

P0641C Study on immunopathogenesis of RSV associated acute lower respiratory tract infections in children with special emphasis on MMP-9 and TIMP-1

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Background: RSV is the most significant causes of severe lower respiratory tract infection in children under 2 years of age mostly in developing countries. In the absence of clarity in the disease pathogenesis, the role of viral load and host cytokines need to be ascertained.

Materials/methods: NPAs were collected from children (n=349) admitted in tertiary care hospital from north India between December 2013-March 2017. Samples positive for RSV by RT PCR targeting N gene were subjected for viral load estimation by Real Time PCR using CDC recommended primer-probes. The level of IL-17A, IFN- γ , TNF- α , IL-10, IL-6 in NPA samples were determined in flow cytometry by CBA and IL-33, MMP-9 and TIMP-1 levels by ELISA. The viral load and cytokine levels were correlated with the WHO specified acute and severe (comprising severe and very severe) ALRTI Patients using Mann Whitney test.

Results: In the study, RSV was positive in 41.4% (146/349) patients. The mean RSV viral load in acute LRTI [$5.9 \times 10^6 \pm 1.2 \times 10^7$ (n=45)] and severe LRTI patients [$1.1 \times 10^7 \pm 2.2 \times 10^7$ (n= 77)] did not differ statistically. However, Pro-inflammatory cytokine TNF- α level turns out to be significantly higher [$p < 0.001$] in severe ALRTI than ALRTI patients [195.52 pg/ml (n=88)] Vs [14.34pg/ml (n=56)] and the same is observed with IL-6 [6552.7pg/ml vs 4548.14pg/m ($p = 0.007$)] and IL-10 [90.6pg/ml vs 25.97pg/ml; ($p < 0.001$)] as well. Th17 cytokine (IL-17) found to be significantly higher ($p < 0.05$) in ALRTI patients [48.86pg/ml (n=56)] than severe patients [31.71pg/ml (n=88)]. In addition, MMP-9 is secreted significantly in higher levels in severe LRTI patients (n=77) in comparison to Acute LRTI patients (n=35) 1119.54ng/ml Vs 30ng/ml with an uphold of thirty seven fold ($p < 0.001$) leading to a significantly higher MMP-9/TIMP-1 ratio in severe LRTI patients; 54.79 Vs 0.67 ($p < 0.001$).

Conclusions: Thus, in the absence of significant viral load, the study highlights the role of TNF - α , IL-6 and Th17 cytokines in the pathogenesis of RSV disease with the possible contibution of MMP-9/TIMP-1 ratio as a bad prognostic marker towards disease severity.