16° CONGRESSO NAZIONALE ICAR Italian Conference on AIDS and Antiviral Research
19-21 GIUGNO ROMA
UNIVERSITA' CATTOLICA DEL SACRO CUORE
CENTRO CONGRESSI EUROPA

ORAL COMMUNICATION

Covid-19 and post-Covid conditions in 2024: data from the EuCARE project

OC 20 Interplay between gut-barrier dysfunction, microbial translocation, microbioma and SARS-CoV-2 RNAemia in acutely ill unvaccinated COVID-19 individuals developing long-covid

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ABSTRACT
Background: The pathogenesis of long-COVID (i.e. LC) is influenced by heterogeneity of clinical manifestations, study populations, time of follow-up, and viro-immunological parameters. The role of gut-barrier dysfunction, microbial translocation (MT), and SARS-CoV-2 RNAemia have not shown conclusive results. We aimed to evaluate their interplay in LC development.
Methods: We consecutively enrolled unvaccinated, hospitalized COVID-19 patients during acute-COVID-19 (T0) who either developed LC (LC+) at a follow-up visit 2 months from viral clearance (T1) or did not (LC-). All virologic and microbial parameters were assessed at both time points: SARS-CoV-2 RNAemia (RT-qPCR, log10(copies/mL), eCAD and IFABP for gut-barrier dysfunction (ELISA), LBP for MT (ELISA) on plasma, as well as microbiome on whole blood (NGS of the 16S bacterial gene).
Results: A total of 21 LC+ and 19 LC- matched for age, gender, co-morbidities and COVID-19 severity were enrolled in the study. Median age in both groups was 55 years (45-69 IQR LC+, 56-67 IQR LC-), 70% in LC+ and 85% LC- group were male. The most frequent symptoms at follow-up in the LC+ were: fatigue (71%), mnestic disorders (33%), dyspnea (19%), pain (19%), and anosmia/dysgeusia (14%).
At baseline, individuals who developed LC showed higher LBP compared to LC- (Fig. 1A); in contrast, gut-barrier dysfunction and amount of bacterial 16S rRNA gene copies were similar in LC+ and LC- (Fig. 1A-B). At the same time-point, blood microbiome analysis revealed a non-significant trend towards lower richness within individuals developing LC, as measured by α-diversity. The blood microbiome of all individuals was dominated by Pseudomonadaceae and Sphingomonadacea families (Fig. 1C).
At viral clearance, LBP decreased in LC+ to the levels observed in LC-, whereas gut damage was similar. SARS-CoV-2 RNAemia did not associate with LC development 2 months from viral clearance (LC-: 0 log10(copies/mL) median T0, 0-3.5 IQR, and 0 log10(copies/mL) median T1, 0-3.5 IQR; LC+: 3

log10(copies/mL) median T0, 0-3.4 IQR, and 3.1 median T1, 0-3.5 IQR; p-values longitudinal analyses: 0.8 LC- and 0.5 LC+; p-values transversal analyses: 0.8 T0 and 0.3 T1), nor with gut-barrier dysfunction and MT. Finally, enrichment of the Oxalobacteraceae family was shown in the LC+ group at T1 (Fig. 1D).

Conclusions: Acutely ill, unvaccinated and hospitalized COVID-19 individuals developing LC feature increased MT and a less rich microbiome in the blood. At viral clearance, despite similar MT and gut barrier dysfunction markers, predominance of blood Oxalobacteraceae was found in LC+ individuals alone. These results, together with the consistent finding of comparable levels of SARS-CoV-2 RNAemia in the two groups at both time-points, suggest that translocation of Gram-negative bacterial families in the peripheral blood, rather than viral RNA, may play a role in the pathogenesis of long-COVID, that merits further investigation.

Figure 1