

# Review of: "A Narrative Review on the Management of Severe COVID-19 Infection Using Stem Cell-based therapies with a Focus on the Registered Clinical Trials"

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Potential competing interests: No potential competing interests to declare.

The current review article with the title "A Narrative Review on the Management of Severe COVID-19 Infection Using Stem Cell-based Therapies with a Focus on the Registered Clinical Trials" is a narrative review article with the aim of investigating the effects of cell therapy on Covid-19 disease. Although the article as a whole is valuable and has useful comments in this field, the correction of the following items can definitely help to improve the quality of the article.

1: The article needs a general correction in terms of grammar, and there are some minor flaws in this field.

2: Since the results of exosome therapy studies (references 2, 3, 5...) are also mentioned in the tables, it is better to discuss a little more about exosomes and their mechanisms of action in the abstract section (briefly) and in the introduction section.

3: In the first paragraph of part 3 (Recent Stem Cell-Based Studies in the Treatment of COVID-19), in this sentence "Different types of stem cells are being applied as an interventional arm, ranging from embryonic stem cells to mesenchymal stem cells," the authors claimed that embryonic stem cells were used in some clinical trials. While, as far as I know, these cells are not licensed for clinical work under normal conditions. Therefore, please correct the sentence or provide the exact relevant reference that used these cells in a specific clinical trial.

4: In table.1, some references, including references 90, 10, etc., do not specify the source of the stem cells and instead write MSC, so it is better to use NM (Not Mentioned) instead if it is not specified.

5: The caption of figure 2 does not express the content well. Can you give a more detailed explanation of this sentence? What was meant by "in the modeling"?

6: Since the time of Covid-19, many clinical trials have been conducted in the field of cell therapy for ARDS patients infected with Covid-19, which have published their results. Also, many works have been done in this field in Iran, and it is better to refer to these articles (instead of referring to the trials that are still in the recruitment phase!). Among others, the following articles in Iran can be cited:

- Kaffash Farkhad N, Sedaghat A, Reihani H, Adhami Moghadam A, Bagheri Moghadam A, Khadem Ghaebi N, Khodadoust MA, Ganjali R, Tafreshian AR, Tavakol-Afshari J. Mesenchymal stromal cell therapy for COVID-19-induced

ARDS patients: a successful phase 1, control-placebo group, clinical trial. *Stem Cell Research & Therapy*. 2022; 13(1):1-13.

- Kaffash Farkhad N, Sedaghat A, Reihani H, Adhami Moghadam A, Bagheri Moghadam A, Khadem Ghaebi N, Khodadoust MA, Nikpoor AR, Tavakol-Afshari J. Specific Clinical and Immunological Changes Following Mesenchymal Stem Cell Transplantation in COVID-19–induced Acute Respiratory Distress Syndrome Patients: A Phase-I Clinical Trial. *Iran J Allergy Asthma Immunol*. 2022. 21(5):687-703.

7- Please be careful in using abbreviations. Every full word needs to be shortened only for the first time, and a word should not be repeated both in full and abbreviated form after that. This case has been repeated several times in the text and for some words, including MSC, and has not been observed.