Seroprevalence and clinical outcome of hepatitis D infection in Qatar

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Abstract

Background: Worldwide, 5–10% of people with chronic hepatitis B virus infection are co-infected with hepatitis D virus. In Qatar, there are no data on hepatitis D virus infection among patients positive for hepatitis B surface antigen (HBsAg).

Aims: To determine the seroprevalence of hepatitis D virus infection among patients with chronic hepatitis B virus infection in Qatar and assess the characteristics of these patients.

Methods: This was a retrospective cohort study of all HBsAg-positive individuals tested for hepatitis D virus between 1 January 2010 and 29 December 2019 within the Hamad Medical Corporation. Data were retrieved from electronic records and included demographic and clinical information of the patients.

Results: Of the 2348 HBsAg-positive patients, 125 were positive for hepatitis D virus (seroprevalence 5.3%). The median age of hepatitis D positive patients was significantly higher than for hepatitis D negative patients (P = 0.001). Most of the patients with hepatitis D had a hepatitis B viral load < 2000 IU/mL (53.6%) and were negative for hepatitis B e antigen (93.6%). A significantly greater proportion of hepatitis D positive patients than hepatitis D negative patients were infected with hepatitis C virus (P < 0.001), and had liver cirrhosis (P < 0.001) and hepatocellular carcinoma (P = 0.006).

Conclusions: Hepatitis D virus infection is associated with lower hepatitis B virus viraemia and more advanced liver disease in the study population.

Keywords: hepatitis D, hepatitis B, co-infection, surface antigen, viraemia, liver disease, Qatar

Citation: Abdallah T; Ibrahim T; Hajmusa M; Abdulgayoom M; Elhassan A; Abusabeib A; et al. Seroprevalence and clinical outcome of hepatitis D infection in Qatar. East Mediterr Health J. 2022;28(11):840–846. https://doi.org/10.26719/emhj.22.081

Received: 15/11/21; accepted: 11/08/22

Introduction

Hepatitis D virus is a hepatotropic virus with a circular ribonucleic acid (RNA) genome. This virus has at least eight genotypes, of which genotype 1 is the most frequent and is distributed worldwide *(1)*. It uses the surface protein of hepatitis B virus as its coating, and hence, its replication and transmission are closely linked to those of the latter *(2)*. In 2015, it was estimated that 257 million people were living with hepatitis B virus infection, defined as hepatitis B surface antigen (HBsAg) positive *(3)*. At least 5% of those people are co-infected with hepatitis D virus, meaning 15–20 million people are infected with hepatitis D virus worldwide *(4)*. A meta-analysis in 2019 showed that hepatitis D virus seroprevalence was 10.58% suggesting more people are infected with this virus *(5)*.

Most people with hepatitis D virus are in Africa, Asia, Eastern Europe, Greenland, Middle East, Pacific Islands and South America *(4)*. People with chronic hepatitis B virus and hepatitis D virus infection have a twofold higher risk of developing cirrhosis, a threefold higher risk of developing hepatocellular carcinoma and a twofold increased mortality rate than individuals only infected with hepatitis B virus (monoinfection) *(6,7)*.

Current guidelines generally recommend treatment with pegylated interferon-alpha for at least 48 weeks for chronic hepatitis D virus infection, irrespective of response patterns while on treatment. This is because the overall rate of sustained virological response is low. However, newer drugs with novel mechanisms of action against hepatitis D virus are more promising. The United States Food and Drug Administration has granted fast-track designation to lonafarnib, a hepatitis D virus prenylation inhibitor, in combination with ritonavir for treatment of hepatitis D virus infection after a phase IIa study showed a decrease in hepatitis D virus RNA during 4 weeks of treatment *(8)*. Another study explored the optimal regimen of lonafarnib and showed that the addition of ritonavir allowed for a lower dose and higher concentration of lonafarnib with better tolerance *(9)*. The European Commission approved the entry inhibitor bulevirtide (also called myrcludex B) as the first drug for chronic hepatitis D virus treatment. An open-label, phase IIb clinical trial assessed the safety and efficacy of bulevirtide in combination with tenofovir in patients with hepatitis B virus and hepatitis D virus co-infection *(10)*. The study showed a dose-dependent decrease in hepatitis D virus RNA in parallel with a decrease in alanine aminotransferase *(11)*.

In Qatar, screening of 78 428 blood donors between January 1994 and December 2001 found that 0.98% were

HBsAg positive and 10.85% were hepatitis B core antibody (HBcAb) positive. Of 915 patients with chronic liver disease in Qatar, 2.5% were attributed to hepatitis B virus *(12)*. However, data are lacking about the hepatitis D virus infection status among HBsAg-positive patients in the country.

This study estimated the seroprevalence of hepatitis D virus antibody among HBsAg carriers in Qatar and assessed the clinical, laboratory and virological characteristics of those positive for hepatitis D virus antibody.

Methods

Study setting, design and population

Hamad Medical Corporation comprises 12 hospitals and provides secondary and tertiary medical care for all the population of Qatar (2.8 million people). This was a retrospective, cohort study conducted in all Hamad Medical Corporation hospitals. The study population included all HBsAg-positive patients (older than 14 years) who were tested for hepatitis D virus antibodies (immunoglobulin G (IgG) and immunoglobulin M (IgM)) at the time of the study.

Study outcome and data collected

The primary outcome was the seroprevalence of hepatitis D virus infection among HBsAg-positive individuals in Qatar. Data were collected on the clinical, laboratory and radiological characteristics of those positive and negative for hepatitis D antibody.

Study procedures

The electronic laboratory system of Hamad Medical Corporation was used to identify HBsAg-positive patients who had also been tested for hepatitis D virus antibody between 1 January 2010 and 29 December 2019. Demographic and clinical data were extracted from all available electronic medical records of identified patients and transcribed into a standardized data collection sheet. Data extracted included: demographic information, hepatitis D virus antibody result, hepatitis D virus polymerase chain reaction (PCR) result, hepatitis B virus serology result, human immunodeficiency virus (HIV) status, abdominal ultrasound and ultrasound elastography results, aspartate aminotransferase (AST) to platelet ratio index score, and cirrhosis and hepatocellular carcinoma status.

Statistical analysis

Demographic and clinical characteristics of individuals who were hepatitis D virus-positive and hepatitis D virus-negative were compared. Continuous data were presented as medians (interquartile ranges [IQR]) and compared using the Wilcoxon rank-sum test. As appropriate, categorical data were summarized as numbers (percentages) and compared using the Fisher exact test or Pearson chi-squared test. Statistical analyses were performed using *Stata*, release 15 (StataCorp., College Station, TX, USA). A P-value ≤ 0.05 was considered statistically significant.

Ethical considerations

This retrospective chart review study involving human participants was conducted in accordance with the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Institutional Review Board at Hamad Medical Corporation approved the study with a waiver of informed consent (MRC-01-19-519).

Results

Between 1 January 2010 and 29 December 2019, we found 2348 patients who were HBsAg positive and screened for hepatitis D virus antibodies; 125 of them tested positive for hepatitis D virus antibodies, giving a seroprevalence of 5.3%. Missing data were reported in the entire data set. Table 1 shows the demographic characteristics of the patients by hepatitis D virus infection. The median age of patients positive for hepatitis D virus was 38 years (IQR 32–49), significantly higher than the patients negative for hepatitis D virus, 35 years (IQR 29–45), $P = 0.001$. There were more males in both groups: 73.6% hepatitis D virus positive and 74.0% hepatitis D virus negative. The patients were categorized by WHO region. The majority of hepatitis D virus positive and hepatitis D virus negative individuals were from the WHO Eastern Mediterranean Region. Within this region significantly more patients were hepatitis D virus positive (80.8%) than the hepatitis D virus negative (61.8%), $P < 0.001$.

Table 2 shows the clinical characteristics of the patients, by hepatitis D virus status. Most of the patients were negative for the hepatitis B e antigen (HBeAg). Of those who were negative for hepatitis D virus, a greater proportion were positive for HBeAg (10.6%) than those who were hepatitis D virus positive (6.4%) but the difference was not statistically significant ($P = 0.170$). No significant differences were seen between hepatitis D virus positive and hepatitis D virus negative groups for other hepatitis B virus markers (HBcAb, HBcIgM and HBeAb). Among hepatitis D virus negative patients, 1775 individuals had PCR results for hepatitis B virus; 46.6% had a result < 2000 IU/mL. A similar percentage was observed for hepatitis D virus positive individuals; 53.6% had hepatitis B virus PCR result < 2000 IU/mL. More patients in the hepatitis D virus positive group had negative hepatitis B virus PCR results (12.0%) than hepatitis D virus negative patients (7.8%) but this difference was not statistically significant ($P = 0.210$).

From the hepatitis D virus positive individuals, 12/112 (9.6%) were positive for hepatitis C antibody, compared with 49/1798 (2.2%) in the hepatitis D virus negative group ($P < 0.001$). Less than half of the patients had been tested for HIV, with only three being positive; all of them were in hepatitis D virus negative group.

Table 1 Demographic characteristics of patients with hepatitis B, by hepatitis D virus infection, Qatar

Variable	Hepatitis D virus status		*P*-value
	Negative (*n* = 2223)	Positive (*n* = 125)	
Age in years, median (IQR)	35 (29–45)	38 (32–49)	0.001
Sex, no. (%)			0.920
Female	577 (26.0)	33 (26.4)	
Male	1646 (74.0)	92 (73.6)	
WHO region, no. (%)			< 0.001
African	266 (12.0)	10 (8.0)	
Americas	12 (0.5)	1 (0.8)	
Eastern Mediterranean	1374 (61.8)	101 (80.8)	
European	43 (1.9)	3 (2.4)	
South-East Asian	405 (18.2)	9 (7.2)	
Western Pacific	123 (5.5)	1 (0.8)	

IQR: interquartile range, WHO: World Health Organization.

The median alanine aminotransferase level was 26 U/L (IQR 17–45) for hepatitis D virus negative patients and 34 U/L (IQR 21–63) for hepatitis D virus positive individuals ($P = 0.004$). There were no significant differences between hepatitis D virus positive and hepatitis D virus negative patients for platelets and international normalization ratio. The median AST to platelet ratio index for hepatitis D virus positive individuals was 0.34 (IQR 0.20–0.90) and 0.30 (IQR 0.2–0.46) for hepatitis D virus negative individuals (Table 2).

A significantly higher percentage of individuals positive for hepatitis D virus had cirrhosis (33.6%) than those negative for hepatitis D virus (14.5%), $P < 0.001$ (Table 3). Similarly, a higher proportion of hepatitis D virus-positive individuals had hepatocellular carcinoma (4.8%) than hepatitis D virus-negative individuals (1.0%), $P = 0.006$. Splenomegaly and ascites were significantly more prevalent in hepatitis D virus-positive patients (19.2% and 8.8%, respectively) than hepatitis D virus-negative patients (5.4% and 2.5%, respectively); $P < 0.001$ for splenomegaly and $P = 0.002$ for ascites (Table 3).

Ultrasound elastography was performed for 665 individuals, 623 were hepatitis D virus-negative, and 42 were positive. Normal to mild stiffness was found in 11.3% of hepatitis D virus-negative patients and 8.8% of positive patients. In comparison, mild to moderate stiffness was found in 16.1% hepatitis D virus-negative individuals and 22.4% of the hepatitis D virus-positive group. Of the patients who were negative for hepatitis D virus, 0.6% had moderate to severe stiffness compared to 2.4% in the hepatitis D virus-positive group, $P = 0.038$ (Table 3).

Discussion

This study is the first to examine the seroprevalence, demographics and clinical characteristics of hepatitis D virus infection in Qatar.

The overall seroprevalence of hepatitis D virus in Qatar of 5.3% was similar to A WHO report *(4)*. A systemic review in 2018 showed the overall prevalence of hepatitis D virus in North Africa to be 5.0%, similar to our figure *(13)*. Another study showed a mean prevalence of hepatitis D virus of 14.7% in the WHO Eastern Mediterranean Region *(14)*. This discrepancy in the prevalence between Qatar and data for the WHO Eastern Mediterranean Region can be explained by the fact that most of the residents in Qatar (more than 80%) are from other countries, mainly Asian countries *(15)*, which are reported to have a lower prevalence of hepatitis D virus infection *(16)*.

Some previous reports have shown that hepatitis D virus co-infection results in a lower level of hepatitis B virus viraemia *(17,18)*. This was consistent with the findings in our study where almost half of the individuals in both groups had low hepatitis B virus PCR results (< 2000 IU/mL) and lower rates of HBeAg. This can affect decisions on management in patients with chronic hepatitis B virus infection since hepatitis B virus viral load and HBeAg are part of the clinical evaluation. We could not find any previous reports on specific association between hepatitis B virus markers and hepatitis D virus infection apart from the previous mentioned association with HBeAg. Since hepatitis D virus PCR was not available in our institution, only 8 patients underwent testing for hepatitis D virus viral load as an outside test. This can be an area for improvement for patients with hepatitis D virus infection management.

In previous experimental studies, it has been suggested that other viruses such as hepatitis C virus can enhance hepatitis D virus transmission *(19)*, which can explain the higher percentage of hepatitis C virus-positive patients among individuals infected with hepatitis D virus than hepatitis D virus-negative patients (9.6% versus 2.2%) in our study. Another study supports this finding where a higher frequency of anti-hepatitis C virus antibodies was found in hepatitis D virus-positive than hepatitis D virus-negative individuals who were HBsAg positive *(20)*. However, these findings are an area for further research to confirm the relationship between hepatitis C virus, hepatitis D virus and chronic liver disease.

Table 2 Clinical characteristics of patients with hepatitis B, by hepatitis D virus infection, Qatar

Variable	Hepatitis D virus status		*P*-value
	Negative (*n* =2223)	Positive (*n* = 125)	
HBcAb, no. (%)			0.210
Negative	27 (1.2)	3 (2.4)	
Positive	2190 (98.8)	122 (97.6)	
Missing	6	0	
HBc IgM, no. (%)			0.240
Negative	2120 (95.8)	123 (98.4)	
Positive	94 (4.2)	2 (1.6)	
Missing	9	0	
HBeAb, no. (%)			0.650
Negative	222 (10.0)	14 (11.2)	
Positive	1993 (90.0)	111 (88.8)	
Missing	8	0	
HBeAg, no. (%)			0.170
Negative	1982 (89.4)	117 (93.6)	
Positive	235 (10.6)	8 (6.4)	
Missing	6	0	
HBV PCR in IU/mL, no. (%)			0.210
< 2000	1036 (58.4)	67 (60.9)	
>2000	565 (31.8)	28 (25.5)	
Negative	174 (9.8)	15 (13.6)	
Missing	448	15	
HCV Ab, no. (%)			< 0.001
Negative	1749 (97.3)	100 (89.3)	
Positive	49 (2.7)	12 (10.7)	
Missing	425	13	
Albumin in g/L, median (IQR)	41.00 (37.00–44.00)	41.00 (36.00–44.00)	0.022
Platelets × 10^3/uL, median (IQR)	225.50 (185.00–269.00)	220.50 (153.00–275.00)	0.088
INR, median (IQR)	1.00 (1.00–1.10)	1.00 (1.00–1.10)	0.180
APRI score, median (IQR)	0.30 (0.20–0.46)	0.34 (0.20–0.90)	0.004
ALT in U/L, median (IQR)	26.00 (17.00–45.00)	34.00 (21.00–63.00)	0.004
AST in U/L, median (IQR)	23.00 (18.00–33.00)	29.00 (21.00–53.00)	< 0.001

HBcAb: hepatitis B core antibody; HBc IgM: hepatitis B core immunoglobulin M; HBeAb: hepatitis B e antibody; HBeAg: hepatitis B e antigen, HBV: hepatitis B virus; PCR: polymerase chain reaction; HCV Ab: hepatitis C virus antibody; IQR: interquartile range; INR: international normalization ratio, APRI: aspartate aminotransferase to platelet ratio index; ALT: alanine aminotransferase; AST: aspartate aminotransferase.

Previous studies have shown that patients with hepatitis B virus and hepatitis D virus co-infection have worse liver disease markers, cirrhosis and decompensation than those without hepatitis D virus co-infection *(6,7,18)* with lower platelets, higher international normalization ratio, higher AST to platelet ratio index scores and higher transaminases. This was not the case in our study, most likely due to a large amount of missing data with our patients. The discrepancy between AST to platelet ratio index scores and percentage of patients with cirrhosis can be explained by the modest sensitivity of the AST to platelet ratio index to detect hepatitis B virus-related fibrosis as found in 2014 meta-analysis *(21)*. Significantly more patients with hepatitis B virus and hepatitis D virus co-infection developed cirrhosis and hepatocellular carcinoma, as demonstrated in previous reports *(7)*. Better management of patients with hepatitis D virus and hepatitis B virus co-infection is needed to address this issue.

A limitation of our study is its retrospective nature. The large number of missing data for some factors may affect the significance of the results. The missing data did not allow us to do a logistic regression analysis to draw any conclusion about the association of hepatitis D virus infection with specific risk factors or markers. Despite these limitations, we believe that our results add to the existing knowledge on hepatitis D virus infection in the region.

Table 3 **Clinical outcome of patients with hepatitis B, by hepatitis D virus infection, Qatar**

Variable	Hepatitis D virus status		*P*-value
	Negative (*n* = 2223)	Positive (*n* = 125)	
Cirrhosis, no. (%)			< 0.001
No	1296 (80.0)	61 (59.2)	
Yes	324 (20.0)	42 (40. 8)	
Missing	603	22	
Splenomegaly, no. (%)			< 0.001
No	1491 (92.5)	79 (76.7)	
Yes	121 (7.5)	24 (23.3)	
Missing	611	22	
Ascites, no. (%)			0.002
No	1562 (96.5)	93 (89.4)	
Yes	56 (3.5)	11 (10.6)	
Missing	605	21	
Hepatocellular carcinoma, no. (%)			0.006
No	1613 (98.6)	97 (94.2)	
Yes	23 (1.4)	6 (5.8)	
Missing	587	22	
Ultrasound elastography in kPa, no. (%)			0.038
Normal–mild (4.5–5.7)	251 (40.3)	11 (26.2)	
Mild–moderate (5.7–12.0)	359 (57.6)	28 (66.7)	
Moderate–severe (12.0–21.0)	13 (2.1)	3 (7.1)	
Missing	1600	83	

Conclusion

Hepatitis D virus infection is associated with lower hepatitis B virus viraemia and more advanced liver disease. Further research is needed on hepatitis D virus infection in Qatar and the region, especially the relation between hepatitis D virus and hepatitis C virus co-infection and their effect on outcomes. With the availability of lonafarnib and bulevirtide as potential effective antivirals for hepatitis D virus treatment, the treatment and outcome for such patients could be improved. This is to be confirmed with more studies. We recommend routine testing of patients with chronic hepatitis B virus infection for hepatitis D virus and, for those who are positive, testing of hepatitis D virus viral load, and evaluation with abdominal ultrasound and elastography.

Funding: Medical Research Centre at Hamad Medical Corporation, Doha, Qatar. The funder was not involved in the conduct of the study, preparation of the manuscript or the decision to submit it for publication.

Competing interests: None declared.

Séroprévalence et issue clinique de l'infection par le virus de l'hépatite D au Qatar

Résumé

Contexte : À l'échelle mondiale, 5 à 10 % des personnes atteintes d'une hépatite B chronique sont co-infectées par le virus de l'hépatite D. Au Qatar, on ne dispose d'aucune donnée sur l'infection par le virus de l'hépatite D chez les patients positifs pour l'antigène de surface du virus de l'hépatite B (HBsAg).

Objectifs : Déterminer la séroprévalence de l'infection par le virus de l'hépatite D chez les patients atteints d'hépatite B chronique au Qatar et évaluer les caractéristiques de ces patients.

Méthodes : Il s'agissait d'une étude de cohorte rétrospective de toutes les personnes positives pour l'antigène de surface du virus de l'hépatite B ayant subi un test de dépistage du virus de l'hépatite D entre le 1er janvier 2010 et le 29 décembre 2019 au sein des établissements de la Hamad Medical Corporation. Les données ont été extraites de dossiers électroniques et comprenaient des informations démographiques et cliniques sur les patients.

Résultats : Sur les 2348 patients positifs pour l'HBsAg, 125 étaient positifs pour le virus de l'hépatite D (séroprévalence de 5,3 %). L'âge médian des patients positifs au virus de l'hépatite D était significativement plus élevé que celui des patients négatifs à ce même virus (p = 0,001). La plupart des patients atteints d'hépatite D avaient

une charge virale pour l'hépatite B inférieure à 2000 UI/mL (53,6 %) et étaient négatifs pour l'antigène e du virus de l'hépatite B (93,6 %). Une proportion significativement plus importante de patients positifs au virus de l'hépatite D par rapport aux patients négatifs à ce même virus étaient infectés par le virus de l'hépatite C (p < 0,001) et présentaient une cirrhose (p < 0,001) et un carcinome hépatocellulaire (p = 0,006).

Conclusions : L'infection par le virus de l'hépatite D est associée à une virémie plus faible du virus de l'hépatite B et à une maladie hépatique plus avancée dans la population de l'étude.

الانتشار المصلي والنتائج السريرية للعدوى بالتهاب الكبد D في قطر

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الخلاصة

الخلفية: لقد وجد أن 5–10٪ من المصابين بعدوى مزمنة بفيروس التهاب الكبد B على مستوى العالم، مصابون أيضًا بفيروس التهاب الكبد D. ولكن في قطر لا توجد بيانات عن عدوى فيروس التهاب الكبد D بين المرضى الإيجابيين للمستضد السطحي لالتهاب الكبد B (HBsAg).

الأهداف: هدفت هذه الدراسة الى تحديد الانتشار المصلي لعدوى فيروس التهاب الكبد D بين المصابين بعدوى مزمنة بفيروس التهاب الكبد B في قطر، وتقييم السمات المميزة لهؤلاء المرضى.

طرق البحث: هذه الدراسة دراسة أترابية استعادية لجميع الأشخاص الإيجابيين للمستضد السطحي لالتهاب الكبد B، الذين أُجري لهم اختبار الكشف عن فيروس التهاب الكبد D بين 1 يناير / كانون الثاني 2010 و 29 ديسمبر / كانون الأول 2019 ضمن مؤسسة حمد الطبية. وقد استُرجعت البيانات من السجلات الإلكترونية وشملت السمات السكانية والبيانات السريرية للمرضى.

النتائج: من بين المرضى الإيجابيين للمستضد السطحي لالتهاب الكبد B، البالغ عددهم 2348 مريضًا، كان هناك 125 مريضًا إيجابيًّا لفيروس التهاب الكبد D (الانتشار المصلي 5.3٪). وكان العمر الوسيط للمرضى الإيجابيين لالتهاب الكبد D أكبر بكثير منه للمرضى السلبيين لالتهاب الكبد D (القيمة الاحتمالية = 0.001). وعند معظم المرضى المصابين بالتهاب الكبد D، كان الحمل الفيروسي لفيروس التهاب الكبد B أقل من 2000 وحدة دولية/ ميلٍّ لتر (53.6٪) وكانت نتائجهم سلبية لمستضد e لالتهاب الكبد B (93.6٪). وعند المقارنة بين المرضى الإيجابيين لالتهاب الكبد D والمرضى السلبيين له، كانت نسبة الإصابة أكبر بكثير بين المرضى الإيجابيين، وذلك لفيروس التهاب الكبد C (القيمة الاحتمالية < 0.001)، وتشمُّع الكبد (القيمة الاحتمالية < 0.001)، والورم الكبدي الخبيث (القيمة الاحتمالية = 0.006).

الاستنتاجات: ترتبط الإصابة بفيروس التهاب الكبد D بانخفاض انتقال فيروس التهاب الكبد B عبر مجرى الدم والإصابة بمرض الكبد الأكثر تقدمًا لدى الفئة الخاضعة للدراسة.

References

1. Rizzetto M. Hepatitis D: thirty years after. J Hepatol. 2009;50:1043–50. https://doi.org/10.1016/j.jhep.2009.01.004
2. Rizzetto M, Ciancio A. Epidemiology of hepatitis D. Semin Liver Dis. 2012;32:211–9. https://doi.org/10.1055/s-0032-1323626
3. Hepatitis B. Geneva: World Health Organization; 2020 (https://www.who.int/news-room/fact-sheets/detail/hepatitis-b, accessed 28 December 2020).
4. Hepatitis D. Geneva: World Health Organization; 2022 (https://www.who.int/news-room/fact-sheets/detail/hepatitis-d, accessed 28 December 2020).
5. Chen HY, Shen DT, Ji DZ, Han PC, Zhang WM, Ma JF, et al. Prevalence and burden of hepatitis D virus infection in the global population: a systematic review and meta-analysis Gut. 2019;68:512–21. https://doi.org/10.1136/gutjnl-2018-316601
6. Fattovich G, Bortolotti F, Donato F. Natural history of chronic hepatitis B: special emphasis on disease progression and prognostic factors. J Hepatol. 2008;48(2):335–52. https://doi.org/10.1016/j.jhep.2007.11.011
7. Fattovich G, Giustina G, Christensen E, Pantalena M, Zagni I, Realdi G, et al. Influence of hepatitis delta virus infection on morbidity and mortality in compensated cirrhosis type B. The European Concerted Action on Viral Hepatitis (Eurohep). Gut. 2000;46(3):420–6. https://doi.org/10.1136/gut.46.3.420
8. Koh C, Canini L, Dahari H, Zhao X, Uprichard SL, Haynes-Williams V, et al. Oral prenylation inhibition with lonafarnib in chronic hepatitis D infection: a proof-of-concept randomised, double-blind, placebo-controlled phase 2A trial. Lancet Infect Dis. 2015;15:1167–74. https://doi.org/10.1016/S1473-3099(15)00074-2
9. Yurdaydin C, Keskin O, Kalkan Ç, et al. Optimizing lonafarnib treatment for the management of chronic delta hepatitis: the LOWR HDV-1 study. Hepatology. 2018;67(4):1224–36. https://doi.org/10.1002/hep.29658.

10. Yardeni D, Koh C. Bulevirtide for HBV and HDV infections. Drugs Today (Barc). 2021;57:433–48. https://doi.org/10.1358/dot.2021.57.7.3283861

11. Wedemeyer H, Schöneweis K, Bogomolov PO, Voronkova N, Chulanov V, Stepanova T, et al. Final results of a multicenter, open-label phase 2 clinical trial (MYR203) to assess safety and efficacy of myrcludex B in with PEG-interferon alpha 2a in patients with chronic HBV/HDV co-infection. J Hepatol. 2019;70:e81. https://doi.org/10.1016/S0618-8278(19)30141-0

12. Rikabi A, Bener A, Al-Marri A, Al-Thani S. Hepatitis B and C viral infections in chronic liver disease: a population based study in Qatar. East Mediterr Health J. 2009;15(4):778–84

13. Daw MA, Daw AM, Sifennasr NEM, Draha AM, Daw AM, Daw AM, et al. The epidemiology of hepatitis D virus in North Africa: a systematic review and meta-analysis. ScientificWorldJournal. 2018;2018:9312650. https://doi.org/10.1155/2018/9312650

14. Amini N, Alavian SM, Kabir A, Aalaei-Andabili SH, Saiedi Hosseini SY, Rizzetto M. Prevalence of hepatitis D in Eastern Mediterranean Region: systematic review and meta-analysis. Hepat Mon. 2013;13:e8210. https://doi.org/10.5812/hepatmon.8210

15. Population statistics quarterly bulletin, 4th quarter 2021. Doha: Planning and Statistics Authority; 2021 (https://www.psa.gov.qa/en/statistics1/pages/topicslisting.aspx?parent=Population&child=Population, accessed 25 September 2022).

16. Abbas Z, Jafri W, Raza S. Hepatitis D: scenario in the Asia-Pacific region. World J Gastroenterol. 2010;16:554–62. https://doi.org/10.3748/wjg.v16.i5.554

17. Giersch K, Dandri M. Hepatitis B and delta virus: advances on studies about interactions between the two viruses and the infected hepatocyte. J Clin Transl Hepatol. 2015;3:220–9. https://doi.org/10.14218/JCTH.2015.00018

18. Coghill S, McNamara J, Woods M, Hajkowicz K. Epidemiology and clinical outcomes of hepatitis delta (D) virus infection in Queensland, Australia. Int J Infect Dis. 2018;74:123–7. https://doi.org/10.1016/j.ijid.2018.07.005.

19. Perez-Vargas J, Amirache F, Boson B, Mialon C, Freitas N, Sureau C, et al. Enveloped viruses distinct from HBV induce dissemination of hepatitis D virus in vivo. Nat. Commun. 2019;10:1–15. https://doi.org/10.1038/s41467-019-10117-z

20. Fattovich G, Tagger A, Brollo L, Giustina G, Pontisso P, Realdi G, et al. Hepatitis C virus infection in chronic hepatitis B virus carriers. J Infect Dis. 1991;163:400–2. https://doi.org/10.1093/infdis/163.2.400

21. Xiao G, Yang J, Yan L. Comparison of diagnostic accuracy of aspartate aminotransferase to platelet ratio index and fibrosis-4 index for detecting liver fibrosis in adult patients with chronic hepatitis B virus infection: a systemic review and meta-analysis. Hepatology. 2014;61:292–302. https://doi.org/10.1002/hep.27382