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INDEXING/ABSTRACTING

The WJH is now abstracted and indexed in PubMed, PubMed Central, Emerging Sources Citation Index (Web of Science), Scopus, China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database.

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Responsible Electronic Editor: *Mei-Yi Lin*

Proofing Production Department Director: *Yun-Xiaojuan Wu*

Responsible Editorial Office Director: *Ruo-Yu Ma*

NAME OF JOURNAL

World Journal of Hepatology

ISSN

ISSN 1948-5182 (online)

LAUNCH DATE

October 31, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Ke-Qin Hu, Koo Jeong Kang, Nikolaos Pyrsopoulos

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-5182/editorialboard.htm>

PUBLICATION DATE

June 27, 2020

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

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<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Case Control Study

Changing delta hepatitis patient profile: A single center experience in Valencia region, Spain

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Author contributions: Hernández-Èvole H performed the research and wrote the manuscript; Berenguer M designed the study and corrected the manuscript; Briz-Redón A was involved in the statistical analysis.

Institutional review board statement: The study was reviewed and approved by the Institutional Review Board.

Conflict-of-interest statement: Marina Berenguer has received a grant from Gilead, has been advisor for Abbvie and Intercept, and has been a speaker and/or moderator in meetings organized by Abbvie, Gilead, Intercept, Novartis and Astellas. All authors have nothing to disclose.

Data sharing statement: No additional data are available.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to

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Abstract

BACKGROUND

Delta hepatitis is a rare infection with an aggressive disease course. For almost three decades, however, there have been no epidemiological studies in our traditionally endemic area.

AIM

To investigate the prevalence of delta hepatitis in a sample of patients with chronic hepatitis B virus (HBV) infection followed at a Hepatology Unit in Valencia, Spain.

METHODS

Retrospective evaluation of anti-hepatitis D virus-immunoglobulin G seroprevalence among patients with chronic HBV infection ($n = 605$) followed at a reference Hepatology Unit in Spain.

RESULTS

The prevalence of anti-hepatitis D virus-immunoglobulin G among HBV-infected patients was 11.5%: Male (63%) and median age of 52 years. The majority were born in Spain (67%) and primarily infected through intravenous drug use. However, a significant percent (24.5%), particularly those diagnosed in more recent years, were migrants presumably nosocomially infected. Comorbidities such as diabetes (8.5%), obesity/overweight (55%), and alcohol consumption (34%) were frequent. A high proportion of patients developed liver complications such as cirrhosis (77%), liver decompensation (81%), hepatocellular carcinoma

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Manuscript source: Unsolicited manuscript

Received: February 9, 2020

Peer-review started: February 9, 2020

First decision: March 18, 2020

Revised: April 7, 2020

Accepted: May 5, 2020

Article in press: May 5, 2020

Published online: June 27, 2020

P-Reviewer: Qi XS, Soldara J, Tajiri K, Zhang XC

S-Editor: Yu XQ

L-Editor: Filipodia

E-Editor: Liu MY



(HCC) (16.5%), or required liver transplantation (LT) (59.5%). Diabetes was associated with progression to cirrhosis, LT, and death. Male sex, increasing age, and alcohol were associated with LT and HCC. Compared to HBV mono-infected patients, delta individuals developed cirrhosis and liver decompensation more frequently, with no differences in HCC rates.

CONCLUSION

Patients infected in the 1980's were mostly locals infected through intravenous drug use, whereas those diagnosed recently are frequently non-Spanish natives from endemic areas. Regardless of their origin, patients are predominantly male with significant comorbidities, which potentially play a major role in disease progression. We confirm a high rate of subsequent liver complications.

Key words: Viral hepatitis; Delta hepatitis; Cirrhosis; Liver transplantation; Immigration; Valencia

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Core tip: Our study shows that there has been a change in the delta hepatitis virus-infected patient profile in our unit. Most patients infected in the 1980s, due to intravenous drug abuse, have progressed to cirrhosis and/or hepatocellular carcinoma and therefore still represent a significant burden on our Hepatology Unit. However, our main concern is with newly diagnosed patients, as there is a clear delay in the diagnosis of infection and cirrhosis. In addition, follow-up in their home countries has been poor. Most of them come from Eastern Europe and prior medical intervention was the main route of infection. We must also take into account the presence of comorbidities, *e.g.*, metabolic syndrome and alcohol intake, which may contribute to the aggressive progression of the disease. Therefore, we must devote our efforts to controlling these aspects and finding an effective treatment, given the poor results offered by pegylated- α -interferon.

Citation: Hernández-Èvole H, Briz-Redón Á, Berenguer M. Changing delta hepatitis patient profile: A single center experience in Valencia region, Spain. *World J Hepatol* 2020; 12(6): 277-287

URL: <https://www.wjgnet.com/1948-5182/full/v12/i6/277.htm>

DOI: <https://dx.doi.org/10.4254/wjh.v12.i6.277>

INTRODUCTION

Delta hepatitis is a rare infectious disease caused by hepatitis D virus (HDV), an RNA defective virus that requires the presence of hepatitis B surface antigen (HBsAg) to infect cells. Roughly 15 million people are infected worldwide. However, there are areas where the prevalence is higher, such as the Mediterranean basin^[1].

The importance of early detection of hepatitis B virus (HBV)-HDV coinfection is due to the aggressive course of the disease demonstrated in these patients compared to those only infected by HBV. At present, the only treatment available and recommended by Scientific Societies is alfa pegylated interferon^[2]. However, its use is restricted to highly selected patients (avoided in cirrhosis, active autoimmune disease and certain psychiatry disorders) and the response rate is low. Consequently, the only possible and effective way to control the spread of the infection currently is HBV vaccination.

In 1988, Buti *et al*^[3] reported a delta seroprevalence among HBV carriers of 15% in Spain; highlighting that intravenous drug users (IDUs) were the major risk group. Most recent studies from northern Spain, a non-traditional immigration area, have reported decreasing rates of infection over a 29-year period. A similar pattern has been documented in other European countries. The prevalence stabilized in the 1990s but was followed by a subsequent increase from 4.7% in 2003-2007 (lowest prevalence) to 7.4% in 2008-2012^[4].

There are no recent epidemiological data for our area, particularly information regarding the current profile of HDV infected patients. This information is especially needed given that the region is an immigration receiving area and the absence of

epidemiological information for almost three decades.

Based on this background, we aimed to update the epidemiological data on HDV infection in our geographical area. We specifically aimed to assess whether there had been changes in the profile of infected individuals, confirm the greater aggressive nature of HDV-HBV coinfection compared to HBV mono-infection, and describe risk factors for progression of disease.

MATERIALS AND METHODS

A retrospective single center study review of a database of HBV-infected patients followed in the Hepatology Unit of the Hospital Universitari I Politècnic “La Fe” (HUP La Fe). Inclusion criteria were: Diagnosis of delta hepatitis (confirmed by the presence of anti-HDV-immunoglobulin G [IgG]). No exclusion criteria were set.

The following data were extracted from the chart review: (1) Demographics including age, sex, country of birth, race, year of diagnosis, and first visit to the Unit, and probable mechanism of acquisition of HBV-HDV infection; (2) Presence of comorbidities such as diabetes mellitus, obesity, and alcohol intake, history of infection with hepatitis C virus (HCV) or human immunodeficiency virus (HIV); and (3) Hepatitis B e (HBe) antigen as well as alanine aminotransferase at diagnosis or first visit. In addition, the presence and time of occurrence of cirrhosis, liver failure, and hepatocellular carcinoma (HCC). The date a patient may have received a transplant or died was also recorded. The follow-up ended at the time of liver transplantation (LT), death or in the absence of these events, at the last visit.

The second part of the research was focused on the differences in disease evolution between HBV-HDV co-infected patients *vs* the HBV mono-infected patients. For this purpose, we designed a case-control study (1:1 match): HBV-infected patients to HBV-HDV-infected patients controlling for the year of diagnosis and sex. The following data were extracted: Presence of HCV or HIV coinfection, cirrhosis, liver decompensation, and liver cancer as well as laboratory tests gathered from the first visit onward including serum creatinine (mg/dL), estimated glomerular filtration rate (mL/min/1.73 m²), total bilirubin (mg/dL), albumin (g/dL), platelets (mm³), international normalized ratio, Child-Turcotte-Pugh, and Model for End-Stage Liver Disease staging.

Diagnostic criteria

HDV infection was defined as the presence of anti-HDV-IgG in patient serum. Chronic HBV infection was confirmed with the presence of HBsAg antigen in serum over a 6 mo period. Coinfection by HCV or HIV was confirmed with the presence of anti-HCV-IgG and anti-HIV-IgG, respectively. The diagnosis of cirrhosis was based on histologic, elastographic (liver stiffness greater than 12.5 kPas), and/or a composite of laboratory/imaging criteria^[5].

Statistical analysis

Continuous variables are expressed as the median and interquartile range, while categorical variables are depicted by the number and corresponding percentage. The comparison of qualitative variables was performed with χ^2 or Fisher's test. For the analysis of continuous variables with a normal distribution, the Student's *t*-test was used while the Mann-Whitney test was used for variables not following a normal distribution. The statistical significance was set at 0.05. To clarify the role of HDV coinfection in the development of the outcomes during the course of the disease previously mentioned, Kaplan-Meier survival analyses were done and the cumulative risk of developing these events was analyzed with Cox regression. All statistical tests performed for the analysis/comparison of variables excluded missing data. Particularly, patients missing one of the dates needed for the computation of a certain survival time outcome (depending on the risk being evaluated) were excluded for the estimation of the corresponding Kaplan-Meier curve.

The statistical analysis was performed using an SPSS program version 24.0 (IBM corporation). The R packages survival^[6] and survminer^[7] were used to produce the survival curves.

Confidentiality and data treatment

The study protocol coded MBH-INT-2018-01 was examined and approved by the Ethics Committee of HUP “La Fe”.

RESULTS

Description of the patient population

A total of 605 HBV-infected patients were included. Delta serology had not been tested in three cases. Seventy ($n = 70$) patients were anti-HDV-IgG positive (11.57%).

The general characteristics of the sample are shown in [Table 1](#). Patients were predominantly male (62.9%) and born in Spain (67.1%) with a median age of 52 years (interquartile range 12) at study entry. A non-negligible proportion (24.3%) were migrants from Eastern European countries. Regarding the route of infection, virtually half of the patients (45.7%) did not remember the possible source of the infection. Of the remaining patients 20% had a probable iatrogenic source of infection and (14.9%) had history of IDU.

Comorbidities

Although no patient was initially diabetic, diabetes developed over the course of the disease in a small proportion of individuals (8.6%). Furthermore, 55.5% were either obese or overweight with a median body mass index of 25.5 kg/m². Alcohol consumption was reported by roughly one-third of the sample (34.1%). Regarding coinfection with other viruses, 10.6% ($n = 7$) and 11.4% ($n = 8$) were HIV and HCV coinfecting, respectively. In most cases, coinfections occurred in Spanish patients with a history of IDU, infected during the peak incidence in the 1980s. Only 11.6% were HBe-antigen positive at diagnosis or first visit to the Unit. The majority (58.6%) of patients had alanine aminotransferase levels 1.5 times the upper limit of normality at diagnosis or first visit to the unit.

Treatment characteristics

One-third of the population (31.4%) had received pegylated interferon alfa therapy at some point in the disease course, with none responding. None of the patients was on interferon treatment at the time of the study. Early treatment discontinuation due to adverse events occurred in 20% of those treated. In contrast to delta therapy, antivirals against HBV were frequently used, with 54.3% of patients having received oral antivirals at some point during their disease course. Tenofovir was the most frequent antiviral used (36.8%) followed by Lamivudine (28.9%). Fifteen patients had never been treated with either pegylated interferon or oral antivirals.

Evolution events

Either at first visit or during follow-up, a large proportion (77.1%) of patients progressed to cirrhosis. Of these, the majority (80.9%) developed some type of decompensation, particularly ascites (71.1%) or upper gastrointestinal bleeding due to varices (26.3%). HCC developed in 16.9% of patients and liver transplantation was performed in 59.3%. Four patients died in the course of the follow-up, with two of the deaths related to their liver disease. Median age at time death was 50.5 years (interquartile range, 23).

Disease course

A survival analysis was performed to determine the cumulative risk of developing the different events during follow up ([Figure 1](#) and [Figure 2](#)). We differentiated the cumulative risk of developing cirrhosis and liver cancer according to whether they were diagnosed before or from 2000 ([Figure 3](#) and [Figure 4](#)). Progression to cirrhosis at 5, 10, 15, and 20 years from diagnosis occurred in 24%, 37%, 54%, and 73% of the patients, respectively. Liver cancer was observed at 5, 10, 15, and 20 years from diagnosis for the 5%, 5%, 8%, and 11%, respectively. In turn, the probability of developing decompensated cirrhosis from diagnosis reached 65%, 76%, 76%, and 88% at 5, 10, 15, and 20 years, respectively. Finally, LT-free mortality at 5, 10, 15, and 20 years from diagnosis was 3%, 3%, 7%, and 12%, respectively.

Factors associated with the development of the different events are shown in [Table 2](#). Diabetes was significantly associated with progression to cirrhosis, LT, and death. Furthermore, men were more frequently transplanted, with LT significantly increasing with patient age. Age was also significantly related to the onset of liver cancer. Alcohol consumption was also found to be associated with the need of LT as well as with liver cancer, but without reaching statistical significance in the latter. Finally, a history of interferon therapy was associated with a higher probability of LT.

Changes over time

We compared those patients diagnosed before the year 2000 to those diagnosed after 2000 to the present to assess the impact of changes in the Spanish population due to migration (based on data provided by the Immigration National Survey)^[8]. Significant differences were noticed regarding the time from diagnosis of infection to cirrhosis

Table 1 General characteristics (n = 70)

Demographic parameters		n (%)	Missing data, %
Sex, men		44 (62.9)	0
Country of birth by region			0
Spain		47 (67.1)	
Eastern Europe		17 (24.3)	
Other		6 (8.6)	
Probable route of infection			0
Unknown		32 (45.7)	
Iatrogenesis		14 (20.9)	
Intravenous drug use		10 (14.9)	
Household contact		6 (8.6)	
Sexual intercourse		4 (5.7)	
Blood transfusion		2 (2.9)	
Other		2 (2.9)	
Diabetes mellitus	Non-diabetic	64 (91.4)	0
Alcohol consumption		24 (34.3)	1.42
Weight			8.7
Underweight		2 (2.9)	
Normal weight		26 (37.1)	
Overweight		23 (32.9)	
Obese		12 (17.2)	
Serologic parameters			
HBe antigen	HBeAg+	8 (11.4)	1.4
HIV	Anti-HIV-IgG +	7 (10)	5.7
HCV	Anti-HCV-IgG +	8 (11.4)	0
Events			
Progression to cirrhosis		54 (77.1)	1.4
Liver decompensation		39 (72.2)	7.4
Most frequent type of liver decompensation			
Ascites		27 (71.1)	
Upper gastrointestinal bleeding		10 (26.3)	
Liver encephalopathy		1 (2.6)	
Hepatorenal syndrome		0 (0)	
Liver cancer		9 (12.9)	0
Liver transplant		32 (45.7)	0
Death		4 (5.7)	0

HBe: Hepatitis B e; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus.

among patients diagnosed before and after the year 2000 (Table 3). The median time interval from diagnosis to cirrhosis was 2 years [95% confidence interval (CI): 0.0-4.1] for those patients seen after the year 2000, while the interval was significantly longer 18.0 years (95%CI: 14.0-22.0); ($P < 0.0001$) for those patients seen before the year 2000.

Comparison between HBV mono-infected and HBV-HDV coinfecting patients

In an attempt to distinguish the effect of delta virus from that of HBV, HDV-HBV patients were paired with HBV-patients of the same sex and diagnosis year. Eventually, 62 HBV patients were included. Mono-infected HBV-patients were also predominantly men with a similar median age of 55.05 years (range: 30-83). Demographic, serological, and evolutive parameters of paired patients are summarized in Table 4. Cirrhosis and liver decompensation developed in a larger proportion of delta patients ($P < 0.000$). In fact, only 14 of HBV-mono-infected patients progressed to cirrhosis compared to 43 of those coinfecting. No differences in HCC development were found between groups.

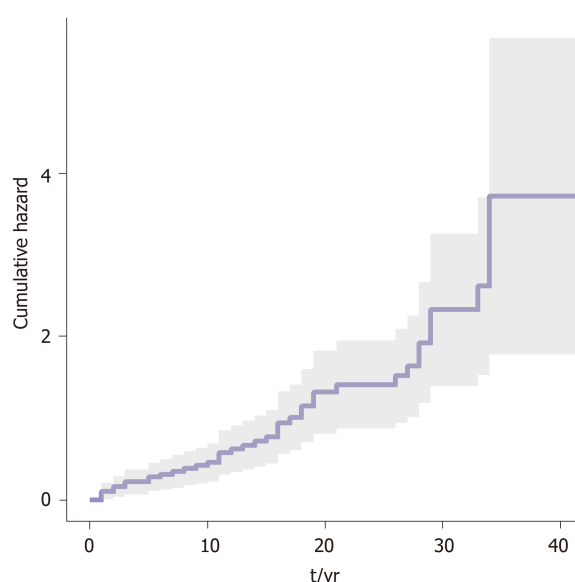


Figure 1 Cumulative risk of developing cirrhosis since diagnosis of infection.

DISCUSSION

The purpose of this study was to describe the prevalence and profile of the delta hepatitis-infected population in our Hepatology Unit over the last 30 years, and the differences due to migration. We also determined current risk factors associated with an unfavorable course and elucidated compliance with clinical practice guidelines.

The major findings can be summarized as follows. (1) Delta-infected patients were middle-aged males in whom HIV or HCV coinfection existed. Alcohol consumption and overweight-obesity were frequently present. (2) A substantial proportion (40%) was non-Spanish born, particularly those diagnosed more recently. (3) The profile of HDV-infected patients has substantially changed over the years, with a higher prevalence of Spanish-born, more frequently infected through IDU, and consequently more frequently coinfecting with either HIV or HCV among those diagnosed before the year 2000. By contrast, in those diagnosed more recently there was a significantly higher proportion of coinfecting immigrants, presumably due to nosocomial infection. (4) A significant proportion of patients progressed to cirrhosis and/or HCC, highlighting the aggressive nature of this co-infection. and (5) A relatively high number of patients (31.4%) had never received therapy with pegylated interferon.

Delta hepatitis is a concern in HBV-infected patients in our region. Indeed, the prevalence of HDV infection in our referral area is 11.57%, a rate higher than that previously reported both in our region as well as in surrounding countries. These findings might be due to our institution being a transplantation referral center and the recent migratory pattern. Recent studies in Spain have reported lower prevalence rates. According to Aguilera *et al*^[9], the delta prevalence in a tertiary hospital in Santiago de Compostela in 2018 was 4% among HBsAg+ patients followed since 2000. As in our study, patients diagnosed before 2000 were preferentially Spanish-born males, with a history of prior IDU. In fact, data from several studies have clearly shown that during the 1980 and 1990s, HDV-infected patients were mostly IDUs, with seroprevalence rates in IDUs ranging from 60% (de Miguel *et al*^[10]) to 68% (Castro Iglesias *et al*^[11]). In our region, a prevalence of 50% among IDUs was reported in the 1980s with no infections found among asymptomatic HBsAg+ carriers without a history of drug addiction^[12]. In the most recent study from 2017, the prevalence was 8.2% among 1215 patients with chronic HBV infection followed since 1983 in Northern Spain^[4]. This study also highlighted a decreasing prevalence among Spanish patients with the migrant population having become the main source of Delta infection nowadays. In addition, they detected an increased number of infections related to sexual practices. In our sample only 4 patients (3 women and 1 men) contracted the virus because of presumably “risky sexual practices,” but they were uniformly distributed between the two groups according to year of diagnosis, before and after 2000. Unfortunately, given the retrospective nature of this study, data on sexual practices were not universally recorded.

As previously reported, a proportion of patients were co-infected with other

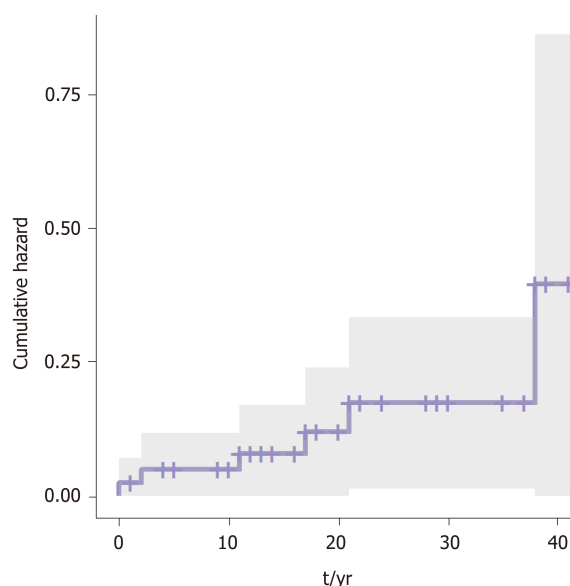


Figure 2 Cumulative risk of developing hepatocellular carcinoma since diagnosis of infection.

viruses. HIV (10.6%) and HCV (11.4%)-coinfection was mainly observed in the Spanish population, where the main risk factor was IDU. Interestingly, 5.7% of the sample had quadruple HBV, HDV, HCV, and HIV infection. As typically described in the Mediterranean area, most of the patients were anti-HBe positive at time of diagnosis.

The profile of currently diagnosed HDV-infected patients is that of middle-aged males, migrating from endemic areas, particularly Eastern Europe, where prior medical contact/intervention seems to be the main risk factor for infection. The few studies in our country evaluating the migrant population have solely focused on people from the African continent. López-Vélez *et al*^[13] found that 10% of HBsAg+ asymptomatic carriers from a cohort of sub-Saharan Africa immigrants residing in Madrid were also anti-HDV-IgG-positive. More recent data among immigrants from Equatorial Guinea living in Madrid demonstrated a prevalence of HDV infection of 20.9% of HBsAg carriers^[14].

Regarding the natural history of this infection, our data confirmed prior studies highlighting the aggressive course of HBV-HDV coinfecting patients. Indeed, three-quarters of patients progressed to cirrhosis and liver decompensation. Furthermore, only 3.3 years elapsed between the diagnosis of compensated cirrhosis and liver transplantation, death or last visit. The lack of response to pegylated interferon as well as the presence of frequent comorbidities, such as diabetes, obesity or alcohol intake may explain these findings. In summary, given the low efficacy rate of interferon, addressing adequately these comorbidities seems the best strategy to improve the long-term outcome of HDV-infected individuals. In addition, it is likely that the very short delay observed between diagnosis and cirrhosis in those diagnosed after the year 2000 may be related to the fact that most of these patients were migrants (46.7%) with no prior liver evaluation.

The main limitation of this study lies in its retrospective design. We cannot exclude selection bias potentially resulting in a prevalence underestimation and errors in estimating the time of infection. Furthermore, as this was a single center study, the sample size was relatively small which may have limited statistical power. Finally, no data on viral load was collected due to substantial missing data in early years and the change in quantitative techniques over time.

Despite these limitations, this research provides epidemiological data in a historically endemic area with new migration, highlighting changes in the patient profile, with a predominance of patients coming from Eastern Europe and the high frequency of comorbidities that may impact disease progression.

In conclusion, 11.5% of our HBV-infected population is coinfecting with HDV. Recently, diagnosed patients are non-Spanish born individuals coming from endemic countries where the main risk factor is presumably prior medical contact/intervention, inadequately diagnosed and followed until their arrival to Spain. Importantly, IDU patients infected during the first outbreak in the 1980s still represent a significant burden as most have progressed to cirrhosis and/or liver cancer.

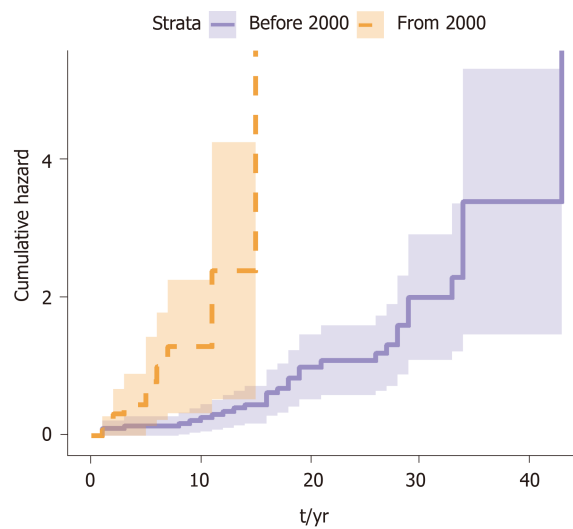


Figure 3 Cumulative risk of developing cirrhosis since delta hepatitis virus infection diagnosis for those patients diagnosed before and from 2000.

Independently from the country of origin, the majority of HDV-infected individuals are men with comorbidities, potentially playing a major role in disease progression. Finally, the low use of pegylated interferon together with its very low efficacy highlights the need for better therapies.

Table 2 Variables associated with the cumulative risk of different end-points since infection¹

	Cirrhosis	Liver cancer	Liver decompensation²	Transplantation	Survival
Age	+ (0.056) ²	++ (0.007)	NS	++ (0.034)	NS
Sex	NS	NS	+ (0.101)	++ (0.040)	NS
Country of birth	NS	NS	NS	NS	NS
Diabetes	++ (0.027)	NS	+ (0.085)	++ (0.013)	++ (0.004)
Overweight	NS	NS	NS	+ (0.104)	NS
Alcohol consumption	NS	+ (0.100)	NS	++ (0.019)	NS
HIV coinfection	NS	NS	NS	NS	NS
HCV coinfection	NS	NS	NS	NS	NS
Log [ALT]	NS	NS	NS	NS	NS
Treatment with IFN	NS	NS	NS	++ 0.034	NS
Antiviral treatment	+ (0.092)	NS	NS	NS	NS

¹>Except for clinical decompensation where baseline was "time of cirrhosis diagnosis" ã

²For this purpose, we only took into consideration cirrhotic patients; ³Underlined values are those with a *P*-value < 0.1, because a tendency towards significance was observed. ALT: Alanine aminotransferase; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus; IFN: Interferon; NS: No statistical significance.

Table 3 Differences according to year of diagnosis of infection, *n* (%)

Demographic parameters		Total	Diagnosis before 2000	Diagnosis after 2000	<i>P</i> value
Country of birth by region					< 0.00
Spain		47 (67.1)	37 (92.5)	10 (33.3)	
Eastern Europe		17 (24.3)	3(7.5)	14 (46.7)	
Other		6 (8.6)	0 (0)	6 (20)	
Diabetes mellitus	Diabetic	6 (8.6)	1 (2.3)	5 (16.7)	0.038
Alcohol consumption	Alcohol consumption	24 (34.3)	12 (30)	12 (41.4)	0.327
Weight					0.038
Underweight		2 (2.9)	1 (2.7)	1 (3.8)	
Normal weight		26 (37.1)	12 (32.4)	14 (53.8)	
Overweight		23 (32.9)	14 (37.8)	9 (34.6)	
Obese		12 (17.1)	10 (27)	2 (7.7)	
Serologic parameters					
HBe antigen	HBeAg +	8 (11.4)	8 (11.4)	0 (0)	0.008
HIV	Anti-HIV-IgG +	7 (10)	7 (10)	0 (0)	0.024
HCV	Anti-HCV-IgG+	8 (11.4)	8 (11.4)	0 (0)	0.009
Events					
Progression to cirrhosis		54 (77.1)	33 (82.5)	21 (72.4)	0.316
Liver decompensation		39 (72.2)	24 (77.4)	15 (75)	0.842
Liver transplant		32 (45.7)	22 (55)	10 (33.3)	0.74
Death		4 (5.7)	2 (5)	2 (6.7)	0.766

HBe: Hepatitis B e; HCV: Hepatitis C virus; HIV: Human immunodeficiency virus.

Table 4 Descriptive characteristics of the paired samples of hepatitis B virus and hepatitis B virus-hepatitis D virus patients ($n = 62$), n (%)

		HBV patient sample	HDV patient sample	<i>P</i> value
Demographic parameters	Age in yr	55.05	48.90	< 0.024
	Sex, men	40 (64.5)	40 (64.5)	-
Serological parameters	HIV	0 (0)	7 (11.9)	< 0.005
	HCV	4 (6.5)	8 (12.9)	NS
Evolution parameters	Liver cirrhosis	14 (23.3)	43 (74.1)	< 0.000
	Liver decompensation	5 (8.2)	33 (57.9)	
	Liver cancer	4 (6.6)	5 (8.5)	NS

HBV: Hepatitis B virus; HCV: Hepatitis C virus; HDV: Hepatitis delta virus; HIV: Human immunodeficiency virus; NS: No statistical significance.

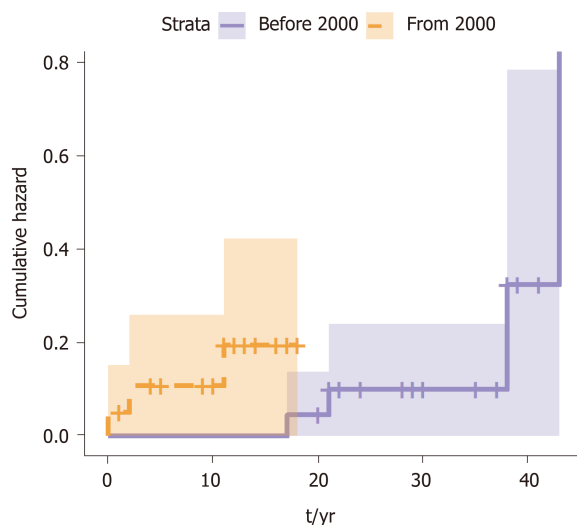


Figure 4 Cumulative risk of developing hepatocellular carcinoma since hepatitis Delta virus infection diagnosis for those patients diagnosed before and after 2000.

ARTICLE HIGHLIGHTS

Research background

At present, epidemiological data and information regarding possible changes in the infected patient's profile are scarce. In addition, there were no updated epidemiological data in our region for three decades.

Research motivation

To carry out this research in Spain is of special interest given the idiosyncrasies of our country, and especially of our Region, Comunidad Valenciana, as an immigration receiving area.

Research objectives

The main objective was to describe the prevalence and profile of the hepatitis D virus (HDV) infection in our referral hospital. Secondary objectives were as follows: (1) To determine the epidemiology of the HDV infection; (2) To assess risk factors associated with this infection and determine whether the disease course is worse than in hepatitis B virus (HBV) mono-infected patients of the same age and sex; and (3) To elucidate whether the recommendations of the European guidelines for treatment are met.

Research methods

Retrospective evaluation of anti-HDV-immunoglobulin G seroprevalence among patients with chronic HBV infection followed in a reference Hepatology Unit. Demographic, clinical, analytic, serologic, and virology parameters were retrieved from chart review together with evolution events (cirrhosis, liver decompensation, liver transplantation, and death). HDV-HBV patients were matched 1:1 by age and year of diagnosis to HBV mono-infected patients.

Research results

Most of anti-HDV-IgG patients were men (63%) with a median age of 52 years. The majority

were Spaniards (67%), who were infected due to intravenous drug use; 24.5% of the population corresponded to migrants, presumably due to a nosocomial infection. Comorbidities (diabetes, alcohol consumption and overweight) were frequent in both groups. A high proportion of patients developed liver complications such as cirrhosis (77%), liver decompensation (81%), or HCC (16.5%), or required liver transplantation (59.5%). Compared to HBV mono-infected patients, delta individuals more frequently developed cirrhosis and liver decompensation, with no differences in HCC rates. The main limitation of this study lies in its retrospective quality. Therefore, we must base our conclusions on the current sample and follow patients prospectively in order to continue updating their data. Future research should collect virological data (HDV viral load) and determine the genotype in order to elucidate the role of these factors and determine if it is possible to ascertain individualized evolutionary courses according to the characteristics previously exposed.

Research conclusions

We confirmed our hypothesis that the HDV-infected population has changed starting in 2000 due to an increase in the immigrant population. However, the disease outcomes remain the same: Cirrhosis, impaired liver function and HCC. We have found a high prevalence of delta hepatitis in our area compared to other Spanish and European regions; probably because increased number of immigrants. This implies that we must be very diligent in screening for this infection in order to be able to offer patients early follow-up.

Research perspectives

Delta hepatitis remains a major concern and must follow these patients carefully given the significant complications seen on follow-up. Future research should elucidate the behavior of patients diagnosed over the last decade.

ACKNOWLEDGEMENTS

We are thankful to the physicians taking care of HDV-infected individuals.

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