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Adjusted estimate of the prevalence of hepatitis delta virus in 25 countries and territories

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Background & Aims: Hepatitis delta virus (HDV) is a satellite RNA virus that requires the hepatitis B virus (HBV) for assembly and propagation. Individuals infected with HDV progress to advanced liver disease faster than HBV-monoinfected individuals. Recent studies have estimated the global prevalence of anti-HDV antibodies among the HBV-infected population to be 5-15%. This study aimed to better understand HDV prevalence at the population level in 25 countries/territories.

Methods: We conducted a literature review to determine the prevalence of anti-HDV and HDV RNA in hepatitis B surface antigen (HBsAg)-positive individuals in 25 countries/territories. Virtual meetings were held with experts from each setting to discuss the findings and collect unpublished data. Data were weighted for patient segments and regional heterogeneity to estimate the prevalence in the HBV-infected population. The findings were then combined with The Polaris Observatory HBV data to estimate the anti-HDV and HDV RNA prevalence in each country/territory at the population level.

Results: After adjusting for geographical distribution, disease stage and special populations, the anti-HDV prevalence among the HBsAg+ population changed from the literature estimate in 19 countries. The highest anti-HDV prevalence was 60.1% in Mongolia. Once adjusted for the size of the HBsAg+ population and HDV RNA positivity rate, China had the highest absolute number of HDV RNA+ cases.

Conclusions: We found substantially lower HDV prevalence than previously reported, as prior meta-analyses primarily focused on studies conducted in groups/regions that have a higher probability of HBV infection: tertiary care centers, specific risk groups or geographical regions. There is large uncertainty in HDV prevalence estimates. The implementation of reflex testing would improve estimates, while also allowing earlier linkage to care for HDV RNA+ individuals. The logistical and economic burden of reflex testing on the health system would be limited, as only HBsAg+ cases would be screened.

Introduction

Globally, an estimated 258 million people were chronically infected with the hepatitis B virus (HBV) in 2022.[1] While only a fraction of these individuals are infected with hepatitis delta virus (HDV), robust epidemiology in the general population has remained limited. HDV is a satellite RNA virus that requires the HBV for assembly and entry of *de novo* viral particles.[2] While the HBV-monoinfected population are at risk of liver-related morbidity and mortality, HDV significantly increases liver disease progression.[2,3] HDV has been demonstrated to accelerate the progression to liver failure or hepatocellular carcinoma (HCC), both of which contribute to early mortality.[4,5] The risk of HCC has been found to be 3-fold higher in anti-HDV+ patients than HBV-monoinfected patients, with mortality being twice as high.[6] In contrast to HBV monoinfection, control of HBV infection with nucleos(t)ide analogue therapy does not improve liver-related outcomes in patients infected with HDV.[7]

Recent studies have estimated the global prevalence of anti-HDV among the HBV-infected population at 5-15%.[8–10] Two of these studies report high prevalence estimates and have been criticized for their wide inclusion criteria.[11,12] The single study with a lower estimate of 4.5% has been criticized for not having wide enough inclusion criteria.[13] While the study by Stockdale *et al.* aims to estimate the population-level prevalence of anti-HDV, unfortunately when calculating the global prevalence, the regional prevalence of HBV was used as opposed to the country-level HBV prevalence.[9] This can have a major impact, particularly with respect to investigating countries with high HBV prevalence, but a relatively low HDV prevalence, such as China.

One of the challenges in attempting to estimate the population-level prevalence of HDV is the high level of bias inherent in most studies. There are few national serosurveys. Instead, most studies are performed either in risk groups or

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among diagnosed individuals who are accessing care.[14] Analyses in either of these groups lead to higher prevalence estimates than would be expected in the general population. This is further complicated by the fact that many regional serosurveys are performed in regions with high prevalence, again skewing estimates of HDV at the national population level. These biases are compounded by the lack of standardized tests for anti-HDV and the lack of HDV RNA data in many HBV studies.

Reflex testing, *i.e.* automatically testing all HBsAg+ specimens for anti-HDV at the laboratory level, is not performed nationally. Even with strong patient registry systems, the lack of reflex testing results in cases of HDV not being diagnosed. For example, recent data from centers in Spain indicate that the consistent implementation of reflex testing may increase the detection rate for HDV-infected cases by 8-10 times.[15] Additionally, the prevalence reported in registry systems are likely to be overestimates, since testing only occurs among patients for whom HDV is suspected.

The current study aimed to overcome these inherent biases in the HDV data. This was accomplished by collecting all available data, and then working with in-country experts to find the optimal way to estimate the adjusted HDV prevalence in their country. This exercise was undertaken in 25 countries and territories.

Materials and methods

A comprehensive literature review was conducted for HDV (including detection of anti-HDV and HDV RNA) prevalence in 25 countries and territories. These papers were then scored and combined with a Delphi process which involved seeking out expert input to fill gaps and to confirm data when available.[1]

The literature review was conducted in PubMed using the search terms “[Country Name] AND [(hepatitis d) or HDV] AND [prevalence]” and “[Country Name] AND (’prevalence’/exp OR prevalence) AND (’hepatitis D’/exp OR ’hepatitis D’ OR ’hdv’/exp OR ’hdv’)”. Abstracts were reviewed for relevance, and only studies that included anti-HDV and/or HDV RNA prevalence were included. Grey literature, including, but not limited to, Ministry of Health reports, working papers, theses, conference presentations, local journals, and publications in local languages were also included in the analysis. Studies solely in non-representative populations (blood donors, people who inject drugs, hemophiliacs, ethnic groups, *etc*.) were excluded from the initial analysis. All studies considered after the exclusion criteria were applied can be found in the supplementary information.

The results of the review were scored utilizing a multi-objective decision analysis approach, resulting in a score of 1–3 for each study, with 1 representing the lowest quality studies.[1] Once scored, two epidemiologists independently reviewed the literature in order to pick the most representative study (supplementary information).

After these data were collected, virtual meetings were held with experts from each setting to discuss the findings, collect additional information, and estimate the population-level prevalence of anti-HDV and HDV RNA positivity among the HBV-infected population (HBsAg+). These data were then combined with The Polaris Observatory HBV national data to estimate the population-weighted prevalence of anti-HDV and HDV RNA in each country/territory at the general population level. The modeled HBV data account for historical and current prophylaxis measures, as well as the impact of treatment.[16]

The quantity and quality of data availability, combined with the known risk factors and drivers of HDV within each country/territory, necessitated additional country/territory-specific methods to estimate the prevalence at the population level.

Results

The results of the literature review and subsequent final estimate by country and territory can be found in Table 1. Of the 25 countries/territories examined, 8 (Mainland China, Canada, Hong Kong, Republic of Korea, Mongolia, Pakistan, Türkiye, and the USA) had published studies that were agreed to be representative of the prevalence at the population level, 8 (Albania, Bulgaria, Brazil, Italy, Mexico, Portugal, Romania, and Spain) were based on weighted averages, 3 (Colombia, Israel, and Sweden) were based on notification data, 3 (France, Germany, and Taiwan) were based on unpublished data, and 3 (England, Japan, and Saudi Arabia) were based on expert opinion.

The highest anti-HDV prevalence among the HBV-infected population (HBsAg+) was recorded in Mongolia at 61.0% (Table 1, Fig. 1A). However, once adjusted for the HBV+ population and HDV RNA positivity, due to the high burden of HBV, China had the highest absolute number of HDV RNA+ cases, represented by the largest blue circle (Table 1, Fig. 1A). In order to better examine the differences between countries and territories, Pakistan and Mongolia were excluded from Fig. 1B since they have significantly higher burden.

None of the countries included have implemented national-level laboratory-based reflex testing following an HBsAg+ test.

The anti-HDV prevalence estimates were then utilized to calculate how many HBsAg+ individuals need to be tested to find one anti-HDV+ case. Results showed that Mongolia would only need to test 1.6 HBV+ individuals to find 1 anti-HDV+ case, but Hong Kong would need to test almost 667 individuals (Table 1, Fig. 2).

Of the 25 countries and territories reported, 13 had general population estimates published in the 2020 article by Stockdale *et al.*[9] The current study had higher estimates for France, Italy, Mongolia, and Pakistan but lower estimates for Brazil, Mainland China, England, Japan, Romania, and the USA when compared to Stockdale *et al.* (Fig. 3).[9] The results in the current study and the aforementioned study for Germany, Türkiye and Saudi Arabia were similar.

By country

Albania

The highest scoring study from Albania reported an anti-HDV prevalence of 9.0% among patients admitted to a hospital in Tirana.[17] Additional data were collected through discussions with the expert panel, and an overall anti-HDV prevalence of 3.3% was estimated by weighting the HBV-infected population by disease stage (supplementary information). The HDV RNA prevalence (in patients who were anti-HDV positive) was estimated to be 63% based on expert clinical experience.

Brazil

In Brazil, the prevalence of both HDV and HBV are highly dependent on the region in which an individual is from. While

Table 1. Anti-HDV and HDV RNA prevalence in 25 countries and territories.

Country/Territory	2023 HBsAg+	Literature % anti-HDV+	Adjusted % anti-HDV+	RNA+ cases	Adjusted HDV RNA+ prevalence	Adjusted HDV RNA+ cases	Anti-HDV tests to diagnose one case
Albania	183,000	9.0%	2.4%	4,400	62.5%	2,800	41.7
Brazil	1,025,000	3.2%	1.7%	17,400	75.3%	13,100	58.8
Bulgaria	169,000	8.6%	3.2%	5,400	80.0%	4,300	31.3
Canada	214,000	1.6%	3.0%	6,400	64.8%	4,100	33.3
China Mainland	78,548,000	1.2%	1.2%	942,600	66.6%	627,800	83.3
Colombia	302,000	5.2%	1.0%	3,000	69.9%	2,100	100.0
England	418,400	2.9%	1.0%	4,200	50.0%	2,100	100.0
France	142,000	1.8%	3.5%	5,000	75.0%	3,800	28.6
Germany	215,000	5.5%	3.0%	6,500	60.0%	3,900	33.3
Hong Kong	332,000	0.2%	0.2%	500	60.0%	300	666.7
Israel	129,000	6.5%	5.4%	7,000	47.0%	3,300	18.5
Italy	336,400	8.3%	3.4%	11,300	60.5%	6,800	29.7
Japan	926,000	8.5%	0.5%	4,600	40.8%	1,900	200.0
Korea, Republic of	1,360,000	0.3%	0.3%	4,100	54.0%	2,200	333.3
Mexico	116,000	2.4%	0.2%	300	69.9%	200	444.4
Mongolia	191,000	61.0%	61.0%	116,500	61.5%	71,600	1.6
Pakistan	3,762,000	16.6%	16.6%	624,500	85.0%	530,800	6.0
Portugal	110,000	12.6%	1.5%	1,700	72.9%	1,200	66.7
Romania	568,000	23.1%	2.9%	16,500	80.0%	13,200	34.5
Saudi Arabia	570,000	5.3%	4.0%	22,800	60.0%	13,700	25.0
Spain	208,000	5.2%	2.3%	4,800	72.9%	3,500	43.5
Sweden	31,000	3.8%	2.8%	900	75.0%	650	35.7
Taiwan	1,864,000	3.3%	0.9%	16,800	60.0%	10,100	111.1
Türkiye	1,962,000	2.8%	2.8%	54,900	68.0%	37,300	35.7
United States	1,650,000	6.0%	3.0%	49,500	66.0%	32,700	33.3

HDV, hepatitis delta virus.

many studies exist that provide estimates in the Amazon, a region with a high burden, fewer studies exist in the major population centers where the prevalence is quite low. The anti-HDV prevalence in the literature was found to be 3.2%. However, this was neither weighted by population nor HBV infections.[18] A previous analysis using data from 2016 and 2017 found that 0.6% of 5 million rapid HBsAg tests conducted among 15-69-year-olds across Brazil were HBsAg+ positive. After adjusting for regional populations and factoring in cases from various special populations (prisoners, drug users, sex workers, men who have sex with men, patients with HIV, patients on dialysis, army conscripts and indigenous peoples), the HBsAg+ prevalence among 15-69-year-olds was estimated to be 0.8%.[19–29] This was then combined with the regional estimates from the aforementioned published study to estimate an anti-HDV prevalence of 1.7%.[18] The details of these calculations can be found in the supplementary information. Based on Ministry of Health data, it was assumed that HDV RNA prevalence was 75%.[30]

Bulgaria

In Bulgaria, the only published study was conducted among patients with chronic liver disease in 1985, reporting an anti-HDV prevalence of 8.6%.[31] Recent unpublished clinical data provided by the expert panel was utilized to weigh the infected population by disease stage, resulting in an anti-HDV prevalence of 3.2% (supplementary information). The HDV RNA prevalence was estimated to be 80% based on unpublished clinical data.

Canada

Data were sparse for Canada, with an anti-HDV estimate of 1.6% from a 1986 study conducted in Western Canada.[32] After discussions with the expert panel, it was agreed upon to use the largest study to date, which is based on specialist referral testing to the National Microbiology Laboratory, and reports an anti-HDV prevalence of 3.0% from 2020-2021.[33,34] The HDV RNA prevalence was assumed to be 65% based on published national notification data.[33]

China, Mainland

In China, a study based on the national HBV serosurveys in 2006 and 2008 found an anti-HDV prevalence of 1.2%.[35] This was agreed to be representative by the expert panel. Based on their clinical experience, the expert panel estimated the HDV RNA prevalence to be 67%.

Colombia

The literature review resulted in one study with an anti-HDV prevalence of 5.2%.[36] However, this study was not representative of the general population, as it was conducted in higher prevalence regions as well as among risk groups such as indigenous peoples. There is a high heterogeneity of HBV and HDV infections in Colombia. We estimated HDV prevalence by dividing the number of delta patients under care in the public system (RIPS) by the number of HBV-infected individuals diagnosed (SIVIGILA).[37,38] The anti-HDV prevalence was found to be 1% (CI 0.6-1.2%). The expert panel estimated an anti-HDV prevalence of ∼1% based on their clinical experience. The HDV RNA prevalence was estimated to be 70% based on a published study from the Amazon.[39]

England

A Public Health England reported an anti-HDV prevalence of 2.9% from their sentinel surveillance system.[40] We estimated

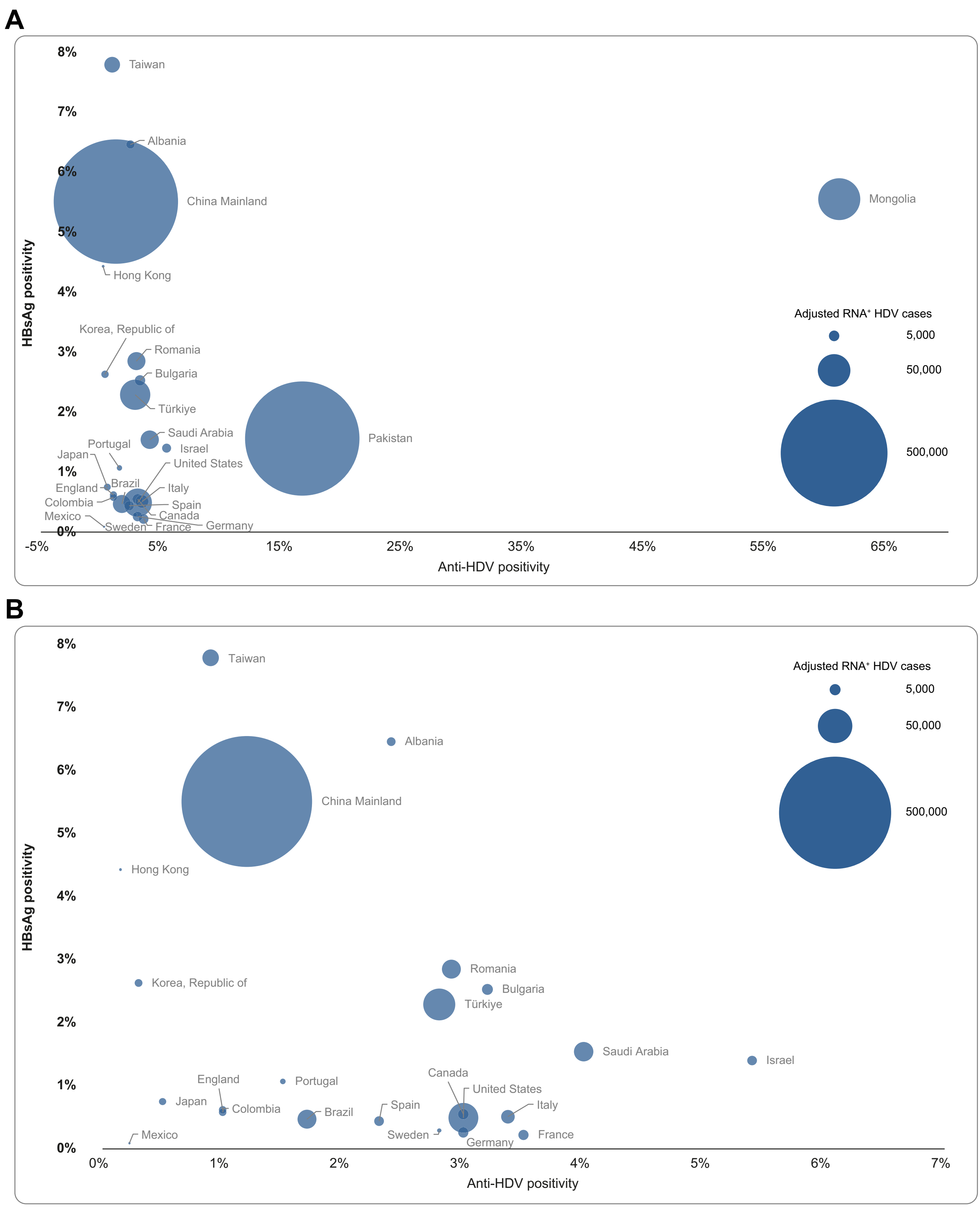

Fig. 1. HBsAg positivity, anti-HDV positivity and HDV RNA+ cases. (A) HBsAg positivity, anti-HDV positivity and HDV RNA+ cases in 25 selected countries and territories. (B) Excluding Pakistan and Mongolia. HBsAg, hepatitis B surface antigen; HDV, hepatitis delta virus.

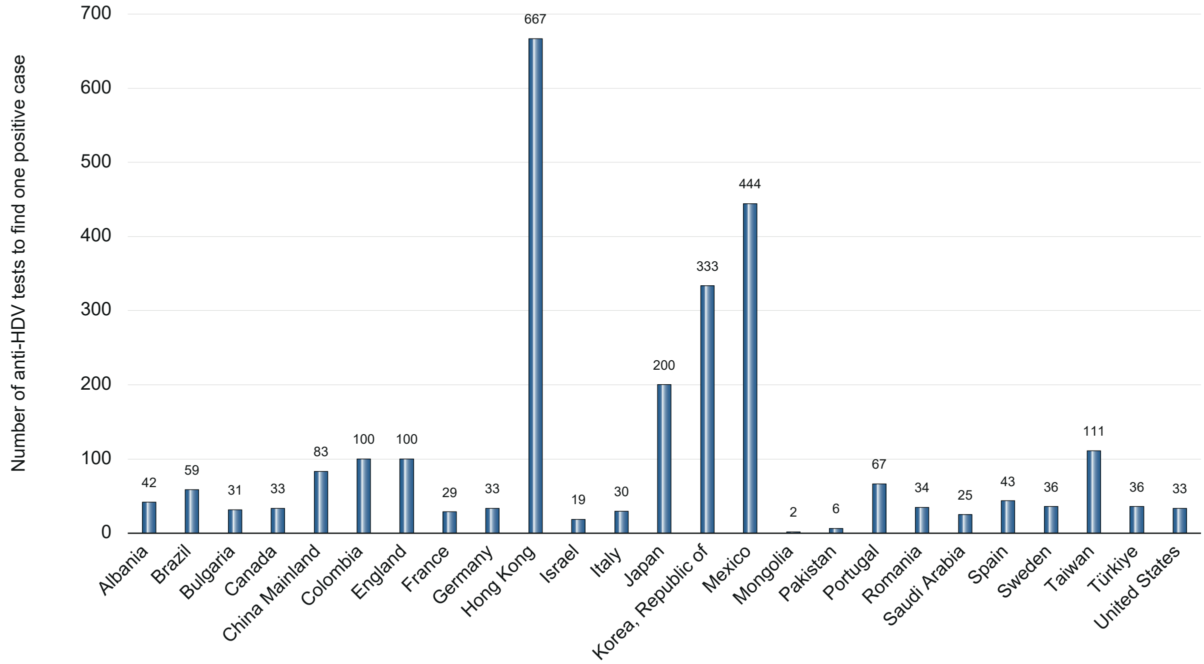

Fig. 2. Number of anti-HDV tests needed to find one positive case. HDV, hepatitis delta virus.

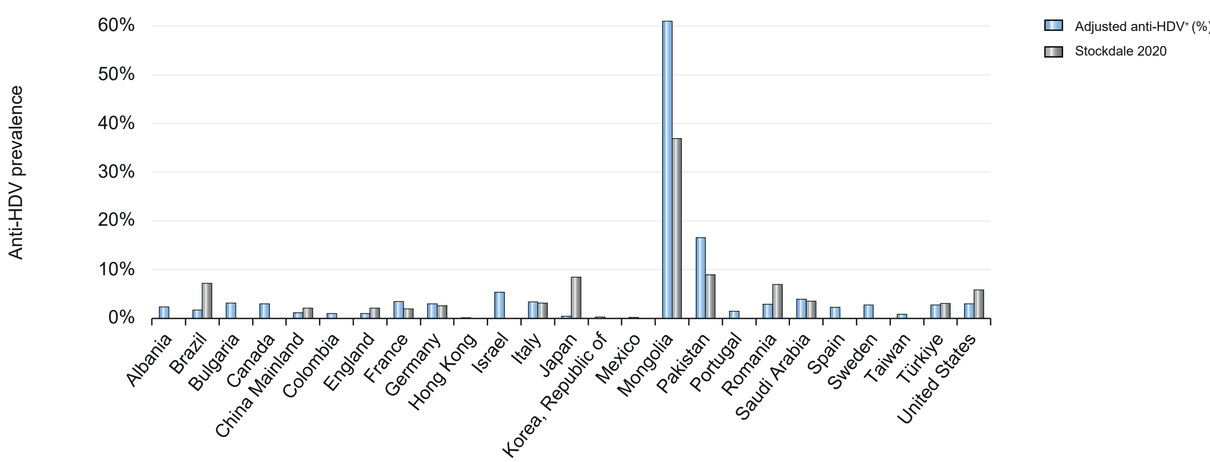

Fig. 3. Comparison of anti-HDV prevalence in current study and Stockdale 2020. HDV, hepatitis delta virus.

an anti-HDV prevalence of 1% and an HDV RNA prevalence of 50% based on expert clinical experience.

France

In 2011, a large study among blood donors found an anti-HDV prevalence of 2.0% in France.[41] When the data was discussed with the expert panel, it was found that over 30 centers in France participate in anti-HDV surveillance. The data from these centers indicate an anti-HDV prevalence of 3.5% and an HDV RNA prevalence of 75%.

Germany

The anti-HDV prevalence in Germany was initially estimated to be 5-6% based on two previously published studies.[42,43] Clinical experience and unpublished single-center data were used to estimate an anti-HDV prevalence of 3% in Germany. Based on expert clinical experience, the HDV RNA prevalence was estimated to be 60%. However, the ongoing migration movement (*e.g.*, due to the war in Ukraine), which may substantially impact HDV prevalence in Germany has not been factored into these estimates.

Hong Kong

HDV prevalence is known to be quite low in Hong Kong. The highest scoring study was a territory-wide assessment conducted between 2015-2016 which found a 0% prevalence among 803 HBV+ individuals.[44] In order to quantify prevalence, we used an older study based on data collected between 1988 and 1990 which found a prevalence of 0.15%.[45] The HDV RNA prevalence was estimated to be 60% based on clinical experience.

Israel

In Israel, the literature reported an anti-HDV prevalence of 6.5% among patients with HBV.[46] Based on data from the Clalit Health Services, which covers 52% of the Israeli population, the anti-HDV prevalence is 5.4% and the HDV RNA prevalence was estimated to be 47%.

Italy

Italy has a number of high-quality cohort studies among patients. The literature reports an anti-HDV prevalence of 8.3%.[47] However, since this study was conducted among a cohort of patients under care, this estimate needs to be weighted by the size of the population at the given disease stage. The anti-HDV prevalence estimates by stage of disease from these studies were combined with the Italian HBV PRoGReSs Model outputs, to estimate an anti-HDV-weighted average of 3.4% (supplementary information).[1,47,48] Based on data from the PITER cohort, the HDV RNA prevalence was estimated to be 61%.[49]

Japan

In Japan, anti-HDV prevalence was found to be 8.5% in one study on a single small island.[50] However, discussions with experts revealed that prevalence from this island is not representative of the national HDV prevalence in Japan. Expert consensus centered on an anti-HDV prevalence of 0.5%. The HDV RNA prevalence was estimated to be 41%.[50]

The Republic of Korea

In Korea, the anti-HDV prevalence of 0.3% from the literature was agreed to be representative by the expert panel.[51] The HDV RNA prevalence was assumed to be 54% based on expert consensus.

Mexico

In Mexico, the highest scoring study found a prevalence of 2.4%.[52] However, once it was reviewed with the experts, it was agreed that this figure was only representative of patients with cirrhosis under care. Thus, a weighted average based on disease stage was calculated resulting in an anti-HDV prevalence of 0.2% (CI 0.2-0.3%). The HDV RNA prevalence was assumed to be 70% based on expert clinical experience.

Mongolia

While many studies on HDV exist in Mongolia, the highest scoring study found an anti-HDV prevalence of 61.0% and an HDV RNA prevalence of 61.5% in 123 apparently healthy HBV-positive adults.[53]

Pakistan

The highest scoring study found an anti-HDV prevalence of 16.6%, although it was among patients visiting a tertiary hospital for liver-related symptoms. Similar prevalence has been found in a serosurvey conducted in Punjab.[54] Based on data from clinics around the country, it was estimated that the HDV RNA prevalence was 85%.

Portugal

In Portugal, an anti-HDV prevalence of 12.6% was found among diagnosed patients attending a hepatology clinic.[55] This value was deemed far too high by the expert panel, since there is believed to be a geographic component to the distribution of HDV in Portugal, driven by immigration. Based on unpublished studies, an anti-HDV prevalence of 1% was applied to the North of Portugal and the city of Lisbon. A range of 3-14% was found in unpublished studies, and so a point estimate of 5% was assumed to be representative of the South of Portugal (supplementary information). This results in an overall anti-HDV prevalence of 1.5%. We arrived at an HDV RNA prevalence of 73% based on expert consensus.

Romania

In Romania, the most prominent study reported an anti-HDV prevalence of 23.1%.[56] Discussions with experts revealed this to be representative of individuals who were hospitalized for HDV in 2011, and so would have already progressed to cirrhosis or a later disease stage. A national serosurvey is currently underway in the country, and the preliminary results from 20,000 individuals screened found an anti-HDV prevalence of 1% among the HBV-infected population. We applied the 23.1% prevalence to the population with cirrhosis or later stage disease in the Romanian PRoGReSs model, and the 1% prevalence to all other patients to get an overall weighted anti-HDV prevalence of 2.9%. Based on clinical experience, HDV RNA prevalence was estimated to be 80%.

Saudi Arabia

In Saudi Arabia, the literature reported an anti-HDV prevalence of 5.3%.[57] Based on expert opinion and clinical experience, it was estimated that the anti-HDV prevalence was 4%. HDV RNA prevalence was estimated to be 60% based on a 2017 publication.[57]

Spain

A 2020 study in Spain found an anti-HDV prevalence of 5.2% among 2,888 patients in teaching hospitals.[58] Spain also recently published a large national serosurvey to estimate the prevalence of HDV. However, there were concerns that the study did not consider the prevalence among specific risk groups such as sex workers, HIV+ individuals, prisoners, injection drug users, and immigrants from Africa. We applied the serosurvey data to the Spanish population less the risk groups, for whom different prevalence estimates were applied, to reach an overall anti-HDV prevalence of 2.3% (supplementary information). HDV RNA prevalence was estimated to be 73% based on a published patient cohort.[58]

Sweden

In Sweden, a study conducted between 1997-2008 estimated that 3.8% of the population accessing healthcare for chronic HBV were positive for anti-HDV.[59] National notification data from 1990 to 2021 for individuals with residency status and an identification number reported an anti-HDV prevalence of 2.0% and an HDV RNA prevalence of 75%. Based on their clinical experience, Swedish experts believe anti-HDV prevalence might be higher in the migrant population without residency status. An undiagnosed population of approximately 200-300 HDV RNA+ Mongolian migrants are believed to live in the Stockholm region. An anti-HDV prevalence of 2.8% has therefore been estimated.

Taiwan

Two hospital-based studies found an anti-HDV prevalence of 4.4% in Taiwan.[60,61] Other data such as the older REVEAL cohort data and recent Taiwan Biobank data were also reviewed.[62] Based on the triangulation of these sources, the anti-HDV prevalence was estimated to be 0.9% in Taiwan, with an HDV RNA prevalence of 60%.

Türkiye

In Türkiye, an anti-HDV prevalence of 2.8% was found among 5,533 volunteers screened between 2009-2010.[63] This was deemed to be representative of the national prevalence by the expert panel. The HDV RNA prevalence was assumed to be 68%, based on a study among blood donors in South-eastern Türkiye.[64]

USA

In the United States, the 1999-2012 National Health and Nutrition Examination Survey reported an anti-HDV prevalence of 6%.[65,66] The expert panel came to a consensus, supported by data from Veteran's Affairs and electronic medical records, that the overall anti-HDV prevalence in the USA is approximately 3%.[67,68] Based on clinical experience, it was estimated that the HDV RNA prevalence was 66%.

Discussion

Many published HDV prevalence studies are conducted among groups who have a higher probability of being infected with HDV, such as patients in tertiary care centers, specific risk groups, or high-prevalence regions. When available data are weighted by population size at the national level, the HDV prevalence often decreases. Thus, literature reviews may result in a higher prevalence estimate than is likely to be seen in the general population. Our approach in this study focused on leveraging the best available HDV data in a country or territory in order to determine the best possible estimate at the national/territorial population level. However, there is a vast heterogeneity in the type of data available and the most common, anti-HDV+ data, is a poor marker of active HDV infection as evidenced by the wide variance (40%-85%) in HDV RNA positivity rates. Although new treatments have become available in some regions, HDV continues to be neglected in research and as a priority in public health policy setting. For example, the global health sector strategies on HIV, viral hepatitis and sexually transmitted infections mention the need to increase awareness, diagnostics, and treatment options for HDV, but define no indicators to be measured and set no targets.[69] Thus, there is clearly a strong need to improve medical education among physicians and nurses regarding this disease and the significant associated morbidity among infected individuals.

A couple of different factors drove high prevalence in countries like Brazil, Mainland China, England, Japan, Romania, and the USA which, in the study by Stockdale and co-authors, reported higher percentages compared to the current study.[9] Brazil, Mainland China, and Japan all have regions with substantially higher prevalence of HDV than the national/territorial average. While these high-prevalence regions are important and should be part of elimination efforts, they are small in terms of population size and thus do not have a large impact on the national/territorial prevalence at the population level.

In England, the published sentinel surveillance data came from high-risk groups and are not representative of what clinicians see in their practice. This explains the lower prevalence presented here. Meanwhile, the national study from the USA has a very small sample size: 168 (supplementary information). Thus, other studies with larger sample sizes were chosen to be more representative and in line with what is seen by clinicians.

The studies cited for the general population in Romania in the Stockdale 2020 study were both 0%. We assumed that the prevalence among hospitalized patients was also considered, thus leading to the overestimate in Stockdale.

The estimates for France, Italy, Mongolia, and Pakistan in the current paper were higher than those reported by Stockdale 2020.[9] In France, the expert panel agreed that the national study was not representative of what they see clinically. For Italy, our study used a weighted average of prevalence by disease stage, whereas Stockdale used an undefined weighting system that appears to be similar to that which they used for Romania. There exists a great deal of uncertainty in the HDV prevalence in Mongolia and Pakistan, with the local experts agreeing that the estimates in our paper are representative of the current data.

The current approach allowed for the collection and reporting of data for countries and territories that have not been included with specific general population data in previous analyses. The flexible approach that was undertaken is a strength of the study; however, it can also be a limitation as the exact same populations are not being utilized and compared across countries and territories. While anti-HDV and HDV RNA positivity were the indicators utilized, there exist many different diagnostics with varying sensitivity and specificity. This likely contributes to the wide variability in the reported proportions of anti-HDV+ cases that are HDV RNA+ and can result in heterogeneity between estimates within a country or territory. These differences may also be due to the predominate modes of transmission in a country, as adults who acquire HBV and HDV simultaneously have a much higher probability of clearing both viruses when compared to individuals who acquire HDV via superinfection.[70]

Another limitation of this study is that none of the countries and territories included were in sub-Saharan Africa or the Pacific Island countries. Both of these regions have had reports of high anti-HDV prevalence that require additional investigation.

Additional research is necessary to better understand the burden of HDV on the total population at the national/territorial level. However, while HBV and HDV serosurveys in the general population can provide strong insights, there is already a large population of HBV-diagnosed individuals, some of whom may be infected with and progressing from HDV. Implementing laboratory reflex testing would increase the knowledge base on HDV prevalence, while also allowing for earlier identification and linkage to care for HDV RNA+ individuals.[71] While this method would not overcome the bias towards a higher prevalence in the absence of a national screening program, as those being diagnosed with hepatitis B are often more likely to have already progressed to later liver disease stages and thus are more likely to be infected with HDV. It would, nonetheless, overcome the major shortcoming currently inherent in notification systems. Since this intervention would only be testing those who are already found to be HBsAg+, the cost would be much lower than a national serosurvey and thus an approach scalable to many different countries and resource settings. However, cost-effectiveness analyses are needed to empirically provide support to these claims.

The number of HBV+ individuals who need to be tested to find one new anti-HDV case can help inform these decisions. This number could be decreased by focusing on the groups and regions that are well known to have a higher probability of anti-HDV+ cases. In countries/territories with a low HBV prevalence, the cost burden of screening for anti-HDV is expected to be low, as the absolute number of individuals who would need to be screened would be relatively small. However, a detailed cost-effectiveness study would be required for countries/territories with a high HBV burden and a low anti-HDV prevalence, such as the East Asian countries presented here.

Concentrating on specific risk groups and regions such as individuals with cirrhosis, the Amazon region, HIV+ individuals, and immigrants from endemic countries can reduce the number of tests needed to find a positive case. However, recent data has shown that this method can miss upwards of 60% of those infected with HDV.[15]

The countries and territories included in the current analysis only represent 37% of the HBV-infected population globally, and the analysis resulted in a much lower anti-HDV prevalence, 2.0%, than previously reported. Expanding these methods to other countries, particularly in sub-Saharan Africa, will be integral to better understanding the burden of HDV globally and thus helping local, regional, and global partners to work towards the elimination of this devastating disease.

Abbreviations

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HDV, hepatitis D virus.

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Conflict of interest

DMR-S, KR-S, AV, and HAR are employees of the CDAF. The CDAF has received funding from the John C Martin Foundation, ZeShan Foundation, The Hepatitis Fund, Gilead Sciences, and AbbVie. AA reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Abbvie, Gilead Sciences, MSD, Sobi, Intercept and Mylan. SA reports payment or honoraria for lectures and educational events from Gilead, AbbVie, MSD, Biogen, not related to this work. TA reports honoraria from consulting for Gilead Sciences, Antios therapeutics, Eiger Biopharmaceutical, Janssen, GSK, and Vir Biotechnology; honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Gilead Sciences, Antios therapeutics, Eiger Biopharmaceutical, Janssen, GSK, and Vir Biotechnology; support for attending meetings and/or travel from Gilead Sciences and Abbvie, and advisory board of ENYO. 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Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

DMR-S and HR conceived the study. DMR-S designed the methodology and was responsible for project administration. DMR-S and HR supervised the study. DMR-S, HR, and KR-S did the formal analysis. HR acquired funding. DMR-S was responsible for data visualization. DMR-S and HR wrote the original draft. DMR-S, HR, and KR-S had access to the underlying data and models. DMR-S, KR-S, HC, ASV, and HR accessed and verified the data. All authors curated data. All authors validated data. All authors reviewed and edited the manuscript. All authors had full access to the data for their country and accepted responsibility to submit for publication.

Data availability statement

The sources of all underlying data and modeling assumptions can be found in the Supplementary Materials. These data can also be found at The Polaris Observatory, https://cdafound.org/dashboard/polaris/. For additional inquiries please contact the authors within 1 year of publication.

Supplementary data

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Supplemental information

Adjusted estimate of the prevalence of hepatitis delta virus in 25 countries and territories

The Polaris Observatory Collaborators

Adjusted estimate of the prevalence of hepatitis delta virus in 25 countries and territories

The Polaris Observatory Collaborators

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Literature search findings

HDV RNA Normalized was a category created normalize studies in which the overall prevalence of anti-HDV and HDV-RNA are reported, but not the portion of anti-HDV positive that are HDV RNA positive. This was done in order to make comparable comparisons across countries. For example, Yolcu 2019 reports an anti-HDV prevalence of 4.1% and an HDV RNA positivity of 2.4%. The authors took 2.4%/4.1% to come to the HDV normalized value of 58.53%.

Country	Year of Estimate	Population	Scope	Scope Size	Surveillance Type	Sample (n)	anti-HDV Prevalence	HDV RNA	HDV RNA Normalized	Source	Combined Score
Albania	1991-1994	Pregnant Women	Urban	Hospital/Clinic/School	Surveillance	67	2.99%	-	-	**(Malamitsi-Puchner et al., 1996)**	1
Albania	2005	Patients	Urban	Hospital/Clinic/School	Surveillance	78	8.97%	-	-	**(Kondili et al., 2010)**	1
Brazil	2013	General Population	Rural	City	Surveillance	623	0.16%	-	-	**(Antonio Ferreira-Junior et al., 2020)**	2
Brazil	2011–2012	General Population	Rural	City	Surveillance	923	-	-	-	**(Caetano et al., 2020)**	2
Brazil	2012–2013	Patients	Rural	Hospital/Clinic/School	Surveillance	498	6.22%	-	-	**(Scarponi et al., 2019)**	1
Brazil	2010–2014	Patients	Rural	Hospital/Clinic/School	Surveillance	409	23.90%	-	-	**(Melo Da Silva et al., 2019)**	1
Brazil	2011–2017	Multiple Groups	Urban/Rural	Region	Surveillance	948	0.30%	-	-	**(Villar et al., 2018)**	2
Brazil	2013–2015	General Population	Urban/Rural	National	Surveillance	1240	3.20%	-	-	**(Lago et al., 2018)**	3
Brazil	2015–2016	Patients	Urban	Hospital/Clinic/School	Surveillance	117	1.70%	-	-	**(Pierre et al., 2018)**	1
Brazil	2014*	Patients	Urban	Hospital/Clinic/School	Surveillance	92	8.70%	-	-	**(Santos et al., 2016)**	1
Brazil	2011–2012	General Population	Rural	Region	Surveillance	467	-	-	-	**(Caetano et al., 2015)**	3
Brazil	2003–2009	Blood Donors	Unknown	Region	Surveillance	130	8.50%	-	-	**(Crispim et al., 2014)**	1
Brazil	2006–2008	General Population	Rural	Unknown	Surveillance	86	65.12%	-	-	**(Dias, Oliveira, Castilho Mda, Silva Mdo, & Braga, 2012)**	1
Brazil	2005–2006	General Population	Rural	City	Surveillance	86	65.10%	-	-	**(Braga et al., 2012)**	1
Brazil	2006–2007	Patients	Urban	Multi-City	Surveillance	3259	1.20%	-	-	**(Mendes-Correa et al., 2011)**	1
Brazil	2008-2010	Patients	Urban	Hospital/Clinic/School	Surveillance	133	3.80%	2.30%	60.53%	**(Barros et al., 2011)**	1
Brazil	2002	General Population	Urban/Rural	Region	Surveillance	2656	1.80%	-	-	**(Souto, 2004)**	2

Country	Year of Estimate	Population	Scope	Scope Size	Surveillance Type	Sample (n)	anti-HDV Prevalence	HDV RNA	HDV RNA Normalized	Source	Combined Score
Brazil	1997	General Population	Rural	Region	Surveillance	18	66.60%	-	-	**(de Paula, Arruda, Vitral, & Gaspar, 2001)**	2
Brazil	1986*	General Population	Rural	Multi-City	Surveillance	96	34.40%	-	-	**(Fonseca et al., 1988)**	2
Brazil	2014–2016	Patients	Rural	Hospital/Clinic/School	Other/Unknown	112	-	-	-	**(Oliveira et al., 2019)**	1
Brazil	2016*	General Population	Rural	Region	Model	0	-	-	-	**(Goyal & Romero-Severson, 2018)**	2
Brazil	1999–2018	General Population	Urban/Rural	National	Surveillance	3984	-	75.30%	75.30%	**(Ministry of Health Brazil, 2019)**	3
Bulgaria		Patients	Unknown	Unknown	Surveillance	105	8.60%			**(Naoumov, Gueorgiev, Ognyanov, & Maleev, 1986)**	0
Canada	1984	Patients	Urban/Rural	Multi-Region	Surveillance	245	1.60%	-	-	**(Cheng, Wang, & Minuk, 1986)**	0
China	2010–2013	Patients	Urban	Hospital/Clinic/School	Surveillance	225	-	4.89%	-	**(Wu et al., 2020)**	1
China	2014	General Population	Urban	Hospital/Clinic/School	Surveillance	672	0.30%	-	-	**(Chen et al., 2017)**	2
China	2005–2011	Patients	Urban	Hospital/Clinic/School	Surveillance	6604	6.50%	-	-	**(Liao et al., 2014)**	1
China	1992–1998	General Population	Urban/Rural	Region	Surveillance	657	2.10%	-	-	**(Li, He, & Zhao, 1998)**	2
China	2006–2008	General Population	Urban/Rural	National	Surveillance	1486	1.20%	-	-	**(Shen et al., 2012)**	3
Colombia	2011	Patients	Urban/Rural	Multi-City	Surveillance	173	5.20%	-	-	**(Alvarado-Mora et al., 2011)**	1
France	2004–2015	Children/Youth	Urban	Hospital/Clinic/School	Surveillance	36	-	-	-	**(Sellier et al., 2018)**	1
France	1997–2011	Blood Donors	Urban/Rural	National	Surveillance	4492	1.98%	22.9%	-	**(Servant-Delmas, Le Gal, Gallian, Gordien, & Laperche, 2014)**	2
France	2012-2022	Patients	Urban	Hospital/Clinic/School	Surveillance	2886	6.00%	61.1%		**(Brichler; et al., 2022)**	1
Germany	2000–2011	Patients	Urban	Hospital/Clinic/School	Surveillance	2844	7.40%	-	-	**(Reinheimer, Doerr, & Berger, 2012)**	1
Germany	2009	Patients	Unknown	Hospital/Clinic/School	Surveillance	410	6.80%	-	-	**(Bissinger & Berg, 2013)**	1
Germany	2011	Pregnant Women	Unknown	Hospital/Clinic/School	Surveillance	243	2.50%	-	-	**(Bissinger & Berg, 2013)**	1
Germany	1992–2006	Patients	Urban	Hospital/Clinic/School	Surveillance	2363	10.90%	64.00%	-	**(Heidrich et al., 2009)**	1
Hong Kong	1988-1990	Patients	Urban	Hospital/Clinic/School	Surveillance	664	0.15%			**(Lok et al., 1992)**	0
Hong Kong	2015-2016	General Population	Urban/Rural	National	Surveillance	803	0.00%			**(Liu et al., 2019)**	3

Country	Year of Estimate	Population	Scope	Scope Size	Surveillance Type	Sample (n)	anti-HDV Prevalence	HDV RNA	HDV RNA Normalized	Source	Combined Score
Israel	2010–2015	Patients	Urban/Rural	National	Surveillance	8969	6.50%	24%	-	**(Shirazi et al., 2018)**	1
Italy	2007–2008	General Population	Urban	Region	Surveillance	488	4.90%	-	-	**(De Paschale et al., 2012)**	2
Italy	2012–2015	Patients	Urban	Multi-Hospital/Clinic/School	Surveillance	2877	8.30%	-	-	**(Brancaccio et al., 2019)**	1
Italy	2005–2007	General Population	Unknown	City	Surveillance	2195	0%	-	-	**(Cozzolongo et al., 2009)**	2
Italy	2007–2008	General Population	Urban	Region	Surveillance	488	4.90%	-	-	**(De Paschale et al., 2012)**	2
Italy	2004–2006	Patients	Urban	Multi-Hospital/Clinic/School	Surveillance	559	5.30%	54%*	-	**(Piccolo et al., 2010)**	1
Italy	2019	Patients	Urban	Multi-Hospital/Clinic/School	Surveillance	786	9.90%	77.80%	-	**(Stroffolini et al., 2020)**	1
Italy	2000-2019	Patients	Urban	Hospital/Clinic/School	Surveillance	2003	5.60%	86.5%		**(Ricco et al., 2023)**	1
Japan	1996	General Population	Urban	City	Surveillance	375	8.50%	3.47%	40.82%	**(Arakawa et al., 2000)**	1
Japan	1994–1995	General Population	Rural	Region	Surveillance	195	23.60%	-	-	**(Sakugawa et al., 1997)**	2
Mexico		Patients	Unknown	Hospital/Clinic/School	Surveillance	85	2.35%			**(Ayala Gaytan, Casillas Romo, & Romero Gonzalez, 1989)**	0
Mexico		Pregnant Women	Unknown	Hospital/Clinic/School	Surveillance	4	0.00%			**(Ortiz-Ibarra, Figueroa-Damian, Lara-Sanchez, Arredondo-Garcia, & Ahued-Ahued, 1996)**	0
Mexico		Patients	Unknown	Hospital/Clinic/School	Surveillance	73	4.0%			**(Munoz Espinosa & Ibarra Salas, 1997)**	0
Mongolia	2002	General Population	Urban/Rural	City	Surveillance	24		83.00%		**(Takahashi et al., 2004)**	1
Mongolia	2002	General Population	Urban/Rural	City	Surveillance	24	91.70%	90.91%		**(Inoue et al., 2005)**	1
Mongolia	2013	General Population	Urban/Rural	National	Surveillance	123	60.98%	61.45%		**(Delgersaikhan Zulkhuu, 2016)**	3
Mongolia	2009	General Population	Urban/Rural	Multi-Region	Surveillance	361	91.69%			**(Dambadarjaa et al., 2022)**	3
Pakistan	1994-2001	General Population	Urban/Rural	National	Surveillance	8721	16.60%			**(Mumtaz et al., 2005)**	3
Pakistan	2007-2011	Patients	Urban	Hospital/Clinic/School	Surveillance	374	28.10%			**(Abbasi, Bhutto, Butt, & Mahmood, 2014)**	1
Pakistan	2016-2017	Pregnant Women	Urban	Multi-Hospital/Clinic/School	Surveillance	63	20.63%	30.80%		**(Aftab et al., 2019)**	2

Country	Year of Estimate	Population	Scope	Scope Size	Surveillance Type	Sample (n)	anti-HDV Prevalence	HDV RNA	HDV RNA Normalized	Source	Combined Score
Pakistan	2020	Patients	Urban	Hospital/Clinic/ School	Surveillance	102		0.98%		**(Ali Khan et al., 2021)**	1
Portugal	1989-1992	Patients	Urban	Hospital/Clinic/ School	Surveillance	532	12.59%			**(Velosa, Ramalho, Serejo, Marinho, & de Moura, 1993)**	0
Portugal	2003-2004	Patients	Urban	Multi-Hospital/Clinic/ School	Surveillance	735	3.50%			**(Carniero de Moura, 2008)**	1
Portugal		Patients	Urban	Hospital/Clinic/ School	Surveillance	354	6.50%	-	-	**(Gamelas, 2021)**	1
Portugal		Patients	Urban	Hospital/Clinic/ School	Surveillance	580	3.40%	-	-	**(Garrido, 2022)**	1
Portugal	2012-2022	Patients	Urban	Hospital/Clinic/ School	Surveillance	835	6.50%	-	-	**(da Costa Coelho, 2023)**	1
Republic of Korea	2008–2010	Patients	Urban	Hospital/Clinic/ School	Surveillance	940	0.32%	-	-	**(Kim et al., 2011)**	1
Romania	2011	Patients	Urban/Rural	National	Surveillance	2761	23.10%	-	-	**(Gheorghe et al., 2015)**	1
Romania	2011	Students	Unknown	Region	Surveillance	44	0%	-	-	**(Iliescu, 2013)**	2
Romania	2011	HCW	Unknown	Region	Surveillance	93	0%	-	-	**(Iliescu, 2013)**	2
Romania	2006	Patients	Urban	Hospital/Clinic/ School	Surveillance	1094	20.40%	-	-	**(Popescu et al., 2013)**	1
Romania	2008	General Population	Unknown	Region	Surveillance	142	-	-	-	**(Voiculescu et al., 2010)**	2
Saudi Arabia	2013–2015	Patients	Urban	Hospital/Clinic/ School	Surveillance	169	5.30%	-	-	**(Jamjoom et al., 2017)**	1
Saudi Arabia	1997	Patients	Urban	Multi-Hospital/Clinic/ School	Surveillance	780	8.60%	-	-	**(Al-Traif, Ali, Dafalla, Al-Tamimi, & Qassem, 2004)**	0
Spain	2005–2018	Patients	Urban	Multi-Hospital/Clinic/ School	Surveillance	2888	5.20%	73.00%	-	**(Palom et al., 2020)**	1
Spain	1983-2012	Patients	Urban	Hospital/Clinic/ School	Surveillance	1215	8.20%	-	-	**(Ordieres et al., 2017)**	1
Sweden	1997–2008	Patients	Urban/Rural	National	Surveillance	9160	3.80%	-	-	**(Ji, Sundquist, & Sundquist, 2012)**	1
Sweden	2000–2005	Patients	Urban/Rural	National	Surveillance	337	-	69.1%	-	**Unpublished Data**	2
Sweden	1990-2015	Patients	Urban/Rural	National	Surveillance	16,410	1.2%	-	-	**(Duberg, Lybeck, Falt, Montgomery, & Aleman, 2022)**	3
Taiwan	1991-1992	General Population	Urban	Multi-City	Surveillance	3,239	2.13%	-	-	**(M. H. Lee et al., 2014)**	2
Taiwan	2006–2019	Patients	Urban	Hospital/Clinic/ School	Surveillance	1147	4.40%	-	-	**(K. C. Lee et al., 2020)**	1
Taiwan	2001–2012	Patients	Urban/Rural	Multi-Hospital/Clinic/ School	Surveillance	2029	4.40%	43.30%	43.30%	**(Lin et al., 2015)**	1

Country	Year of Estimate	Population	Scope	Scope Size	Surveillance Type	Sample (n)	anti-HDV Prevalence	HDV RNA	HDV RNA Normalized	Source	Combined Score
Taiwan	2018*	Other/Unknown	Unknown	Unknown	Surveillance	2850	2.70%	0.90%	33.33%	**(Jang et al., 2020)**	1
Taiwan	2008*	General Population	Rural	Other	Surveillance	26	3.84%	-	-	**(Chang, Chiang, Lu, & Wang, 2010)**	1
Turkey	2012–2014	Patients	Urban/Rural	Region	Surveillance	1118	15.30%	19.90%	-	**(Dulger et al., 2016)**	1
Turkey	2009–2010	General Population	Urban/Rural	Region	Surveillance	218	2.80%	-	-	**(Tozun et al., 2015)**	2
Turkey	2011	Other/Unknown	Urban/Rural	National	Surveillance	7871	5.90%	-	-	**(Kemal Celen et al., 2014)**	1
Turkey	2010–2011	Blood Donors	Urban	Hospital/Clinic/School	Surveillance	88	3.40%	2.30%	67.65%	**(Uzun, Sener, Gungor, Afsar, & Demirci, 2014)**	1
Turkey	2012*	Blood Donors	Urban	Hospital/Clinic/School	Surveillance	186	6.98%	15.39%	-	**(Mese, Nergiz, Tekes, & Gul, 2014)**	1
Turkey	2007–2009	Patients	Urban	Hospital/Clinic/School	Surveillance	3094	2.50%	-	-	**(Kose, Ece, Gozaydin, & Turken, 2012)**	1
Turkey	2015-2019	Patients	Urban	Hospital/Clinic/School	Surveillance	2548	2.90%	33.30%	-	**(Ergen, 2020)**	1
Turkey	2015-2017	Patients	Urban	Multi-City	Surveillance	2089	4.10%	2.40%	58.53%	**(Yolcu, 2019)**	1
England	2016*	Patients	Urban	City	Surveillance	991	1.60%	-	-	**(Jackson et al., 2018)**	1
England	2016*	Patients	Urban	City	Surveillance	142	4.90%	-	-	**(Jackson et al., 2018)**	1
England	2019	Patients	Urban/Rural	Multi-Region	Surveillance	1119	1.9%			**(England, 2020)**	1
England	2005–2010	Blood Donors	Urban/Rural	Region	Surveillance	344	2.03%	-	-	**(Rosenberg et al., 2013)**	1
England	2008–2012	Patients	Urban	Hospital/Clinic/School	Surveillance	1048	2.10%	1.43%	68%	**(William Tong et al., 2013)**	1
United States	2011–2016	General Population	Urban/Rural	National	Surveillance	113	42.00%	-	-	**(Patel, Thio, Boon, Thomas, & Tobian, 2019)**	3
United States	1999–2012	General Population	Urban/Rural	National	Surveillance	168	6.00%	-	-	**(Njei, Do, & Lim, 2016; Roberts et al., 2016)**	3
United States	1999–2013	Soldiers	Urban/Rural	National	Surveillance	2008	3.60%	-	-	**(Kushner, Serper, & Kaplan, 2015)**	2

* Year of publication less two years

Adjusted prevalence calculations

Albania

Patient Group	HBV Prevalence - Modeled Outputs	% Anti-HDV	Source	Anti-HDV+
CHB	178,370	2.7%	(Malamitsi-Puchner et al., 1996) PITER Cohort Albanian Refugees	4,741
Cirrhosis	10,573	8.5%	(Kondili et al., 2010; Sadiku, 2012)	899
Decompensated Cirrhosis	801	40%	PITER Cohort Albanian Refugees	320
HCC	835	40%	PITER Cohort Albanian Refugees	334
Total Infected	**190,579**	**3.3%**		**6,294**

Brazil

Location	Population (n)	% HBV+	HBV+	Lago 2018 anti-HDV Regional Data	Anti-HDV+
Acre	816,687	1.09%	8,925	8.50%	759
Amapa	782,295	0.10%	812	8.50%	69
Amazonas - Total	4,001,667	0.9%	36,857	8.50%	3,133
Para - Total	8,305,359	0.3%	25,184	8.50%	2,141
Roraima	514,229	0.6%	3,327	8.50%	283
Rondonia	1,787,279	1.4%	24,182	8.50%	2,055
Tocantins	1,532,902	0.2%	3,504	8.50%	298
Alagoas	3,358,963	1.6%	54,967	0.80%	440
Ceara	8,963,663	0.2%	18,778	0.80%	150
Maranhao	6,954,036	2.3%	159,943	0.80%	1,280
Paraiba	3,999,415	0.4%	14,775	0.80%	118
Piaui	3,212,180	0.0%	1,123	0.80%	9
Pernambuco	9,410,336	0.3%	25,614	0.80%	205
Rio Grande do Norte	3,474,998	2.1%	72,748	0.80%	582
Sergipe	2,265,779	0.4%	8,995	0.80%	72
Minas Gerais	20,997,560	1.0%	207,198	1.70%	3,522
Espirito Santo	3,973,697	0.3%	13,506	1.70%	230
Rio de Janeiro	16,635,996	1.5%	247,375	1.70%	4,205
Sao Paulo - Total	44,749,699	0.3%	117,448	1.70%	1,997
Distrito Federal	2,977,216	0.0%	51	2.50%	1
Goias	6,695,855	0.2%	15,769	2.50%	394
Mato Grosso do Sul	2,682,386	0.7%	19,326	2.50%	483
Mato Grosso	3,305,531	0.7%	24,703	2.50%	618
Parana	11,242,720	0.8%	88,987	-	0
Rio Grande do Sul	11,286,500	0.2%	27,785	-	0
Population-weighted	**206,114,100**	**0.67%**	**1,388,700**	**1.7%**	**13,600**

Bulgaria

Patient Group	HBV Prevalence - Modeled Outputs	% Anti-HDV	Source	Anti-HDV+
CHB	168,025	3.10%	Unpublished Clinical Data	5,209
Cirrhosis	14,802	3.80%	Unpublished Clinical Data	562
Decompensated Cirrhosis	1,257	5.40%	Unpublished Clinical Data	68

HCC	1,202	5.40%	Unpublished Clinical Data	65
Liver Transplant	10	5.40%	Unpublished Clinical Data	1
Total Infected	**185,294**	**3.2%**		**5,905**

Italy

Patient Group	HBV Prevalence - Modeled Outputs	% Anti-HDV	Source	Anti-HDV+
CHB	266,082			
Normal ALT, <2K	115,214	0.50%	ICEBERG	576
Normal ALT, >2k	33,526	1.70%	(Stroffolini et al., 2020)	570
ALT>ULN	117,342	3.14%	(Brancaccio et al., 2023) and Dr. Brunetto's cohort	3,680
Cirrhosis	30,932	17.50%	(Brancaccio et al., 2019)	5,413
Decompensated Cirrhosis	871	17.50%	(Brancaccio et al., 2019)	152
HCC	1,389	17.50%	(Brancaccio et al., 2019)	243
Liver Transplant	2,311	30.00%	(Brancaccio, Vitale, Signoriello, Gaeta, & Cillo, 2020)	693
Total Infected	**336,414**	**3.37%**		**11,330**

Portugal

Region	Population(n)	% Anti-HDV	Source	Anti-HDV+
North	5,813,825	1%	Jose Presa's center	58,138
South	1,171,876	5%	(da Costa Coelho, 2023; Gamelas, 2021)	58,594
Lisbon	2,870,208	1%	Jose Presa's center	28,702
Total	**9,855,909**	**1.48%**		**145,434**

Romania

Population	HBV+	% Anti-HDV	Source	Anti-HDV+
Non-cirrhotic population	569,300	1%	Unpublished National Serosurvey	5,690
Cirrhosis or greater	52,900	23.1%	(Gheorghe et al., 2015)	12,160
Total	**622,100**	**2.9%**		**17,860**

Spain

Population	Population (n)	% HBV+	Source	% anti-HDV+	Source	HBV+	anti-HDV+
General population	44,563,113	0.47%	Modeling Output	1.20%	MOH 2021	209,447	2,513
Sex Workers	68,894	4.60%	(Bratos et al., 1993)	11.80%	(Bratos et al., 1993)	3,169	374
MSM	789,607			-	Leon 1993	-	-
HIV+	150,000	4.80%	(Gonzalez-Garcia et al., 2005)	44.40%	(Arribas et al., 2005)	7,200	3,197
Prisoners	52,408	1.20%	(Saiz de la Hoya, Marco, Garcia-Guerrero, & Rivera, 2011)	37.50%	(Bayas et al., 1990)	629	236
IDUs	8,352	6.40%	(Aguilera et al., 2018)	4.20%	(Aguilera et al., 2018)	535	22
Immigrants							
North Africa (Magreb)	883,086	9.39%	(Cuenca-Gomez et al., 2016)	0%	(Cuenca-Gomez et al., 2016)	82,922	-

Sub-Saharan Africa	239,323	9.90%	(Picchio et al., 2021)	4.80%	(Cuenca-Gomez et al., 2016)	23,693	1,137
Total	**46,754,783**	**0.7%**		**2.3%**		**327,600**	**7,500**

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