

**Title: CYTOKINE AND CYTOKINE ANTAGONIST LEVELS IN HEALTHY INDIVIDUALS AND IN SEPSIS: AN ETIOLOGY AND RISK SYSTEMATIC REVIEW PROTOCOL.** Amal A. Gharamti, M.D., Omar Samara, MD Candidate in the School of Medicine, Anthony Monzon, Andrés Henao-Martínez, M.D., Department of Infectious Disease, university of Colorado, Denver, CO.

**Abstract:**

**Objective:** The main aim of this review is to characterize levels of key cytokines and cytokine antagonists in the circulation in healthy individuals and patients with sepsis.

**Introduction:** Research hypothesis has implicated multiple cytokines in the pathogenesis of sepsis. The levels of key cytokines, mainly TNF- $\alpha$ , IL-1 $\beta$  and IFN- $\gamma$  and antagonistic (anti-cytokine) molecules TNF soluble receptors (TNFRp55 and TNFRp75) and IL-1 receptor antagonist (IL-1ra) are poorly characterized during sepsis or in healthy volunteers. A systematic review of this topic will contribute to a better understanding of the pathophysiology of sepsis and inform therapeutic approaches to anticytokine therapy in patients with sepsis.

**Inclusion criteria:** Clinical trials and prospective cohort studies that measure relevant cytokine or cytokine antagonists will be included. We would include reports of any design with key information for healthy individuals as well as patients with sepsis. Sepsis patients will comprise those with a diagnosis of sepsis, severe sepsis, or septic shock. The primary outcome is levels of pro-inflammatory and anti-inflammatory cytokines (6 molecules total, see above). Studies will be restricted to the English language. We will limit to studies published from 1985 forward.

**Methods:** Medline, Embase, Cochrane Library, and Web of Science Core Collection will be searched for eligible studies. Two reviewers will independently screen and select studies, assess methodological quality, and extract data. A meta-analysis will be performed, if possible, and the Grading of Recommendations Assessment Development and Evaluation (GRADE) Summary of Findings presented.

**What is left:** We are at the stage of statistical analysis of the entire data set. After completing the statistical analysis, we will move on to write up the conclusion and report out results before submitting to a journal.