Acute hepatitis E incidence and seroprevalence in a UK population

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BACKGROUND: Hepatitis E (HEV) is a food- and water-borne, non-enveloped single-stranded RNA (7.2 kbp) *Orthohepevirus,* previously mostly associated with travel-related infections. In recent years, there have been concerns about non-travel-related HEV infections in France [**1**] and Singapore [**2**], leading to a call for the screening of blood and haematological transplant donations [**1,2,3**].

A recent UK study screening 225,000 blood donations found 79 that were HEV RNA positive (viraemic), giving a prevalence of 1 in 2848 (0.035%). Of the 43 recipients of affected blood products, 18 (42%) were found to be HEV-infected [**4**]. On the basis of these findings, guidelines have been published for the inclusion of HEV testing in suspected acute viral hepatitis cases [**5**], as well as for the routine screening of blood and tissue donors **[6,7**].

Other reports have found that zoonotic HEV infections, most likely from HEV-infected swine populations, are increasing with seroprevalence estimates ranging from 0.6% to 52.5% **[8]** in some populations. Routine HEV serology and molecular testing has been introduced recently into our diagnostic laboratory. We reviewed all HEV test data to date, to obtain a better understanding of the local HEV disease burden in this Leicester population. Hepatitis E IgM and RNA positive samples were sent to the national reference laboratory at Colindale for further characterisation

METHODS: Data from all HEV testing during Jan-Sep 2017 was included. Laboratory results for HEV serology (IgM, IgG, total Abs - Diagnostic BioProbes s.r.l., Sesto San Giovanni, Italy), HEV RNA (Micropathology Ltd., Coventry, UK), liver function tests and patient demographic data were reviewed. Acute cases were initially defined as HEV IgM POS and/or HEV RNA POS (regardless of HEV IgG status).

RESULTS: Of the total 339 patients tested 227 (67%, mean age: 53.9 years, s.d. 21.05, 52% male) were tested as part of an acute hepatitis screen and all but one of the remaining 112 patients (33%, mean age 53.3 years, s.d. 13.7, 53% male) tested as part of pre-transplant screening.

Of the 227 patients presenting with symptoms and signs of acute hepatitis that were screened, 113 (49.8%) were HEV IgM and HEV IgG NEG. Twenty-eight cases of acute HEV were identified (see Table 1). Men were more commonly affected (16 vs. 12 cases), however affected women were slightly older (median 62.5 years vs. 59.5 years). Hepatitis E RNA was detected in 9 of these cases (range <100 to 333,000 IU/ml). Alanine aminotransferase (ALT) levels were higher in acute HEV vs. non-HEV cases (median 673 vs. 375 IU/ml, IQR 215.25 vs. 224.5), and also higher in HEV RNA POS acute cases vs. those with undetectable HEV RNA (median 1374 vs. 405 IU/ml, IQR 817.5 vs. 113). Isolated HEV IgG seropositivity increased with age (years): 0% (0-17), 14% (18-64), 20% (>65). This effect was most notable in those aged >40 years.

Table 1: Acute HEV cases by serological profile

	Acute HEV	HEV RNA Positive
HEV IgM EQU, IgG NEG	1	1 (strongly POS)
HEV IgM POS, IgG NEG	2	-
HEV IgM POS, IgG EQU	1	-
HEV IgM POS, IgG POS	24	8

We have been screening for HEV as part of our renal and bone marrow transplant programme. Of the 112 patients in this category (4 donor, 108 recipient), 104 were HEV IgM and IgG NEG; in this group median ALT was 20 IU/ml (IQR 14). 2 patients were HEV IgM and IgG POS but HEV RNA NEG and were likely non-specific reactions on the HEV IgM/ IgG assays. Of these, one had normal ALT. No further information was available for the other. In addition, a further 41 of these patients had HEV RNA levels checked and all were undetectable. HEV IgG seropositivity was 7% (n=8/112) in this pre-transplant screening population.

DISCUSSION: From this single-site study, it is clear that hepatitis E is an increasingly recognised cause of acute hepatitis in the UK. In our study patients with acute/recent HEV had higher ALT than in non-HEV cases and were mostly middle-aged or older, consistent with published data. Despite recent concerns around HEV in transplant populations we found no cases of either acute HEV infection or asymptomatic viraemia in those screened pre-transplant.

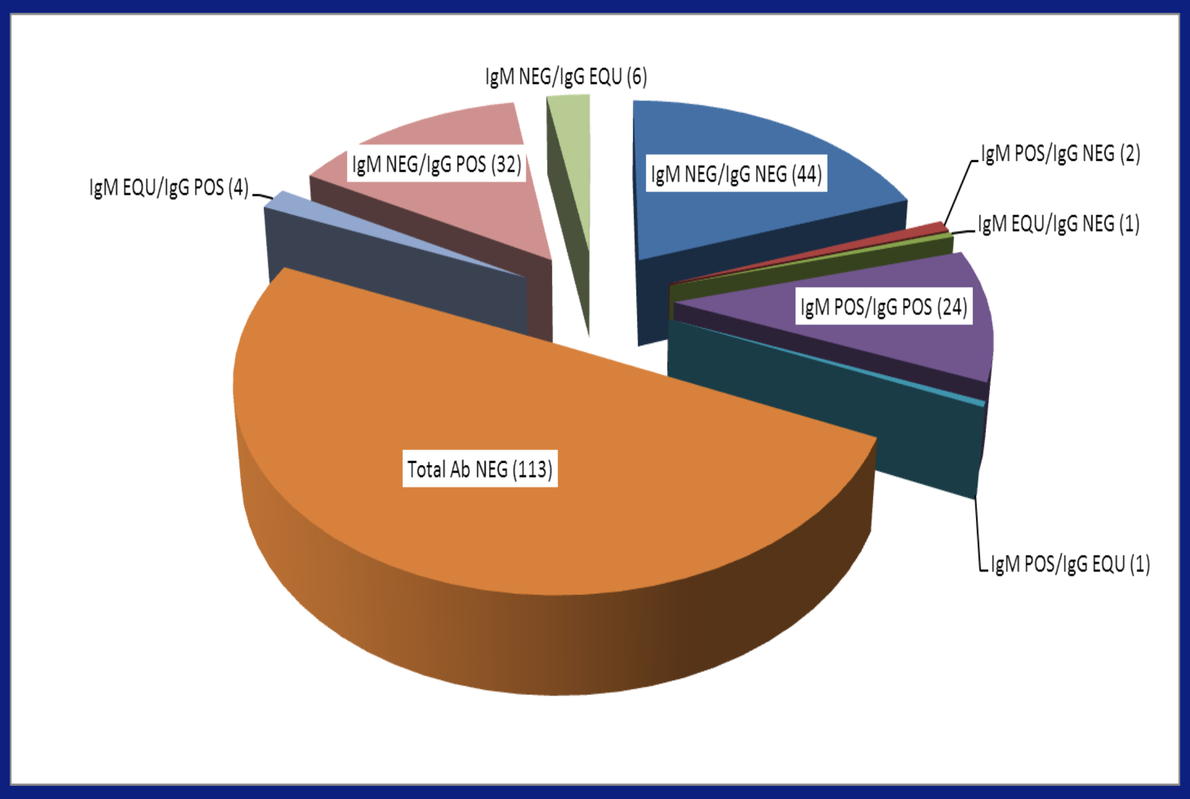


Figure 1: Acute hepatitis screening: HEV serological profile

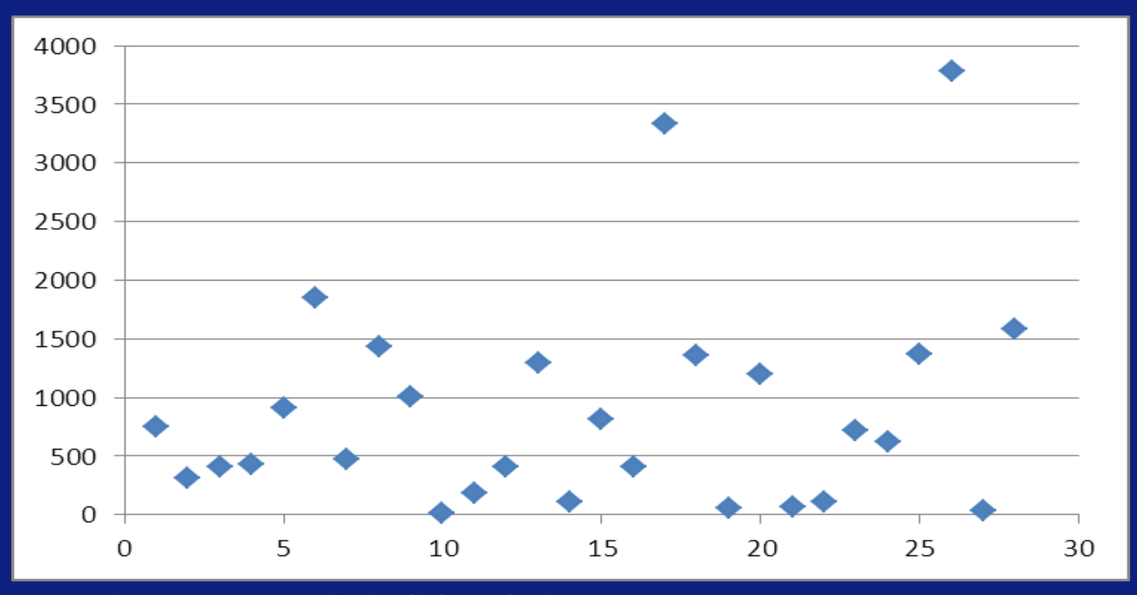
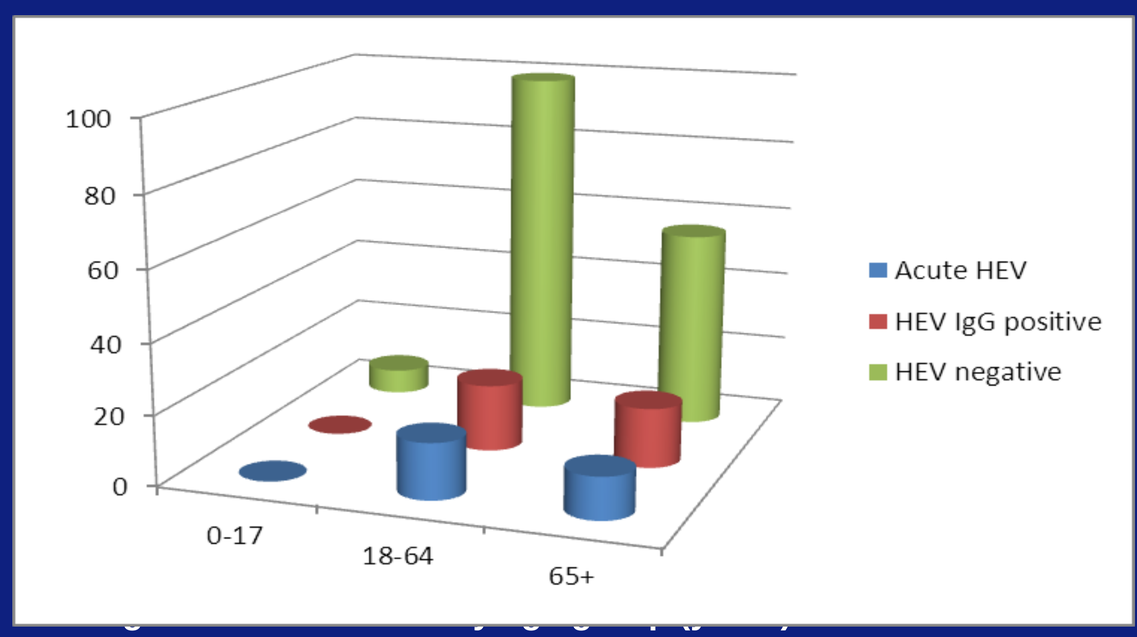


Figure 2: ALT (IU/ml) levels in acute HEV cases



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