The prognosis of hepatitis delta infections in Belgium is poor and determined by the hepatitis delta viremia

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Background and Aims: Hepatitis B virus (HBV) – hepatitis delta virus (HDV) co-infection is considered the most severe form of chronic viral hepatitis and remains a major global health problem worldwide. Long-term studies that investigate the disease severity are of crucial importance to identify the factors that define the prognosis of this population.

Method: In the present study we retrospectively performed a medical chart review of hepatitis delta patients seen at 8 Belgian hospitals. All relevant data was uniformly collected from July 2001 until January 2023. The inclusion criteria were a) HBsAg or HBV DNA positive at admission; b) anti-HDV or HDV RNA positive; c) at least 1 follow-up visit.

Results: A total of 138 patients were included. The patients were predominantly male (64.5%), had a median age of 36.6 years and had a median follow-up of 5.4 (max 20.4) years. 35.6%, 47.8% and 16.7% of patients respectively were from African, Caucasian and Asian descent. The median AST, ALT and MELD score at admission were 55 (range 9 – 1735) U/L, 62 (range 13 – 5463) U/L and 7.9 (range 6 – 37) respectively. Cirrhosis was diagnosed in 40.6% (52/128) of the patients using liver biopsy (n = 27), liver stiffness measurement (n = 19) or the combination of clinical and radiological findings (n = 6) and did not differ between ethnicity groups (p = 0.06). A total of 33 patients (23.9%) had at least one severe adverse outcome during follow-up: 27 liver decompensations (19.6%), 12 HCC's (8.7%), 10 liver transplantations (7.2%) and 9 deaths (6.5%). Patients of Caucasian ethnicity had more frequently an adverse outcome than the other ethnicities (p = 0.04). The mean age at time of outcome was 48.6 years. The 1-, 5- and 10-year cumulative outcome probability is 8%, 15% and 49% respectively. The last available HDV RNA was positive in 80/120 (66.7%) patients. These patients had a higher AST (89 vs 49 U/L, p < 0.001), ALT (121 vs 61 U/L, p < 0.001) at admission and had more frequently cirrhosis (46.7% vs 24.3%, p = 0.02) than the patients with a negative last HDV RNA. There was no significant difference in gender (p = 0.11), age (p = 0.74) and MELD score at admission (p = 0.08) between these groups. A detectable HDV viremia at last evaluation was associated with a higher frequency of severe adverse outcomes compared to patients without HDV viremia (1-, 5- and 10-year cumulative outcome probabilities of 10% vs 0%, 18% vs 4% and 59% vs 14% respectively; Kaplan Meier p = 0.005). In

addition, having a negative HDV RNA at any point during follow-up was associated with not having an outcome (p = 0.009).

Conclusion: In this real-world national cohort study, approximately half of HBV-HDV co-infected patients develop a severe liver-related outcome within 10 years of diagnosis. Caucasian patients and those with a positive HDV RNA have a worse prognosis during long-term follow-up.

Figure: