The main part of the research was a retrospective case-case study of all available adult cases of acute hepatitis E and A admitted in The Teaching Hospital of Infectious Diseases of Cluj-Napoca, Romania, between 2017 January 1 and 2019 August 30.

Hepatitis A was chosen due to similar (mainly enteral) transmission and usually self-limited evolution. Since hepatitis E is not common in children, we decided to only include adult patients.

Inclusion criteria were defined as a diagnosis of acute hepatitis E or A at discharge (ICM10 codes: B17.2 and B15.\*, respectively), admission date between 2017 January 1 and 2019 August 30 and age > 18 years old. No specific exclusion criteria were used.

All clinical departments within our hospital were considered similar regarding diagnosis and management of the patients and the judgment of all doctors assigned to each patient was considered equivalent. We gathered information on laboratory parameters at admission (total and direct bilirubin, INR, prothrombin index, ALT, AST, γ-GT and ALP), final diagnosis and doctors’ description of each patient’s presentation and evolution.

The etiology of hepatitis A and E was established from blood samples by qualitative anti-HAV and anti-HEV IgM respectively using *bioMérieux VIDAS® Hepatitis panel* electrochemiluminescence immunoassays [1]. According to our hospital’s protocol, valid since 2016 and during the whole study period, all suspected cases of acute viral hepatitis were tested simultaneously for hepatitis A – E from the same blood sample as a single laboratory request.

To put the main study into context, we counted all confirmed cases of acute viral hepatitis A-E IMC10 codes B15-B17.2), of all ages, registered in our hospital during the same period.

We further investigated the severe cases of both hepatitis E and A within the main study as case series. *We defined* severe cases of hepatitis E if INR >1.5, hepatic encephalopathy grades 2-4 and/or comorbidities (acute-on-chronic liver disease, confirmed immunosuppression) or neurological manifestations were found (according to EASL guideline 2018 and our hospital’s protocol) [2]. The therapeutic approach for these patients was supportive treatment *plus* ribavirin (600-800 mg/day). *We defined* severe cases of hepatitis A if INR >1.5, hepatic encephalopathy grades 2-4 were present (according to EASL 2016 guidelines and our hospital’s protocol) [3]. The therapeutic approach for these patients was supportive treatment *plus* plasma products. Therefore, all patients received appropriate supportive treatment according to our hospital’s protocols and general recommendations, as needed: hepatoprotective agents (ursodeoxycholic acid, L-arginine supplementation), ammonia-reducing agents (rifaximin, lactulose), glycemia correction, liquid repletion, cholecystitis treatment [3]. *We defined* additional treatment as ribavirin in hepatitis E patients and plasma products in hepatitis A patients.

In assessing disease severity we gathered information on common signs and symptoms of acute viral hepatitis, neurologic manifestations and hepatic encephalopathy grading by West-Heaven criteria [4]. We reported a short summary of each selected patient’s comorbidities, evolution and possible causes of death.

All patients signed an informed consent form at admission allowing anonymous research on data included in the electronic records. This study was approved by the ethics committee of our hospital.

Data were centralized in a spreadsheet, checked for consistency, anonymized and imported into R 3.6.1 [5] on Linux where all subsequent statistical analyses were performed. We used absolute and relative frequencies to describe categorical data and means with standard deviations or medians with IQR and ranges to describe numerical data. Comparisons between hepatitis A and hepatitis E groups were performed using both univariate methods (t-test for continuous variables with normal distribution according to the Shapiro-Wilk test, Mann-Whitney test for continuous variables with non-normal distribution, Fisher test for binary variables) as well as two multivariate logistic regression models adjusting for (model 1): age & gender and (model 2): all variables taken into account. Prior to logistic models, right-skewed data were transformed using the decimal logarithm. All statistical tests used a significance cut-off value at p<.05.

Supplementary data, available online, include the R script used to generate the statistical analysis, randomly generated sample data, technical details on all variables, detailed explanation of the methods and details on our hospital’s protocols for diagnosis and management of hepatitis A and E.