Parallel Session 2: Implementing Research Findings in Clinical Practice

T2b - Comprehensive Clinical, Virological, Microbiological, Immunological and Laboratory Monitoring of Patients Hospitalized with Coronavirus Diseases (COVID-19)

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Introduction and Project Objectives: The SARS-CoV-2 emerged in late 2019 and became a pandemic of devastating disease (COVID-19). Our project aimed at: (i) Evaluating the diagnostic performance of various specimen types; (ii) Delineating the profiles of virological and immunological markers; and (iii) Exploring alternative detection methods targeting different gene regions.

Methods: Prospective studies were performed on hospitalized COVID-19 patients. Diagnostic performance of self-collected samples was evlauted. Cytokine profile in association with clinical outcome was delineated. Clinical value of subgenomic viral RNA profiling from serial respiratory and stool specimens was examined.

Diagnostic value of self-collect samples: Deep throat saliva (DTS) had the lowest PCR positive rate (68.7% vs 89.4% [sputum] and 80.9% [pooled nasopharyngeal and throat swabs, NPSTS]), and the lowest viral RNA concentration (mean log copy/mL 3.54 vs 5.03 [sputum] and 4.63 [NPSTS]).

Mouth gargle (MG) was not different from DTS in the positive rates across test platforms (ranged from 89.9% to 96.3%, p=0.46 to 1.00). A positive correlation between the paired MG and DTS was observed (Spearman's correlation: 0.662-0.727).

Nasal strip showed significant correlation with NPSTS (p=0.0003) and DTS (p=0.01). Nasal strip and NPSTS showed 94% and 100% agreement for NPSTS-positive and -negative samples, respectively.

Cytokine/chemokine immune response: IL-38 showed a regulatory and protective role in SARS-CoV-2 infection. Proinflammatory Th1 helper (IL-18, IP-10, MIG, IL-10) and ARDS-associated cytokines (IL-6, MCP-1, IL-1RA and IL-8) were enhanced progressively with severity. Furthermore, 11 cytokines were consistently different in both early and late phases, including 7 (GROα, IL-1RA, IL-6, IL-8, IL-10, IP-10, MIG) that increased and 4 (FGF-2, IL-5, MDC, MIP-1α) that decreased from mild to severe/critical patients.

Subgenomic viral RNA profile: While conventional diagnostic PCR targeting genomic viral RNA often remained positive for 3-4 weeks, it was rare to have PCR targeting subgenomic viral RNA remained positive beyond 10 days after illness onset. Most stool specimens tested positive by diagnostic PCR were negative by subgenomic PCR, suggesting non-viable viruses.

Conclusion: DTS is suboptimal in diagnostic yield, whereas mouth gargle can be applied for massive screening. Nasal strip provides a good diagnostic yield and is particularly feasible for children. Th1 helper response and ARDS-associated cytokines correlate with severity. MCP-1 predicts day of mechanical ventilation, vasopressor requirement and length of ICU stay. PCR targeting subgenomic viral RNA and does not require a high biosafety containment facilities, and is a feasible and reliable tool to monitor infectivity.

Project Number: COVID190107