Title: Long-term Immune Reprogramming in Sepsis Survivors Versus Severe COVID-19 Survivors: A Comparative Study

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**Introduction:** Both sepsis and severe COVID-19 can trigger persistent immune alterations, but their long-term inflammatory profiles remain poorly characterized. This study directly compares monocyte reprogramming patterns in survivors of these conditions to identify distinct immunological trajectories.

**Methods:** We analyzed 34 sepsis survivors (3-year longitudinal follow-up) and 46 severe COVID-19 survivors (2-year post-discharge). qPCR assessed M1/M2 polarization markers (IL-1 $\beta$ , NLRP3, TGF- $\beta$ ) and inflammasome components. Clinical outcomes including mortality and readmissions were tracked.

**Results:** Sepsis survivors maintained elevated IL-1 $\beta$  (M1) and TGF- $\beta$  (M2) for 3 years (p<0.01), indicating chronic inflammation. COVID-19 survivors showed TLR4/MYD88 suppression (p<0.05) and reduced IL-1 $\beta$  at 2 years, suggesting immune exhaustion. IL-1 $\alpha$  dynamics differed significantly: transient elevation in sepsis survivors (resolving by 1 year) versus persistent increase in COVID-19 (p<0.001). Sepsis had higher 1-year mortality (30-44% vs 28%, p<0.01), with distinct causes: recurrent infections (47%) dominated in sepsis versus thrombotic events (32.8%) in COVID-19.

**Conclusion:** This first direct comparison reveals sepsis drives sustained inflammation while COVID-19 leads to immune suppression. These findings support tailored surveillance strategies: immunomodulation for sepsis survivors and thrombotic risk management for COVID-19 survivors.

## References

(Gritte et al. Frontiers in immunology, 2021; Gritte et al. Crit Care Explor, 2022; Klauss et al. Braz J Med Biol Res 2024)