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Paper Poster Session IV

Updates on viral hepatitis

Influence of viral load and host cytokines in the pathogenesis of acute and fulminant hepatitis E

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Introduction: Hepatitis E virus (HEV) infection is endemic in India with a reported 70,000 mortality globally. The disease manifestation ranges from self-limiting acute viral hepatitis (AVH) to acute liver failure (ALF). The varied clinical course of the disease might be contributed to viral load and genotypes or due to the interplay between various host cytokines.

Objectives: To evaluate the HEV viral load, genotypes and cytokine response of IL4, IL10, IL12, TNF-α, IFN-γ and TGF-β and their correlation with the disease severity.

Materials and Methods: A total of 50 AVH, 30 ALF and 50 HC were recruited for the study. The serum samples were tested for anti-HEV IgM by MicroElisa and HEV RNA by neste reverse transcriptase PCR. HEV genotyping was carried targeting RdRp region of ORF1 gene using the nested RT-PCR. For viral load estimation HEV RNA was amplified by single step Real Time PCR for quantification using *in-house* RNA standards. Cytokine levels were estimated by multiplexed cytokine Bead Array.

Results: The mean circulating HEV viral load was significantly higher in AVH as compared to ALF patients ($1.13x10^6 \pm 4.1x10^5$ Vs $1.97x10^3 \pm 6.14x10^2$; $p<0.0001$). Circulating levels of the serum cytokines were in general low. A Th2 bias was observed in ALF patients with an IFNγ: IL4 ratio of 0.647, while a Th1 response was evident in AVH patients with a ratio of 3.4. TGF-β levels were significantly elevated in patients as compared to HC (HC: 57.40±27.48 ng/ml, AVH: 322.8±212.2 ng/ml, ALF: 334.5±203.8 ng/ml). The sequencing results confirmed the HEV strains as Genotype 1.

Conclusions: The low viral load in ALF cases might be suggestive of immune mediated hepatic damage and sequestration of the virus in liver. Serum cytokine levels in ALF exhibited a shift towards Th2 bias with an increase in circulating TGF-ß indicating the role played by T-regulatory cells in the disease pathogenesis.