

# The effectiveness of convalescent plasma for the treatment of patients with Coronavirus: a systematic review and meta-analysis

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## Abstract

Convalescent plasma may be of clinical benefit for treatment of 2019 Novel Coronavirus. We conducted a systematic review and meta-analysis of these interventions, including Middle East respiratory syndrome-Coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV) to summarize reliable evidences of the treatment. Methods: Three major electronic databases (PubMed, Google scholar) were searched, Several studies were collected for Meta-analysis. Results: Seven studies were included in Meta-analysis, including a total number of 416 patients with SARS and 169 patients with MERS infection. Meta-analysis shows that in critically ill patients, the Convalescent plasma can reduced mortality significantly. (odds ratio [OR]=0.27; 95% confidence interval [CI]=0.15-0.50; I<sup>2</sup>=0%; P = 0.47). Conclusions: The therapy of Convalescent plasma can reduce mortality of patients with Coronavirus, and it need to be further verified with Large-scale clinical trial.

## INTRODUCTION

As of 17 March 2020, China had been informed of 81116 confirmed cases of coronavirus disease 2019 (COVID-19), of whom 3231 (3.98%) have died. Until now, the virus still spread and have not been fully controlled<sup>[1]</sup>. The treatment of COVID-19 was mainly general supportive therapy<sup>[2]</sup>. Recently, It had been suggested that Convalescent plasma therapy will yield a clinical effect for the treatment of severe patients especially with cytokine storm<sup>[3]</sup>. However, The effectiveness were not yet verified, the underlying evidence is based on studies of other viral infections including Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome coronavirus (SARS-CoV)<sup>[4]</sup>. We conducted a systematic review and meta-analysis to evaluate the clinical effectiveness of convalescent plasma for the treatment of MERS-CoV and SARS-CoV, to help inform clinical management of COVID-19.

## 2. Material and Methods

2.1 We searched the databases containing PubMed, and Google scholar. We used the following keywords: “2019 Novel coronavirus” or “2019 novel coronavirus infection” or “COVID19” or “coronavirus disease 2019” or “coronavirus disease-19” or “2019-nCoV disease” or “2019 novel coronavirus disease” or “2019-nCoV infection” or “Wuhanvirus” or “coronavirus” or “SARS” or “MERS” AND “convalescent plasma” or “Blood Plasma” “Blood Fresh Frozen Plasma” or “Frozen Plasma, Fresh” or “Plasma, Fresh Frozen”.

2.2 The inclusive and exclusive criteria

2.2.1 Inclusive criteria: studies that include randomized controlled trials, non-randomized controlled trials, and patients in hospital or sent to the Intensive Care Unit (ICU) for treatment.

2.2.2 Exclusive criteria: repeated articles; reviews; studies on animals or In vitro studies.

2.2.3 paper quality evaluation

Two members of the team evaluated the quality using the Newcastle-Ottawa Scale (NOS).

#### 2.2.4 Statistical analysis

All statistical analyses were carried out with RevMan5.3 (Cochrane ), Statistical significance was assumed at the 5% level.

### 3. Results

An initial search identified a total of 35 articles from PubMed, 615 from Google scholar. After reviewing for inclusion and exclusion and the removal of duplications, a total of 7 studies were used for the full review (Figure 1). The mortality from the 7 trials showed convalescent plasma for the treatment of patients with Coronavirus was associated with lower mortality (odds ratio [OR]=0.27;95% confidence interval [CI]=0.15-0.50; Figure 2). Visual inspection of a funnel plot, did not exclude publication bias (Figure 3).

Figure 1. Flow of studies through the meta-analysis.

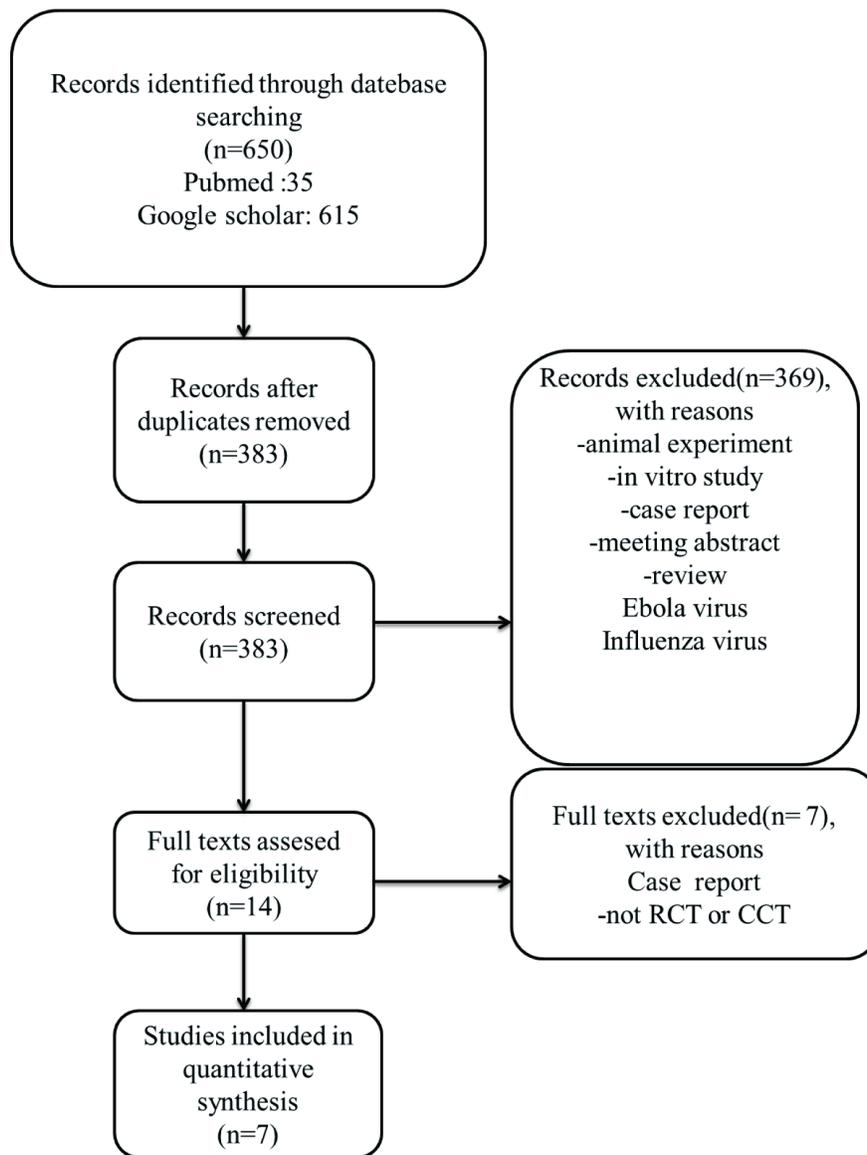


Figure 2. The outcome of convalescent plasma for the treatment of patients with Coronavirus

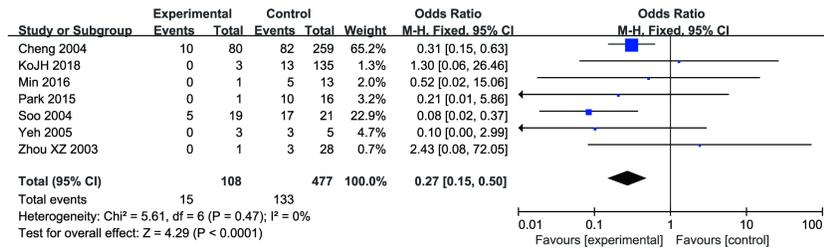


Figure 3. A funnel plot for analysis of mortality to show publication bias

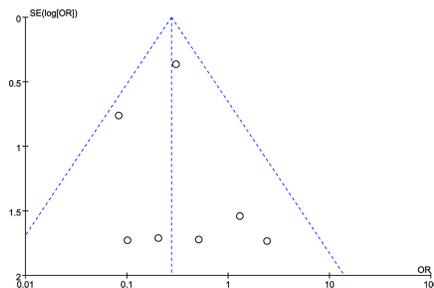
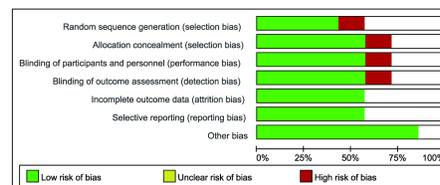


Figure 4. Risk of bias graph: each of item presented as percentages across all included studies



## Discussion

Coronavirus disease 2019 (COVID-19), which was identified due to the case of viral pneumonia in 2019, and was named by the world health organization on January 12, 2020<sup>[1]</sup>. Coronavirus is a large family of viruses known to cause serious illnesses such as MERS and SARS<sup>[5]</sup>. The novel coronavirus is a new strain of coronavirus that has never been found in humans before. Since December 2019, A lot of viral pneumonia cases have been detected, which have been diagnosed as viral pneumonia infection. People infected with coronavirus after the common signs of respiratory symptoms, fever, cough, gas and breathing difficulties. In more severe cases, the infection can lead to pneumonia, severe acute respiratory syndrome, kidney failure, and even death<sup>[6, 7]</sup>. There is no specific treatment for diseases caused by novel coronaviruses currently<sup>[8]</sup>. The generally susceptible and high mortality associated with COVID-19 led us to conduct this systematic review and meta-analysis to summarize the available options for treatment of novel coronavirus infection based on previous reports of therapy of SARS, MERS.

Convalescent plasma plays an important role in the treatment of SARS and MERS for severe respiratory infections<sup>[9]</sup>. Cheng<sup>[10]</sup> found that convalescent plasma therapy had benefits effect for SARS, especially in the early phase. Soo<sup>[11]</sup> Conformed that Patients with convalescent plasma therapy had a shorter hospital stay, lower mortality and no immediate adverse effects were observed. Yeh<sup>[12]</sup> made a conclusion that infected SARS in Taiwan hospital whose condition had progressed severely survived after transfusion with convalescent plasma. Chun<sup>[13]</sup> reported Transfusion-Related Acute Lung Injury occurred after Convalescent Plasma Transfusion in a Patient With Middle East Respiratory Syndrome. Jae-Hoon Ko<sup>[14]</sup> reported donor convalescent plasma with a neutralization activity of a PRNT titer 1:80 should be used in MERS.

This study revealed that the therapy of Convalescent plasma can reduce mortality of patients with Coronavirus. The study provided a high sample size and the conclusions drawn by the study are highly credible because of the comprehensive data collection strategy. However, there were several limitations to this study. The distribution of studies between locations was not uniform. We were able to find and extract data for the meta-analysis from Hong Kong, Taiwan, Korea. In addition, most of the selected studies were from hospital and no strict control group. There was no convalescent plasma for the treatment of patients with Coronavirus in the early stages. There may be reporting bias in some details. Moreover, the systematic review is likely to have publication bias as some articles used other languages. Therefore, the conclusions of this Meta-analysis still need to be verified by further studies to clarify the associations.

We hope this study will provide important information for policy-makers pay more attention to The effectiveness of convalescent plasma for the treatment of patients with Coronavirus, Improve survival of critically ill patients<sup>[15]</sup>.

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