Reply to the query “Chronic hepatitis E virus infection by genotype 1”

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Sir,

We are obliged by the keen interest of the author of this letter on our article and thankful to her for continuing the discussion on this extremely important subject of chronic infections caused by hepatitis E virus (HEV).

We agree with the authors that it is still not the time to call off the role of virological factors in causing chronic infections especially in the predominant circulating genotype 1 of HEV from our region. The same has been concluded by us in our study [1]. But the limited evidence available from our study and from another study in kidney transplant recipients pose a very bleak possibility of the same. On the other hand, the recent report of chronic hepatitis by HEV genotype 1 in a child with leukemia (which we have acknowledged in our article) cautions us against complacency too soon [2].

The authors have discussed the findings of Lhomme et al. [3] wherein greater quasi species heterogeneity of open reading frame 1 (ORF1) is associated with persistence in HEV genotype 3 infections, and pondered if the same would hold true for genotype 1.

The genetic divergence in HEV is highest in the polypropylene region (PPR) of the ORF1 of HEV genome. This region shows more divergence in genotypes 3 and 4 than genotype 1 reflecting the better host adaptability of the virus. The homoplastic density of the PPR reflecting the convergence of evolution also was found to be higher in genotypes 3 and 4 of HEV as compared to genotype 1 [4]. The influence of genetic divergence, host adaptability modulating the pathogenicity of the virus is a known phenomenon in most of the viruses especially RNA viruses with high replication rates like in hepatitis C, influenza viruses, and chikungunya [5]. The findings of Ikram et al. [6] in their comprehensive study highlights that HEV is under continuous evolutionary pressure and

changes in its pathogenicity is reflective of the same. However, in their study V1213A, the only characteristic mutation associated with chronic hepatitis was found in 95% of genotype 3 ORF1 sequences (125 of 131) as compared to none in genotype 1 ($n = 57$) or genotype 4 ($n = 99$). This stark finding could account for the comparatively limited potential of HEV genotype 1 to cause persistent infections and thus the extreme scarcity of such reports.

To conclude, preliminary evidence suggests that HEV genotype 1 possesses a limited potential of chronicity. However, it is too early to give up and we should be on an active lookout for the same. Large multicentric longitudinal studies of similar nature are the need of the hour.

Compliance with ethical standards

Conflicts of interest EG, and PA declare that they have no conflict of interest.

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