HHS Public Access

Author manuscript

J Immigr Minor Health. Author manuscript; available in PMC 2019 May 14.

Published in final edited form as:

J Immigr Minor Health. 2013 April ; 15(2): 390–397. doi:10.1007/s10903-012-9604-8.

Acute Viral Hepatitis in the United States–Mexico Border Region: Data from the Border Infectious Disease Surveillance (BIDS) Project, 2000–2009

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Conflict of interest None.

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Abstract

Little is known about the characteristics of acute viral hepatitis cases in the United States (US)–Mexico border region. We analyzed characteristics of acute viral hepatitis cases collected from the Border Infectious Disease Surveillance Project from January 2000–December 2009. Over the study period, 1,437 acute hepatitis A, 311 acute hepatitis B, and 362 acute hepatitis C cases were reported from 5 Mexico and 2 US sites. Mexican hepatitis A cases most frequently reported close personal contact with a known case, whereas, US cases most often reported crossborder travel. Injection drug use was common among Mexican and US acute hepatitis B and C cases. Cross-border travel during the incubation period was common among acute viral hepatitis cases in both countries. Assiduous adherence to vaccination and prevention guidelines in the US is needed and strategic implementation of hepatitis vaccination and prevention programs south of the border should be considered.

Keywords

Acute viral hepatitis; Border; Mexico; Surveillance

Introduction

The border region, as defined in the La Paz Agreement of 1983, is the area extending 100 km (62 miles) north and south of the 2,000-mile-long United States (US)–Mexico border, which comprises four US and six Mexican states and is home to a population of over 21 million people [1, 2]. Almost 500,000 people crossed the border daily in the year 2010 [3], and economic exchange between the two countries has grown rapidly. The combination of poverty, migration, drug use, crime, poor environmental and sanitation conditions, and limited public and private healthcare, have contributed to the US–Mexico border region experiencing higher rates of illness, including infectious disease, compared with other regions of the US [4] and Mexico [5, 6].

Efforts to improve health in the border region have been limited by lack of adequate systems for gathering and analyzing comparable data. Exchange of surveillance data may be further complicated by disparate disease case definitions used for public health reporting in the two countries. For instance, while laboratory confirmatory data are required for many reportable diseases in the US, it is often unavailable in laboratories in Mexican border states. Until recently, there was no system for sharing infectious disease surveillance data and

coordinating public health interventions between the US and Mexico. To overcome these obstacles, the Border Infectious Disease Surveillance (BIDS) project was established in 1997 as a binational approach to the control and prevention of infectious diseases, including viral hepatitis, across the US–Mexico border [7]. This report is the first to summarize trends in and characteristics of acute viral hepatitis cases along the United States (US)–Mexico border region collected in BIDS from 2000 through 2009.

Methods

Border Infectious Disease Surveillance

BIDS involves a binational collaboration between the US and Mexico that includes the US Centers for Disease Control and Prevention (CDC), the Mexican Secretariat of Health (General Directorate of Epidemiology [Direccion General de Epidemiologia, or DGE]) and the National Institute of Epdemiological Diagnosis and Reference (Instituto de Diagnostico y Referencia Epidemiologicos [InDRE]), US and Mexican border state and local health officials, and academic institutions. The purpose of this collaboration is to have a unified, enhanced epidemiologic and laboratory-based surveillance system that monitors the occurrence of specific infectious diseases in the US–Mexico border population. BIDS was initially established with pilot sites at nine clinics and hospitals in four sister-city regions along the US–Mexico border and later expanded to include 81 clinics and hospitals in the same four sister-city regions (Fig. 1). The BIDS network has conducted syndromic sentinel surveillance for three major conditions, including acute hepatitis syndrome [7].

Acute Viral Hepatitis Surveillance

In BIDS, the acute hepatitis syndrome was defined as either: (1) an acute illness with jaundice or dark urine or (2) an acute illness of at least 6 days without jaundice and at least three of the following: abdominal pain, acholic stools, nausea/vomiting, fever, or anorexia. To confirm the presence of viral hepatitis infection, serum from patients with acute hepatitis syndrome was tested for IgM antibody to hepatitis A virus (anti-HAV) (using DiaSorin IgM anti-HAV, ETI-HA-IGMK Plus], IgM antibody to hepatitis B core antigen (IgM anti-HBc) (using DiaSorin IgM anti-HBc, ETI-CORE-IGMK Plus, ETI-AB-COREX-PLUS) and hepatitis B surface antigen (HBsAg) (using DiaSorin ETI-MAK-2 PLUS HBsAg), and IgG antibody to hepatitis C virus (anti-HCV) (using Abbott HCV EIA 2.0 and Ortho HCV Version 3.0 ELISA Test System). Anti-HCV screening-reactive specimens that had a signal to cutoff (S/CO) ratio predictive of a true positive result (as evaluated by CDC for various manufacturers) were considered confirmed to be positive for anti-HCV [8]. The specimens with S/CO ratio lower than that predictive of a true positive were tested using a confirmatory recombinant immunoblot assay (The Chiron RIBA HCV 3.0 SIA; Novartis Vaccines & Diagnostics, Inc., Emeryville, CA). The laboratory criteria for acute viral hepatitis infection were, for hepatitis A, positive IgM anti-HAV; for hepatitis B, positive IgM anti-HBc or HBsAg and negative IgM anti-HAV; and for hepatitis C, positive anti-HCV and positive RIBA or S/CO consistent with true positive and negative IgM anti-HAV and negative IgM anti-HBc and negative HBsAg.

In BIDS, a case of acute viral hepatitis was defined as a person who: (1) had one of the criteria for acute hepatitis syndrome and (2) had a positive serologic test consistent with current hepatitis A, B, or C virus infection. A case was confirmed when an epidemiologic investigation using a standardized questionnaire was completed by the surveillance officer (a physician or epidemiologist), a final diagnosis was assigned, and all associated case data were entered into the BIDS database and approved by InDRE/DGE and CDC.

BIDS Sites, Study Population, and Data Collection

BIDS sites were included in the analysis based on the consecutive calendar years of participation and the degree to which each consistently collected case data for the project. From January 2000 through December 2009, 11 study sites participated in BIDS; however, because of resource constraints not all were consistently active. Four sites (Nogales, AZ, USA; Las Cruces, NM, USA; Tucson, AZ, USA; McAllen, TX, USA) only reported cases during 2000–2004. Of the remaining seven sites, three (San Diego, CA, USA; Tijuana, B.C., MX; and Ciudad Juarez, Chih, MX) reported acute viral hepatitis annually during 2000–2009, and four sites (Nogales, Son., MX, 2000–2006; El Paso, TX, USA, 2000–2005; Reynosa, T.M., MX, 2000–2007; Mexicali, B.C., MX, 2002–2009) reported cases annually for at least six consecutive years. Therefore, data from these seven sites (five Mexico, two US) were included in this analysis. The Mexican sites comprised one general hospital and four primary-care clinics; the US institutions were one primary-care clinic and one non-profit public hospital. The primary-care institutions service 10,000–20,000 acute-care visits per site annually, while the hospitals service 23,000–51,000 acute-care visits per site annually [7].

Persons with an illness meeting the case definition for acute hepatitis A, B, or C from January 1, 2000 through December 31, 2009 were included in the analysis. Demographic, risk factor, and travel history data were collected by a surveillance officer during a patient interview using a standardized questionnaire. The list of potential risk factors for infection was obtained from CDC viral hepatitis surveillance case report forms; multiple risk factors could be recorded for each patient. Determination of risk factors was based on engagement in the respective risk behavior during the incubation periods of acute hepatitis A, B, and C (e.g., for hepatitis C, during 2 weeks to 6 months before symptoms), and not relative to lifetime behavior. Cases were classified by country according to the primary residence of the patient. A cross border case was defined as a person with acute viral hepatitis who reported having traveled to the country opposite their country of primary residence during the incubation period of the resulting illness. The CDC Institutional Review Board conferred a “non-research” determination for the BIDS Project, as the data collected were de-identified and used for disease surveillance purposes.

Calculation of Disease Case Rates

Population estimates were not available for the geographic catchment areas associated with particular BIDS-affiliated clinics and hospital; therefore, typical population-based incidence rates could not be reliably calculated. In order to provide a surrogate case rate with which to compare disease trends, the number of acute viral hepatitis cases per/1,000 patient clinic visits was used as a proxy for viral hepatitis incidence among US and Mexican BIDS sites.

Case rates for viral hepatitis were calculated based on the number of acute viral hepatitis cases at a specific BIDS site divided by the total number of patient clinic visits at that same site, multiplied by 1,000.

Statistical Analyses

Principal characteristics and risk factors among reported acute viral hepatitis A, B and C cases from US and Mexico were analyzed using SAS (SAS Institute Inc., Cary, NC). We used the Pearson Chi-square statistic to determine whether there was a significant difference between the proportion of cases with a given characteristic or risk factor reported from US sites compared with those reported from Mexican BIDS sites. *P* values less than 0.05 were considered significant.

Results

BIDS Sites, Study Population, and Data Collection

From the seven consistently active BIDS sites (Tijuana, B.C., MX; Ciudad Juarez, Chih, MX; Nogales, Son., MX; Reynosa, T.M., MX; Mexicali, B.C., MX; San Diego, CA, USA; El Paso, TX, USA), 2,110 reported acute viral hepatitis cases met the case definitions of acute hepatitis A, acute hepatitis B, or acute hepatitis C (Fig. 2). Of these 2,110 acute cases, 1,437 were hepatitis A (1,178 [82 %] Mexico, 259 [18 %] US), 311 were hepatitis B (248 [80 %] Mexico, 63 [20 %] US), and 362 were hepatitis C (293 [81 %] Mexico, 69 [19 %] US).

Viral Hepatitis Cases by Age and Gender

Table 1 shows the principal demographic characteristics of reported acute viral hepatitis cases in BIDS. For each type of acute viral hepatitis, the median age of US cases was consistently greater than that of Mexican cases; in both countries, hepatitis C cases were oldest and hepatitis A cases were youngest. Among all hepatitis A cases, 65 % of Mexico cases were age ≤10 years compared with only 7 % of US cases; four Mexican infants (i.e., <12 months old) had serologic evidence of infection. Acute hepatitis B (79.8 % Mexico, 79.4 % US) and acute hepatitis C (79.5 % Mexico, 79.7 % US) cases were more predominantly male than were hepatitis A cases (52.1 % Mexico, 57.9 % US).

Risk Factors for Viral Hepatitis

The principal risk factors, as well as cross border case status, among reported acute viral hepatitis cases in BIDS from 2000 to 2009 are shown in Table 1 (less frequently reported risk data are not shown). As mentioned, reported characteristics were not mutually exclusive and were assessed relative to behavior during the incubation period only. Among acute hepatitis A cases, Mexican cases most frequently reported household contact with a known case (40.9 %), whereas US cases most commonly reported cross border travel (45.1 %). Among acute hepatitis B cases, Mexican cases most frequently reported injection drug use (40.4 %) and tattooing/acupuncture/piercing (35.6 %), whereas US hepatitis B cases most often reported injection drug use (28.9 %) and cross border travel (25.7 %). Similarly, acute hepatitis C cases from Mexico most commonly reported injection drug use (52.1 %) and

tattooing/acupuncture/piercing (33.6 %), whereas US hepatitis C cases reported cross border travel (45.8 %) and injection drug use (42.6 %).

Viral Hepatitis Case Rates

Rates of acute viral hepatitis among cases reported from five Mexican and two US BIDS sites, expressed as the number of cases per 1,000 patient-clinic visits, are shown in Table 2. From 2000 through 2009, among 1,719 Mexico and 391 US cases, 891 (52 %) Mexico and 172 (44 %) US cases had clinic visit data for which case rates could be calculated. While acute hepatitis A case rates were higher in Mexico compared with the US, acute hepatitis B and acute hepatitis C case rates were higher in the US. During 2000–2009, case rates for acute hepatitis A, B, and C, respectively, were 0.18, 0.19, and 0.28 cases per 1,000 clinic visits among US cases compared with 0.60, 0.12, and 0.14 cases per 1,000 clinic visits among Mexican cases.

Discussion

We found that hepatitis A remains endemic on the Mexican side of the border, and that almost half of US BIDS hepatitis A cases traveled across the border during the disease incubation period. On both sides of the border, injection drug use and cross-border travel were commonly reported among BIDS acute hepatitis B and acute hepatitis C cases. In the US, national data have shown dramatic reductions in the burden of acute disease attributed to infection with HAV and HBV over the last two decades, largely attributed to the availability of safe and effective vaccines for hepatitis B since 1981 and for hepatitis A since 1995 [9]. Even without a vaccine, acute hepatitis C incidence declined 90 % to 0.5 cases per 100,000 population; however, annual incidence has not changed since 2003 [9].

Less is known about the incidence of acute viral hepatitis in Mexico. Several studies have suggested that the epidemiology of hepatitis A is undergoing a shift from high to intermediate endemicity, attributed to improvements in socioeconomic conditions, sanitation, and water supply [10–12]. Three nationwide hepatitis B surveys in Mexico revealed a hepatitis B surface antigen prevalence of 0.3 %, similar to the US, with transmission of HBV infection having occurred mainly via sexual activity and exposure to contaminated surgical equipment or body fluids [13]. Seroprevalence studies of HCV infection in Mexico reported ranges in anti-HCV from 1 to 2.5 %, with blood transfusion and unprotected sex or having multiple sex partners as principal risk factors [14, 15]. Other studies, however, have reported injection drug use as the principal risk factor, particularly in Northern Mexico, where anti-HCV seroprevalence among injection drug users was greater than 90 % [16, 17]. Thus, the epidemiology of viral hepatitis in Mexico shows substantial geographic variation and seems attributable to differences in the mode of disease transmission and associated risk factors.

Among BIDS hepatitis A cases, those from Mexico were predominantly aged 10 years or less, suggestive of the persistence of endemic hepatitis A in Mexican border communities. In contrast, the median age of US BIDS hepatitis A cases was 31 years. Most US BIDS hepatitis A cases (i.e., primary residence in the US), unlike Mexican cases (primary residence in Mexico), reported cross-border travel during the incubation period, a feature

noted among US hepatitis A cases in other studies [18]. It may be that cross-border travel is common among persons from both countries living in the region; however, our data suggest that US hepatitis A cases were more likely to have done so during the 2–6 weeks before developing illness. This association does not prove that infection necessarily occurred in Mexico. However, others have reported hepatitis A among US residents who cross the border to visit friends and relatives, and among US residents making brief excursions across the border for shopping, entertainment, and even for medical care and pharmaceuticals [19]. In such circumstances, persons may not consider themselves “international travelers,” and therefore also may not consider a need for hepatitis A vaccination [18, 19]. Partial molecular characterization of HAV BIDS isolates, recovered from both sides of the border, has shown that viral strains circulating along the US–Mexico border are rather homogeneous and genetically related (CDC, unpublished data). This is consistent with reported data that showed that the vast majority of viral strains collected throughout the border belong to the same subgenotype (IA) and group tightly together, forming a characteristic cluster which also includes most of US isolates related to international travelers (to Mexico mainly), infections among Hispanic children, and food-borne outbreaks [20, 21].

The association of cross-border travel with the acquisition of HBV or HCV infection, however, is more tenuous given the longer disease incubation periods and because a single cross-border visit, even if only for a day, classifies a case as “cross-border.” Relative to certain hepatitis B and C risk factors, such as injection drug use, unsafe sex, and tattooing, risk behavior in one’s country of residence may be more relevant than behavior across the border. Several papers have reported HCV infection risk associated with unsafe, non-commercial tattooing among persons in high-risk networks on both sides of the border [22–24]. Even if not a reliable indicator of cross-border infection, the relatively high proportion of cross border cases among all viral hepatitis cases nonetheless reflects the frequency and pervasiveness of cross border travel.

Case rates for acute hepatitis A, B, and C were calculated using total clinic visits because population estimates were unavailable for the catchment areas of clinic sites. These case rates cannot be converted to compare with national incidence estimates; they permit only a crude comparison of rates among the BIDS sites and assessment of disease trends during the study period. Compared with US sites, overall rates were higher in Mexico for acute hepatitis A (over three times the US case rate) but lower for acute hepatitis B (two-thirds the US rate) and acute hepatitis C (one-half the US rate). While case rates were similar among all types of viral hepatitis among US BIDS sites, among Mexican sites, rates of hepatitis A were five times and four times the rate of hepatitis B and hepatitis C, respectively. At all sites, there was relatively little fluctuation in case rates over the study period, except for an increase in hepatitis A case rates in Ciudad Juárez in 2004–2005. Review of individual case reports from Ciudad Juárez during these years revealed a cluster of symptomatic hepatitis A among children ≤10 years of age, many of whom were seen in the same clinic over a 4-month interval in late 2004/early 2005.

There were several limitations. First, not all BIDS sites were active over the study period because of inconsistent availability of resources; therefore, case data may not be representative of all BIDS cases or of US and Mexican national data. Several BIDS sites,

particularly US sites, did not participate consistently in viral hepatitis surveillance over the course of this study; however, a quorum of sites regularly provided data during the 10-year observation period described in this report. Second, case rate and risk factor data for BIDS cases were limited, particularly among US cases, and because case rate data were dependent upon the enumeration of clinic visits as a denominator, some rates may have been affected by substantial changes in reported total clinic visits from year to year. Third, from a case definition standpoint, over-reporting of acute hepatitis C cases was probable, as persons presenting without jaundice and with non-specific symptoms could have been pre-existing chronic hepatitis C cases. On the whole, however, consistent methodology relative to case ascertainment and calculation of disease rates permitted comparison among the sites and evaluation of trends during the study period.

In summary, we found that hepatitis A remains endemic on the Mexican side of the border, and that almost half of US BIDS hepatitis A cases traveled across the border during the disease incubation period. Socioeconomic and environmental conditions south of the border and the underutilization of hepatitis A vaccine among adult US travelers to Mexico likely contributed to these findings. Currently, the World Health Organization does not recommend large-scale vaccination programs where hepatitis A is endemic [25]; however, continuous improvements in socioeconomic conditions will further shift countries such as Mexico toward intermediate endemicity. In such places, an increasing proportion of the population becomes susceptible to HAV infection during adolescence and adulthood. Routine hepatitis A vaccination of young children in endemic settings, including Mexico’s northern border region, would likely result in a substantial reduction in hepatitis A [26–28]. On both sides of the border, injection drug use and cross-border travel were most commonly reported among BIDS acute hepatitis B and acute hepatitis C cases, reflecting the overlap of sexual and injection drug use networks. Hepatitis B vaccination and hepatitis C prevention programs can be improved by providing services at sexually transmitted disease clinics and drug treatment centers [29]. For all efforts to be effective, binational cooperation with disease interventions and ongoing surveillance is essential.

Acknowledgments

The authors would like to thank the many public health and medical professionals in the US and Mexico who contributed to the Border Infectious Disease Surveillance (BIDS) project. The financial support for this study is given by Centers for Disease Control and Prevention.

Appendix

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Fig. 1.
Sentinel surveillance sites, BIDS, 2000–2009

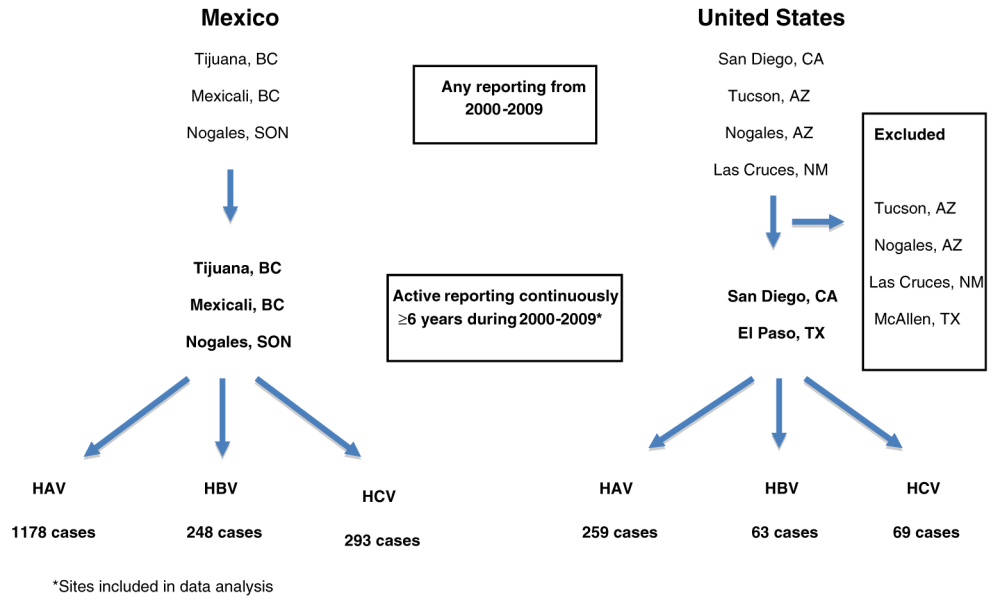

Fig. 2.

Reported acute viral hepatitis cases from Mexico and United States project sites, BIDS, 2000–2009

Table 1

Principal characteristics and risk factors among reported acute viral hepatitis cases (N), United States and Mexico, BIDS, 2000–2009

Characteristic	Hepatitis A			Hepatitis B			Hepatitis C		
	US (N = 259)	Mexico (N = 1,178)	*P**	US (N = 63)	Mexico (N = 248)	*P*	US (N = 69)	Mexico (N = 293)	*P*
Median age, years (range)	31 (0–82)	7 (0–65)		38 (8–86)	33 (0–90)		43 (16–68)	39 (0–66)	
Male	57.9 %† (150/259)	52.1 % (613/1,176)	0.091	79.4 % (50/63)	79.8 % (198/248)	0.93	79.7 % (55/69)	79.5 % (233/293)	0.972
Cross border[a]	45.1 % (105/233)	17.0 % (200/1,176)	<0.001	25.7 % (9/35)	17.6 % (43/245)	0.245	45.8 % (27/59)	23.9 % (70/293)	0.001
Risk factor									
Household/contact	7.7 % (20/259)	40.9 % (482/1,178)	<0.001	11.1 % (7/63)	21.4 % (53/248)	0.065	5.8 % (4/69)	25.3 % (74/293)	<0.001
Sexual contact	1.9 % (5/259)	0.8 % (9/1,178)	0.084	4.8 % (3/63)	3.6 % (9/248)	0.677	(0/0)	5.5 % (16/293)	
IDU	2.6 % (6/231)	1.0 % (12/1,173)	0.052	28.9 % (1¾5)	40.4 % (99/245)	0.145	42.6 % (26/61)	52.1 % (152/292)	0.180
Medical/Dental employment or procedure (including transfusion)	(0/0)	1.9 % (4/210)	-	10.3 % (4/39)	4.4 % (11/248)	0.129	1.7 % (1/59)	4.1 % (12/292)	0.370
Tattooing/piercing/needle puncture	(0/0)	1.9 % (4/210)	-	5.0 % (2/40)	35.6 % (88/247)	<0.001	3.5 % (2/58)	33.6 % (98/292)	<0.001

*Pearson Chi-square statistic

†Values associated with characteristics and risk factors are shown as the quotient of the number of cases with a particular characteristic divided by the number of cases with available data for that characteristic (in parenthesis), along with the associated percentage

[a]Cross border case was defined as a person with acute viral hepatitis who reported having traveled to the country opposite their country of primary residence during the incubation period of the resulting illness

Table 2

Rates* of acute hepatitis A, B and C, by BIDS site, 2000–2009

Site	Hepatitis A			Hepatitis B			Hepatitis C		
	Cases	Visits	Rate	Cases	Visits	Rate	Cases	Visits	Rates
Mexico total	684	1,146,308	0.60	115	990,007	0.12	92	638,354	0.14
US total	74	421,044	0.18	39	205,131	0.19	59	213,709	0.28
San Diego, CA, USA**	18	261,356	0.07	1	45,443	0.02	4	79,269	0.05
Tijuana, BC, MX	25	167,205	0.15	14	167,205	0.08	7	47,264	0.15
Mexicali, BC, MX**	32	27,413	1.17	4	27,413	0.15	16	27,413	0.58
Nogales, SON, MX	70	203,081	0.34	39	203,081	0.19	37	203,081	0.18
El Paso, TX, USA	56	159,688	0.35	38	159,688	0.24	55	134,440	0.41
Ciudad Juarez, CHIH, MX	370	479,525	0.77	46	382,315	0.12	25	255,921	0.10
Reynosa, TAM, MX	187	269,084	0.69	12	209,993	0.06	7	104,675	0.07

*Number of cases/Total number clinic visits ×1,000

**San Diego and Mexicali hepatitis B and C data for 2005 only; Mexicali hepatitis A data for 2000 only

J Immigr Minor Health. Author manuscript; available in PMC 2019 May 14.