

# THE ASSOCIATION BETWEEN CYTOKINE LEVELS, SEPSIS SEVERITY, AND CLINICAL OUTCOMES IN SEPSIS: A QUANTITATIVE SYSTEMATIC REVIEW PROTOCOL

Amal A. Gharamti<sup>1</sup>, Omar Samara<sup>2</sup>, Anthony Monzon<sup>2</sup>, Carlos Franco-Paredes<sup>3,4</sup>, Andrés F. Henao-Martínez<sup>3</sup>



<sup>1</sup>Department of Internal Medicine, American University of Beirut, Beirut, Lebanon

<sup>2</sup>University of Colorado – Denver, Anschutz Medical Campus

<sup>3</sup>Department of Medicine, Division of Infectious Diseases, University of Colorado Denver

<sup>4</sup>Hospital Infantil de México, Federico Gómez, México City, México

## INTRODUCTION

- Sepsis is an important global health problem that has been poorly understood and coined with the vague terms of, “Cytokine storm,” or “Cytokine release syndrome.”
- Cytokines, specifically: TNF- $\alpha$ , IL-1 $\beta$  and IFN- $\gamma$  and the antagonists TNFRp55, TNFRp75, and IL-1 RA, are poorly characterized during disease progression.
- **Aim:** To characterize the levels of key cytokines and cytokine antagonists in the circulation of healthy and septic individuals with the hope to better aid therapeutic approaches. These findings will help us better characterize the host-pathogen response during sepsis and possible new therapeutics pathways.

## BACKGROUND

- Sepsis is an important global health problem associated with significant morbidity and mortality.
- In 2017, there were an estimated 48.9 million cases of sepsis and 11 million sepsis-related deaths. Approximately 19.7% of all deaths recorded in 2017 were attributed to sepsis.<sup>1</sup>
- In the United States (US) in 2013, the annual cost of sepsis was estimated at \$23.7 billion, representing the largest expenditure for any disease treated in US hospitals.<sup>2</sup>
- In 1992, sepsis was defined as a systemic inflammatory response syndrome in the presence of a documented or clinically suspected infection.<sup>3</sup>
- In 2016, sepsis-3 diagnostic criteria were introduced, and sepsis was defined as "life-threatening organ dysfunction due to a dysregulated host response to infection." SEPSIS-3 defined SEPSIS as an increase in sequential organ failure assessment (SOFA) score by two or more points.
- At present, there is no standard diagnostic clinical or laboratory test for sepsis.<sup>4</sup>

## METHODS

Study Design	<ul style="list-style-type: none"> <li>• Meta Analysis</li> </ul>
Databases	<ul style="list-style-type: none"> <li>• Medline, Embase, Cochrane Library, Web Science Core Collection.</li> <li>• Studies included: 1985 to present.</li> <li>• Language restricted to English.</li> </ul>
Exclusion Criteria	<ul style="list-style-type: none"> <li>• Case reports and retrospective cohort studies</li> <li>• Cytokines measure via Radio-Immuno-Assay</li> </ul>
Inclusion Criteria	<ul style="list-style-type: none"> <li>• Healthy and septic patients whose cytokine measurement came from plasma, serum, or peripheral blood.</li> <li>• Cytokines measured via ELISA or Immunological beads</li> </ul>
Primary Outcome	<ul style="list-style-type: none"> <li>• Mortality rate</li> </ul>
Secondary Outcomes	<ul style="list-style-type: none"> <li>• ICU and hospital length of stay</li> <li>• Progression/Resolution of organ dysfunction: change in SOFA score.</li> <li>• Time until shock resolution</li> <li>• Requirement for vasopressors and duration of use</li> <li>• Need for mechanical ventilation and time spent on the ventilator</li> <li>• Need for renal replacement therapy (RRT) and duration of RRT</li> </ul>

## RESULTS

- All data extraction is done. Currently performing the statistical analysis of the study and looking at the results before reporting out the data.

## CONCLUSIONS

- We will hopefully characterize the different cytokines and their response during sepsis.

## STRENGTHS /LIMITATIONS

- This study will systematically assess the levels of key cytokines in sepsis patients and study the relationship between these levels and sepsis outcomes such as organ dysfunction and mortality.
- A systematic review of this topic will contribute to a better understanding of the pathophysiology of sepsis and inform therapeutic approaches to anti-cytokine therapy in patients with sepsis.
- A possible publication bias might limit this study as we will include only peer-reviewed published data. Therefore, this systematic review might not capture evidence from other sources.
- Guide to therapeutic approach.

## REFERENCES

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