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Hepatitis E virus genotype 3 subtype dependent clinical outcomes in Belgium 2010–2018

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Background and Aims: Except for immunosuppression, male gender, age >50 and chronic liver disease, no correlators with clinical outcomes of a Hepatitis E Virus (HEV) genotype (gt) 3 infection have been identified. In Belgium, diagnosis of HEV is centralized at the National Reference Center (NRC) for Viral Hepatitis, Sciensano. We analyzed virological factors and clinical outcomes in a nationwide cohort of HEV patients.

Method: Demographic, clinical and biochemical parameters of HEV infections documented at the NRC were collected between 2010–2018. Serum HEV –IgM, –IgG and HEV RNA were determined by ELISA and RT qPCR. HEV was subtyped by Sanger sequencing of an ORF2 fragment. Odds ratios (OR), risk ratios (RR) and 95% confidence intervals (95% CI) were calculated using STATA.

Results: 402 cases were identified. Among 300 cases with clinical data, the median age was 57 years and 69% were males. HEV viremia was detected in 211 patients with an available genotype in 177. HEV

gt3 infections largely predominate (93% [165/177]) with subtypes 3c (38% [67/177]) and 3f (44% [78/177]) almost equally represented. The percent of immunocompromised patients (30% vs 16%; OR3c=2,2 [1.0-4.7] p = 0.045) was higher for patients infected with a virus from the clade of gt3c (achi), compared to a virus from the clade of gt3f (efg), while a similar but non-significant trend was observed for preexisting liver cirrhosis (9.9% vs 3.4%; OR3c = 3.1 [0.8-12.5]). Patients with a HEV gt3f infection had higher peak values of ALT (mean of 2199 vs 1528 U/L; p = 0.005) and bilirubin (mean of 8.6 vs 4.1 mg/dl; p = 0.001) compared to a HEV gt3c infection. In addition, HEV gt3c infections were treated more in ambulatory settings, while the percent of patients admitted to the hospital was higher for HEV gt3f cases (36% for 3c; 61% for 3f; RR3f = 1.7 [1.2-2.4] p = 0.003). There were no differences between the subtypes in intensive care unit admissions (5.7%), in hospitalization durations (median of 4.0 weeks), in chronicity (18% vs 14%, RR3f=0.8 [0.4-2.0]) nor in deaths (1.4% vs 4.8%; RR3f = 3.4 [0.4-30]).

Conclusion: A similar number of HEV gt3c and gt3f infections have been diagnosed in Belgium. Despite more pre-existing comorbidity in patients infected with HEV gt3c, HEV gt3f infections are associated with a more severe disease course according to laboratory values and hospitalization rates. Our nationwide analysis is the first to identify a correlation between HEV gt3 subtype and clinical outcomes.

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Background and Aims: Liver-transplanted patients with acute hepatitis E virus (HEV) infection are at risk developing a chronic infection, which may rapidly progress to severe liver damage if not treated. However, the prevalence of HEV infection after liver transplantation remains largely unclear and likely varies geographically. Thus the aim of this study was to investigate the prevalence of acute and chronic HEV infection among liver transplant recipients in an HEV endemic region.

Method: During 2013–2018, 116 liver-transplant recipients were prospectively enrolled. They were evaluated for anti-HEV IgM and IgG antibodies as well as HEV RNA at the time of liver transplantation, and 6 and 12 months post transplantation. Additionally, medical records were reviewed.

Results: Seven (6%) had detectable HEV RNA, of whom six acquired their infection post-transplantation and one had detectable HEV RNA prior to transplantation. Additionally, 4 (3%) patients had serological markers indicative of HEV infection without detectable HEV RNA. Signs and symptoms of HEV infection were subtle, none were diagnosed in routine clinical care, and none developed a chronic HEV infection. Furthermore 15 patients (13%) had reactive anti-HEV IgG serologies in pre-transplant samples.

Conclusion: A substantial proportion of liver transplant recipients in Sweden are at risk of acquiring acute HEV infection, but surprisingly, no chronic HEV infection were detected in the present study. As HEV infections are often discrete and not diagnosed by current clinical practise, and as ribavirin therapy is available, the introduction of routine prospective HEV RNA screening of liver transplant recipients may be warranted.