified by presence or absence of behavior risky for hepatitis B virus (HBV).*

Results: *865 cases of acute hepatitis B in people aged ≥23 years; 95 (11.0%) were diagnosed with diabetes. The incidence of diabetes mellitus in the comparative group was 9.1%. Among adults without hepatitis B risk behaviors and with a reported diabetes status, the OR for acute hepatitis B compared to non-diabetic and diabetic adults was 1.9 (95% confidence interval [CI] = 1.4; 2.6;); ORs for adults aged 23–59 and ≥ 60 years were 2.1 (95% CI = 1.6, 2.8) and 1.5 (95% = CI 0.9, 2.5), respectively.*

Conclusions: *Diabetes mellitus was independently associated with an increased risk of acute hepatitis B in adults without HBV risk behavior.*

Key words: *blood glucose monitoring, diabetes, hepatitis B, prophylaxis*

Corresponding author:
Dr. Muhammad Adeel,
Central Park Medical College, Lahore.

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INTRODUCTION:

In 2010, an estimated 18.6 million adults ≥20 years of age in the United States were diagnosed with type 1 or type 2 diabetes and the annual incidence of diabetes is expected to increase. People with diabetes require comprehensive medical care to control blood glucose levels and prevent diabetes complications such as cardiovascular disease, kidney disease, retinopathy, and neuropathy. Regardless of treatment (insulin, oral medications or nutrition), 86% of people with diabetes self-monitor their blood glucose levels at least once a month. Assisted monitoring also takes place at a variety of locations, including doctor's offices, hospitals, health fairs, schools, and nursing homes. The potential for transmission of blood-borne pathogens exists when patients are exposed to the blood or body fluids of people infected by contaminated equipment or surfaces (e.g., on blood glucose monitoring equipment, when insulin pens are used by more than one person, or during some procedures)). Hepatitis B virus (HBV) is a highly infectious bloodborne pathogen that is transmitted by transcutaneous or mucosal contact with the blood or body fluids of an infected person; HBV remains stable on environmental surfaces for ≥7 days. Known behaviors that increase the risk of getting HBV include injection drug use (IDU), male sex with another male (MSM), and sex with multiple partners. Unvaccinated health care workers and households or sexual intercourse of someone infected with HBV are also at increased risk of contracting HBV. About 5% of healthy adults with acute or asymptomatic HBV infection become chronically infected, which can lead to cirrhosis, hepatocellular carcinoma, and liver failure. Outbreaks of hepatitis B among people with diabetes in long-term care facilities (e.g., nursing homes and nursing homes) suggest that there may be an increased risk of HBV infection in these locations. However, the prevalence and magnitude of the risk of acute hepatitis B is unknown in the general adult population with diabetes or after excluding those for whom HBV infection can reasonably be attributed to other recognized risk behaviors. For the purposes of this analysis, we tried to determine the relationship between diabetes and acute hepatitis B in adults with no known HBV risk behaviors.

METHODS:

This study was held in the Medicine Unit-II of Jinnah Hospital Lahore for one-year duration from August 2019 to August 2020. Patient information collected during standard medical history or review of medical records by healthcare professionals included demographics (e.g., age and race). HBV risk behaviors (e.g., IDU and MSM) performed within six weeks to six months of symptom onset, other potential HBV exposure, and data on hospitalization and deaths attributed to acute hepatitis B. Diabetes status determines based on the diagnosis of diabetes by a physician (type 1 or 2). If the patient was not at the interview, the doctor presented the diabetes status or reviewed medical records. If neither of these sources were available, the state of diabetes was considered unknown. Cases with pregnancy or pre-diabetes, or diagnosed with diabetes mellitus within the 6-month incubation period prior to the onset of acute symptoms of hepatitis B, were classified as nondiabetic. Unidentified data on acute hepatitis B cases have been reported to the Centers for Disease Control and Prevention (CDC) as part of routine hepatitis B surveillance; since the effect was considered 'disease control' rather than 'human research', it was excluded from the human research review. Respondent data was weighted against the overall population of each EIP site based on age, gender, and race / ethnicity. Diabetes status was determined by self-report based on the following question: "Has your doctor ever told you have diabetes?" Respondents with pregnancy or pre-diabetes were classified as non-diabetic. HBV risk behavior was assessed using the BRFSS variable for the risk of human immunodeficiency virus (HIV) infection (HIVRISK), defined by IDU history, treating sexually transmitted infection, giving or receiving money or drugs in exchange for sex or anal sex without a condom in the past year. HIV RISK information was available to respondents <65 years of age.

RESULTS:

In total, a total of 865 confirmed cases of acute hepatitis B in adults ≥23 years of age (Table 1).

There were no significant differences between adult and nondiabetic adults with respect to race / ethnicity, LTC residency, HBV hospitalization or HBV-related deaths (Table 2).

Table 1.
Characteristics of Acute Hepatitis B Cases and Behavioral Risk Factor Surveillance System Comparison

Characteristic	Acute hepatitis B cases *N* = 865		BRFSS comparison group[a] Unweighted *N* = 90,941	
	n	%*b*	Unweighted *n*	Weighted %[b]
Age (years)				
23–59	756	87.4	50,866	74.4
≥60	109	12.6	40,075	25.6
Sex				
Male	561	64.9	33,997	48.0
Female	303	35.0	56,944	52.0
Race/ethnicity				
Non-Hispanic white	398	46.0	74,476	71.9
Non-Hispanic black	220	25.4	6533	12.5
Hispanic	81	9.4	5116	8.4
Asian or Pacific Islander	35	4.1	1285	2.8
Other	15	1.7	2502	3.3
Other HBV Risk Behaviors[c]				
Yes	247	28.6	1259	2.4
No	503	58.2	56,723	74.8
Diagnosed diabetes				
Yes	95	11.0	10,076	9.1
No	707	81.7	80,766	90.8

Table 2.
Demographics, HBV Risk Behaviors,[a] and Health Outcomes for 865 Acute Hepatitis B Cases

Characteristic	Diagnosed diabetes mellitus		No diagnosed diabetes mellitus		Unknown diagnosis of diabetes mellitus		*P* value[b]
	n	%[c]	*n*	%	*n*	%	
N	95	11.0	707	81.7	63	7.3	—
Age (years)							
23–59[d]	68	71.6	633	89.5	55	87.3	<0.001
≥60	27	28.4	74	10.5	8	12.7	
Sex							
Male	59	62.1	457	64.7	45	71.4	0.616
Female	36	37.9	249	35.3	18	28.6	
Race/ethnicity							
Non-Hispanic white	38	43.2	329	54.1	31	58.5	0.055[e]
Non-Hispanic black	34	38.6	176	28.9	10	18.9	
Hispanic	10	11.4	64	10.5	7	13.2	
Asian or Pacific Islander	4	4.5	28	4.6	3	5.7	
Other	2	2.3	11	1.8	2	3.8	
Long-term care residence							
Yes	2	3.0	7	1.3	2	5.9	0.1669[f]
No	64	97.0	531	98.7	32	94.1	
Injection drug use							
Yes	1	1.5	60	10.8	5	14.3	0.009[f]
No	68	98.5	495	89.2	30	85.7	
Male sex with another male							
Yes	6	8.2	62	11.6	6	14.0	0.392
No	67	91.8	473	88.4	37	86.0	—
Multiple sex partners							
Yes	11	16.4	110	22.4	8	21.6	0.265
No	56	83.6	381	77.6	29	78.4	
Other HBV Risk Behaviors[g]							
Yes	16	19.5	215	34.6	16	34.8	0.006
No	66	80.5	407	65.4	30	65.2	
Hospitalization due to acute hepatitis B							
Yes	42	52.5	287	45.4	13	31.0	0.231
No	38	47.5	345	54.6	29	69.0	
Death due to acute hepatitis B							

Yes	4	4.6	12	2.0	3	5.4	0.127[f]
No	83	95.4	599	98.0	52	94.6	

The estimated annual incidence of acute hepatitis B among adults ≥23 years of age with and without diabetes mellitus between 2009 and 2010 was 1.8 per 100,000 (95% CI = 1.5, 2.2) and 1.3 per 100,000 (95% CI = 1.2, 1.4), respectively. In a two-dimensional analysis, the covariates associated with acute hepatitis B were age (23-59 years versus ≥60 years, OR 2.4, 95% CI = 2.0, 2.9), gender (male versus female, OR 2.0, 95% CI = 1.7, 2.3), Race / Ethnicity (all others vs non-human whites, OR 2.4, 95% CI = 2.0, 2.7), other behaviors related to the risk of HBV (OR 15.4, 95% CI = 12.9, 18.4) and diabetes (OR 1.3, 95% CI = 1.1, 1.7; Table 3).

Table 3.
Bivariate Analysis of Covariates Associated with Acute Hepatitis B among Adults Aged ≥23 Years

Characteristic	OR (95% CI)
Age[a]	2.4 (2.0, 2.9)
Sex[b]	2.0 (1.7, 2.3)
Race/ethnicity[c]	2.4 (2.0, 2.7)
Other HBV Risk Behaviors	15.4 (12.9, 18.4)[d]
Diagnosed diabetes	1.3 (1.1, 1.7)

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DISCUSSION:

For adults without some well-established risk factors for HBV infection, our results suggest that adults diagnosed with overall diabetes and adults with diabetes aged 23–59 years are approximately twice as likely to develop acute hepatitis B as non-diabetic adults. The increased risk was maintained in the sensitivity analyzes which investigated the effect of cases of unknown diabetes status. Diabetic adults ≥ 60 years of age may also be at increased risk of acute hepatitis B, although the results were not statistically significant. The main advantage of the analysis is the large sample size (approximately 17% of the US adult population), which makes it possible to determine the likelihood of developing acute hepatitis B while controlling the demographic characteristics of people with diabetes who did not report other behaviors associated with the risk of HBV. Age, race / ethnicity, and other behaviors associated with the risk of HBV were covariates that may have influenced the interpretation of the results. Diabetes mellitus and hepatitis B have a disproportionate impact across age, race and ethnicity. In 2005–2008, the elderly (≥65 years old) had the highest incidence of diabetes; 1 while data from the national surveillance from 2009 showed the highest frequency of acute hepatitis B among adults aged 30–59 years. The 2007-2009 National Health Interview Survey found that diagnosed diabetes was 18% higher in Asian Americans, 66% in Hispanics and 77% in non-Hispanic blacks compared to non-Hispanic whites.1 Results 1996–1 The 2006 National Health and Nutritional Examination Survey (NHANES) showed a higher seroprevalence of past or present HBV infection [total antibodies to hepatitis B core antigen (anti-HBc)] among non-Hispanic blacks compared to non-Hispanic whites (12 2% versus 2.8%, p = 0.001). In our study, cases of acute hepatitis B without diagnosed diabetes were more likely to report IDU and other behaviors associated with the risk of HBV than people diagnosed with diabetes. Of 1,715 reported cases of acute hepatitis B with available risk information collected by the national CDC surveillance in 2009, 39.9% reported at least one risky behavior / exposure to HBV, including IDU, MSM and having sex with ≥2 partners . Results were

supported by age and race / ethnicity adaptation and limitation of the analysis to cases and comparators without other behaviors associated with HBV risk. While this study is the first to assess the risk of acute hepatitis B in adult diabetics in the United States, the seroprevalence data support our findings. In 1999–2010, NHANES, a national study that excludes institutionalized adults, found 60% ($p < 0.001$) higher anti-HBc seroprevalence among adults with diabetes than in adults without diabetes. In Turkey, Gulcan and colleagues compared 630 people with diabetes and 314 people without diabetes who visited an internal medicine clinic and found that HBV infections increased but were not significantly more common among people with diabetes compared to people without diabetes (5.1 % compared to 3.8%); However, researchers found significant correlations between HBsAg-positive serology (indicative of chronic hepatitis B) and history of hospitalization, long duration of diabetes, and insulin use. Halota et al. Found anti-HBc seropositive among 123 (39.0%) out of 315 people with diabetes in Poland. The percentage of anti-HBc study participants increased with age and duration of diabetes. In Italy, Sangiorgio and co-authors identified a higher proportion of people with HBsAg-positive diabetes compared to a blood donor control group (7.1% versus 1.6%, $p < 0.001$), and in another Italian study, higher HBc seroprevalence was observed among people with diabetes compared to blood donors. This study has several limitations. A cohort study of people with diabetes would provide the best measure of risk for acute hepatitis B. In the absence of such a study, we used two data sources from the same population that provided information from a large part of the United States. and had enough detail to estimate the risk of acute hepatitis B by controlling important potential confounding factors. However, the definition of other HBV risk behaviors differed between comparators and cases of acute hepatitis B, which might have affected the reliability of the estimates. Compared to non-diabetic adults, adults with diabetes may have had greater use of healthcare, which could lead to more frequent testing and therefore a greater likelihood of being diagnosed with acute hepatitis B. Unlike surveillance of EIP cases, BRFSS was limited to non-institutionalized adults. Of the cases of acute hepatitis B, 11 (1.3%) reported a history of LTC, and the percentage of acute hepatitis B in LTC did not differ by diabetes status. Therefore, not excluding cases of long-term care would not be likely to affect the results. We assumed that none of the BRFSS respondents included in the sample had acute hepatitis B and the analysis did not include vaccination as vaccination histories are not available for the 2009-2010 BRFSS data. The direction of any resulting error would depend on the variability in the incidence of acute hepatitis B and the extent of vaccination by diabetes status among comparators. Other data were limited or unavailable for variables including healthcare profession, history of hemodialysis or dental care, HepB vaccine, and frequency of blood glucose monitoring or insulin use.

CONCLUSIONS:

Our results suggest an increased risk of acute hepatitis B in adults diagnosed with diabetes. Hepatitis B vaccination and the continuous infection control practice associated with diabetes care and monitoring can reduce the transmission of blood borne pathogens and prevent HBV-related morbidity and mortality.

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