INPLASY PROTOCOL

Corresponding author:
Mohammad Safiqul Islam

research_safiq@yahoo.com

Author Affiliation:
Noakhali Science and Technology University.

Elevated levels of pleiotropic interleukin-6 (IL-6) and interleukin-10 (IL-10) are critically involved with the severity and mortality of COVID-19: An updated longitudinal meta-analysis and systematic review on 147 studies

Jafrin, S[1]; Aziz, MA[2]; Islam, MS[3].

Review question / Objective: How were serum IL-6 and IL-10 linked with the severity and mortality of COVID-19 patients? To evaluate the role of IL-6 and IL-10 in the development of the severity or morality of COVID-19 patients. The outcomes (mean difference) were calculated between the severe vs. non-severe COVID-19 patients and non-survival vs. survival patients to evaluate the risk of severity or mortality.
Condition being studied: Severity and mortality among the COVID-19 patients.
Information sources: The international scientific authorized databases such as Google Scholar, PubMed, Embase, CNKI, Cochrane Library, and Web of science were used as primary sources to identify and collect the eligible literature. Additional secondary databases were also comprehensively searched to extract more related studies.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 April 2022 and was last updated on 08 April 2022 (registration number INPLASY202240046).

INTRODUCTION

Review question / Objective: How were serum IL-6 and IL-10 linked with the severity and mortality of COVID-19 patients? To evaluate the role of IL-6 and IL-10 in the development of the severity or morality of COVID-19 patients. The outcomes (mean difference) were calculated between the severe vs. non-severe COVID-19 patients and non-survival

vs. survival patients to evaluate the risk of severity or mortality.

Rationale: Disruption in the natural immune reaction due to SARS-CoV-2 infection can initiate potent cytokine storm among COVID-19 patients. An elevated level of IL-6 and IL-10 during a hyperinflammatory state plays a vital role in increasing the risk of severity and mortality. In this study, we aimed to evaluate the potential of circulating IL-6 and IL-10 levels as biomarkers for detecting the severity and mortality of COVID-19.

Condition being studied: Severity and mortality among the COVID-19 patients.

METHODS

Search strategy: The specific search terms used for this study were: "COVID-19" OR "SARS-Cov-2"; "interleukin-6 " OR "IL-6"; and "interleukin-10" OR "IL-10".

Participant or population: Global population.

Intervention: Association of severity and mortality of COVID-19 with IL-6 and IL-10 levels was detected as mean difference with 95% confidence interval.

Comparator: Serum Il-6 and IL-10 levels of severe cases and non-survival COVD-19 cases were compared with non-severe and survival COVID-19 cases, respectively.

Study designs to be included: The serum levels of IL-6 or IL-10 or both were provided in the severe and non-severe cases or survival or non-survival cases.

Eligibility criteria: Inclusion criteria: 1) clinical studies, case-control investigations or cohort studies; 2) articles representing severity and mortality in COVID-19 patients; 3) articles providing information on IL-6 and IL-10 level among mild-to-severe COVID-19 patients; 4) articles reporting IL-6 and IL-10 level in the COVID-19 survivors and deceased patients.

Information sources: The international scientific authorized databases such as Google Scholar, PubMed, Embase, CNKI, Cochrane Library, and Web of science were used as primary sources to identify and collect the eligible literature. Additional secondary databases were also comprehensively searched to extract more related studies.

Main outcome(s): The pooled mean difference with a 95% confidence interval is the main outcome of this meta-analysis.

Additional outcome(s): Publication bias.

Data management: Two authors independently extracted the data, and the corresponding authors solved if there was any disagreement between them. The data was analyzed with RevMan 5.4 and all the related data was archived by the corresponding authors. The corresponding authors will provide the data with a valid request.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Scale (NOS) can determine the quality range of studies by rating them from 0 to 10 stars based on some specific features. Egger regression test and Begg & Mazumdar test were performed to detect the presence of publication bias.

Strategy of data synthesis: RevMan 5.4 was applied for the meta-analysis. The outcome was continuous and mean difference with standard deviation was used for data synthesis. The pooled mean difference with 95% confidence interval was obtained as outcome. A random effect model was applied for this meta -analysis as I2≥50% was obtained.

Subgroup analysis: No subgroup analysis was required as we performed analysis of serum IL-6 and IL-10 levels between severe vs. non-severe patients and non-survival vs. survival patients.

Sensitivity analysis: A sensitivity analysis was performed by removing each included

study and no significant impact was found on the pooled outcome.

Language: Manuscript was written in English but there was no language restriction for literature search.

Country(ies) involved: Bangladesh.

Keywords: COVID-19; Interleukin-6; Interleukin-10; Meta-analysis; Cytokine storm.

Contributions of each author:
Author 1 - Sarah Jafrin - Data collection, quality assessment, data analysis, and initial draft preparation.
Email: sarahjafrin1215@gmail.com
Author 2 - Md. Abdul Aziz - Data collection, quality assessment, data analysis, and initial draft preparation.
Email: aziz.nstupharma@gmail.com
Author 3 - Mohammad Safiqul Islam - Concept, study design, data-analysis, edition, and correction of the manuscript and overall supervision.
Email: research_safiq@yahoo.com