



Beyond serology: integrating PCR to clarify HEV infection stage and liver injury in a Catalan healthcare area

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Background

Hepatitis E virus (HEV) is an emerging cause of acute hepatitis in Europe. Diagnosis relies on anti-HEV IgM/IgG and/or HEV RNA detection, which appear at different stages of infection, complicating interpretation. This study aimed to evaluate concordance between HEV PCR and serology on the same serum sample, assess IgG positivity among IgM-positive cases, and explore associations with liver enzyme levels.

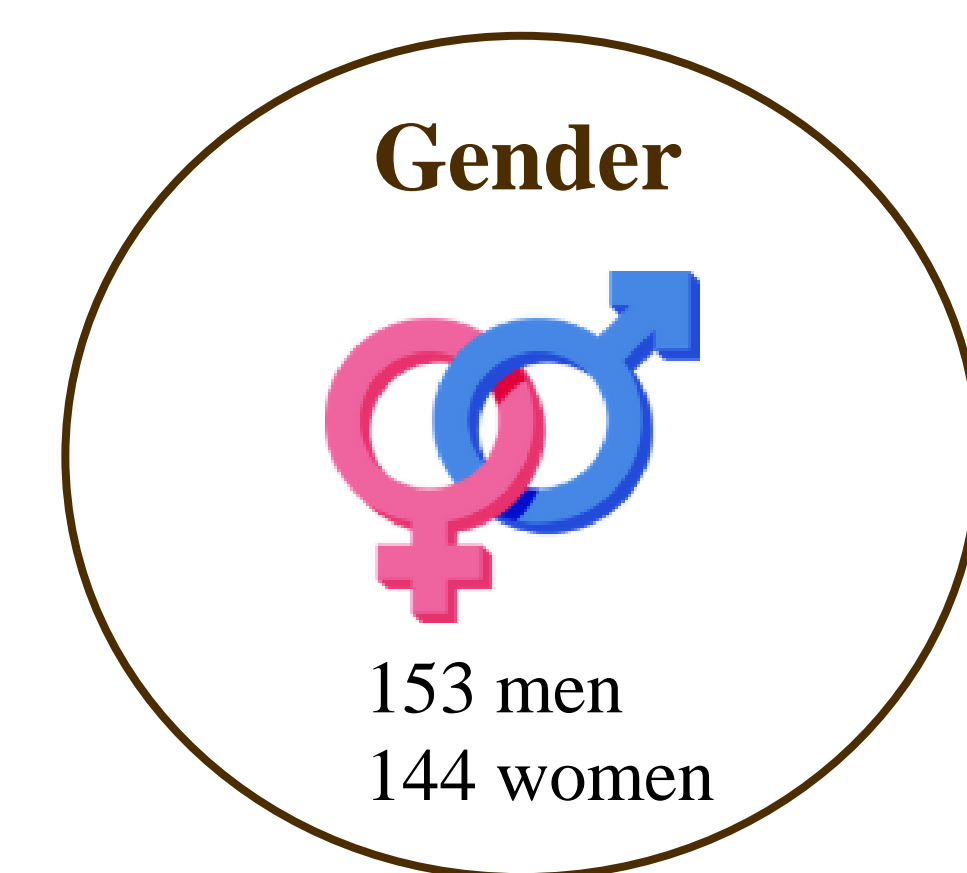
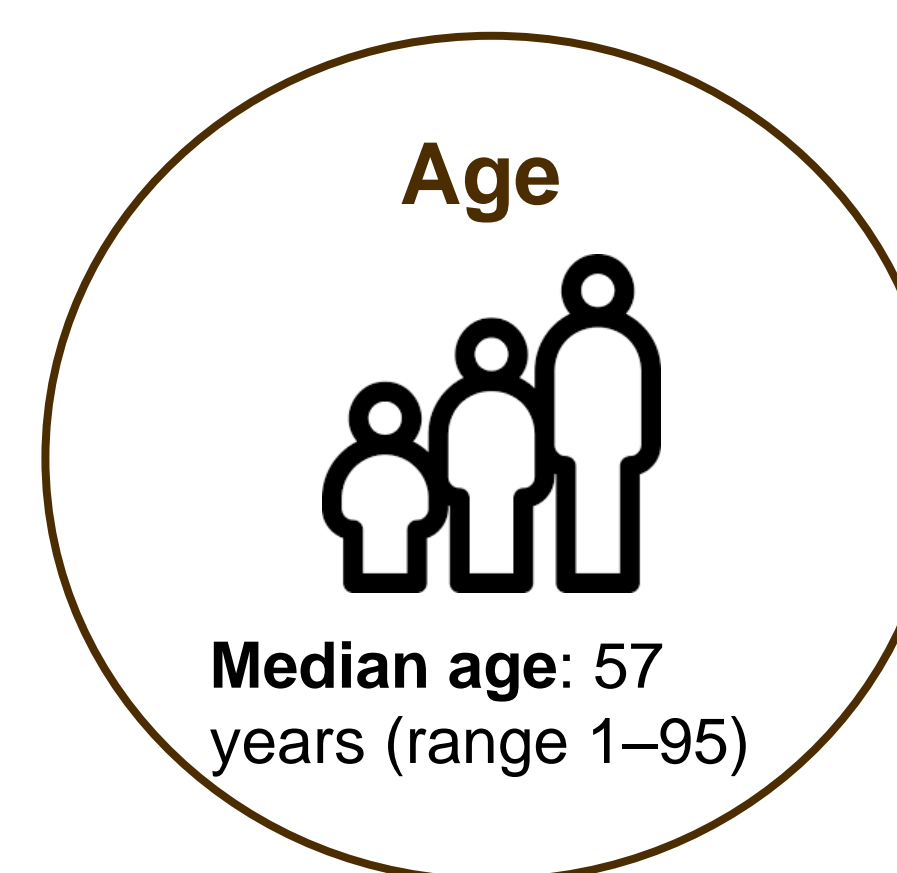
Methods

A **retrospective analysis** was conducted on serum samples tested for **HEV** (Hepatitis E Virus) between **September 2021 and December 2025** in the **Vallès Occidental healthcare area** (Barcelona, Spain). **Active or recent infection** was defined according to the **EASL criteria** (European Association for the Study of the Liver).

- **HEV RNA Detection:** **RealStar® HEV RT-PCR Kit** was used for the detection of HEV RNA in the serum samples.
- **Anti-HEV IgM/IgG Detection:** **VirClia® chemiluminescence** was used to detect anti-HEV IgM and IgG antibodies.
- **Liver function markers:** Values of **AST, ALT, and total bilirubin** corresponding to the test date were retrieved to assess liver function.

Results

A total of **318 serum samples** from **287 patients** were analyzed, with **HEV RNA detected in 20/318 samples** (6.3%). Additionally, **stool PCR** was performed in **61 cases**.



1. HEV RNA Detection and IgM/IgG Correlation

- HEV RNA was detected in **20/318 samples (6.3%)**.
- Among PCR-positive samples, 17 were IgM-positive, 2 IgM-negative (early infection or possible false-positive), and 1 lacked IgM testing.
- Conversely, **28 IgM-positive** samples were **PCR-negative**, most also IgG-positive, suggesting ongoing or recent infection.
- **Serum–stool PCR concordance was 60/61**, and overall agreement between serum PCR and IgM was 90.9%. See Table 1.

Table 1. HEV RNA Detection and IgM/IgG correlation and concordance with stool HEV PCR.

SERUM HEV PCR	IgM POSITIVE	IgM NEGATIVE	IgM NOT PERFORMED	TOTAL	STOOL HEV PCR (performed in parallel)
POSITIVE	18	2	1	21	7 positive* (1 only stool positive)
NEGATIVE	28	260	10	298	54 (100% concordant)
TOTAL	46	262	11	318	61

2. Correlation Between HEV RNA Detection, Liver Enzymes, and IgG Seroconversion in IgM-Positive Hepatitis E Samples

- **PCR Detection in IgM-Positive Samples:** 18 out of 50 IgM-positive samples (36%) were HEV RNA-positive.
- **Liver Enzyme and Bilirubin Comparison:** PCR-positive samples had significantly higher AST (34 vs 6.5 U/L), ALT (24 vs 7.2 U/L), and bilirubin (85 vs 40 μmol/L) compared to PCR-negative samples (p-values < 0.001 for AST and ALT, p = 0.02 for bilirubin).
- **IgG Seroconversion:** IgG was detected in **42 of 50 IgM-positive samples (84%)**, including all PCR-negative cases, suggesting ongoing or completed seroconversion.

Table 2. Correlation Between HEV RNA Detection, Liver Enzymes, and IgG Seroconversion in IgM-Positive Hepatitis E Samples

ANTI-VHE IGM POSITIVE SERUM SAMPLES	N	AST (U/L) MEDIAN (RANGE)	ALT (U/L) MEDIAN (RANGE)	BILIRUBIN (μMOL/L) MEDIAN (RANGE)
PCR POSITIVE	18	34 (5-80)	24 (1.5-65)	85 (8.5-201)
PCR NEGATIVE	28	6.5 (0.3-47)	7.2 (0.3-46.8)	40 (1.4-238)
PCR NOT PERFORMED	4	20 (5-55)	10 (3-20)	38.5 (11-65)
TOTAL	50	16.8 (0.3-80)	12.4 (0.3-65)	52 (0.3-238)

Conclusions

- PCR may help **detect patients with active virus** and higher liver enzyme elevations.
- IgM positivity, even if PCR is negative, particularly when accompanied by IgG seroconversion, could indicate active or resolving infection.
- Using **PCR and serology together** on the same sample could improve understanding of **infection stage**.
- Combining PCR, IgM, and IgG results may provide a clearer picture of liver injury and support patient management.