



Biomarkers of CRP, IL-6, and D-Dimer COVID-19 Patients That Are Giving Convalescence Plasma Therapy – Literature Review

Ainul Rofik^{1*}, Reza Hery Mahendra¹, Bastiana¹, Yekti Tunjungsari²

¹Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya

²UPPM FK Universitas Nahdlatul Ulama Surabaya

*Corresponding author: dr.ainul@unusa.ac.id

ARTICLE INFO

Keywords:

D-Dimer level, CRP level, IL-6 level, convalescent plasm, COVID-19 outcomes.

Submission: December 4th, 2021

Review: December 8th, 2021

Publish: January 20th, 2022

ABSTRACT

Background: Convalescent plasma therapy is the only antibody-based therapy used to treat COVID-19 Patients. The use of convalescent plasma therapy has been recommended by the FDA as a therapy for COVID-19 patients (FDA in Asep, 2020). Several routine biomarker parameters used as indicators in the diagnosis of COVID-19 are IL-6, CRP and D-Dimer. There was a change between the three biomarker values of IL-6, CRP and D-Dimer between COVID-19 patients on convalescent plasma therapy and COVID-19 patients who did not receive convalescent plasma therapy.

Objective: This review article is how effective of convalescent plasma usage as therapy for COVID-19 patients is by looking at changes in the biomarkers of IL-6, CRP and D-Dimer in patients receiving convalescent plasma therapy.

Methods: This literature review uses 3 fulltext articles obtained by combining keywords in an electronic database: Scopus, Cochrane Library, PubMed, and Google Scholar. Articles were eliminated using predefined inclusion and exclusion criteria, then analyzed systematically. The preparation of the discussion uses a systematic analysis based on the themes and topics of discussion obtained in the research article.

Conclusion: There were changes in the biomarker values of CRP, IL-6 and D-Dimer in COVID-19 patients who receiving convalescent plasma therapy and COVID-19 patients who did not.

Introduction

More than 30.6 million cases and the death of 950.000 people caused by COVID-19 have been reported to WHO. From 14 to 20 September 2020, there were almost 2 million new cases of COVID-19, representing a 6% increase over the previous week, and at the single week of the pandemic begin the highest number of

cases was reported (World Health Organization, 2020).

Common abnormalities of hematology in COVID-19 are thrombocytopenia, elevation of D-dimer levels, and lymphopenia. These changes are significantly more common in severe COVID-19 disease, and thus may serve as

a possible biomarker for those requiring hospitalization and ICU care.

The results of several studies indicate that the usage of convalescent plasma in patients recovering from Ebola, SARS-CoV, and H5N1 is effective. Serum taken from recovered patients can completely neutralize the cellular infectious ability of the isolated virus. Based on the research of Shen et al, reported that regulation of convalescent plasma have substance of neutralizing antibody in 5 critical cases, gave an improvement in their clinical status. However, the characteristics of these antibodies have not been studied in depth in conjunction with the patient's clinical manifestations.

Then the question arises whether a patient who has been given convalescent plasma therapy will show better routine biomarker results than patients who do not receive convalescent plasma therapy? Based on these questions, this literature review is intended to analyze the comparison of biomarkers patients who receiving a convalescent plasma therapy and COVID-19 patients not receiving convalescent plasma therapy. In addition, it will also be further identified how effective the convalescent plasma usage as therapy for COVID-19 is by looking at changes in the biomarkers CRP, IL-6 and D-Dimer in patients receiving convalescent plasma therapy.

Methods

Article searches were conducted in credible journals through 4 electronic databases (Scopus, Cochrane Library, PubMed, and Google Scholar). The keywords used were: C-Reactive protein level, D-Dimer level, Interleukin 6 level, convalescent plasma, and COVID-19 patients outcomes. The scope of the search was expanded to include a combination of Medical Subject Headings (MeSH) while making use of the Boolean operator combined with the keywords used. The articles obtained were then eliminated using the inclusion and exclusion criteria set by the author. The inclusion criteria used were: full text articles, research conducted in 2020 – 2021 and all studies containing CRP, D-Dimer, and IL-6 values. Meanwhile, the exclusion criteria used were all studies that did not use English or Indonesian. The preparation of the discussion uses a systematic analysis based on the themes and topics of discussion obtained in the research article.

Result and Discussion

A total of 3 full text articles were used in this literature review. There is one article published in 2020 and two articles in 2021. The research was taken in 3 different countries, namely Italy, China, and Iran. The characteristics of each article are described in the following table 1.1.

Convalescent Plasma Therapy (TPK)

Based on the diagnosis of Pneumonitis and the infection of SARS-CoV-2 treatment program, doctors in China turn to convalescent plasma transfusions, when drug therapy is unsatisfactory. Convalescent plasma is used as a last treatment to increase the survival chance of patients with acute respiratory syndrome infections. Although the potential for antivirals and immunomodulators is still being evaluated in COVID-19 patients, according to physiopathology, convalescent plasma therapy can reduce mortality (Hung in Sukohar, 2020).

The convalescent plasma therapy usage has been recommended by the Food and Drug Administration (FDA) since May, to health services and researchers regarding the use of convalescent plasma taken from recovered patients (FDA in Sukohar, 2020).

Convalescent plasma therapy is the regulation of passive polyclonal antibodies (Ab) to supply immediate immunity which has been used for more than a century to prevent and treat many infectious diseases and has been shown to reduce patient mortality in hospitals (Duan in Sukohar, 2020). Convalescent plasma therapy in 2009 H1N1 infection can reduce viral load, clear the respiratory tract, decrease serum cytokine response, and patient mortality

(Hung in Sukohar, 2020). In addition, convalescent plasma has been used as a therapy for Ebola virus outbreaks in Africa, based on research conducted by Edwads et al (in Sukohar, 2020) who reported that there was a reduction in mortality and no adverse reactions were found in the use of convalescent plasma therapy. In SARS Coronavirus and severe influenza, there was a significant decrease in the group of patients who had been treated with placebo or without therapy (Mair-Jenkins in Sukohar, 2020).

CRP and IL-6 in COVID-19 Patients

In COVID-19, an inflammatory processes occur in the body. Some evidence suggests that disease worsening in COVID-19 patients is closely related to dysregulation and excessive cytokine release. Observations in one study in Wuhan showed that patients who eventually died from complications of COVID-19 showed high interleukin (IL) 6, serum C-reactive protein (CRP), and ferritin, indicating that there was a hyperinflammatory process.

In a study on the interleukin-6 cohort conducted in China in 2020, it was found that the movement of the amount of IL-6 in patients who experienced an increase in serum interleukin, when compared at the time of admission to when they were declared cured of COVID-19, the

interleukin yield remained high so that the study supports its use for severity stratification (Zhang et al., in Haithani, 2021).

D-Dimer in COVID-19 Patients

Examination of hematological parameters becomes important especially in asymptomatic patients, suspected of having positive PCR results. Parameters that are often carried out in hematology and homeostasis examinations are Complete Blood, while for homeostasis include D-Dimer, Activated Partial Thromboplastin Time (APTT), and Prothrombin Time (PT) (Atna et al, 2021). In a case study by Luca Spezia et al (in Rostami, 2020), found that patients with COVID-19 experienced an increase in D-Dimer values.

Research conducted by Abdulgader et al (in Permana, 2021) concluded, cases of VTE in COVID-19 patients treated in the ICU showed a significant increase in D-Dimer levels, thus recommending anticoagulant prophylactic therapy. This increase in D-Dimer levels indicates plasmin-mediated hyperfibrinolysis, but it is interestingly not in accordance with the picture on Thrombo Elastography (TEG) which shows fibrinolysis Shutdown. The study of Uemura et al (in Kahar, 2021) found significantly high levels of D-Dimer

and fibrin/ fibrinogen degradation product (FDP) in COVID-19 patients.

Conclusion

There were changes in the biomarker values of IL-6, CRP and D-Dimer in COVID-19 patients who received convalescent plasma therapy and who did not.

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