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LETTER

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The role of mesenchymal stem cells in the treatment of ARDS and cytokine storms in COVID-19

Muhammad Waseem[1], Hamza Altaf[2], Nageen Hussain[3], Sobia Mushtaq[4], Samavia Siddique[5]

1. Research Cell, University College of Medicine and Dentistry, University of Lahore, Pakistan.
2. Public Health, Department of Experimental Medicine, University of Campania Luigi Vanvitelli, Naples, Italy
3. Institute of Microbiology and Molecular Genetics, University of the Punjab, Lahore, Pakistan
4. University Institute of Biochemistry and Bio Technology-Pir Mehr Ali Shah Arid Agriculture University - PMAS AAUR, Rawalpindi, Pakistan
5. Institute of Microbiology and Molecular Genetics, University of the Punjab, Lahore, Pakistan.

Correspondence
Muhammad Waseem, Research Cell, University College of Medicine and Dentistry, University of Lahore, Pakistan

e-mail
waseem.mmg.pu@gmail.com

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ORCID ID of the author(s):
MW: 0000-0002-0819-129X
HA: 0000-0002-7573-6157
NH: 0000-0002-4944-1881
SM: 0009 0001 2086 8304
SS: 0009-0006-0043-7503

Dear Editor,

The COVID-19 pandemic continues to challenge global healthcare systems, particularly due to the lack of effective treatment options for patients who develop acute respiratory distress syndrome (ARDS), cytokine storms, and long-term pulmonary complications. While antiviral agents and vaccines have mitigated some of the burden, these approaches are not universally effective—especially against emerging variants. In this context, mesenchymal stem cells (MSCs) have emerged as a promising therapeutic strategy due to their unique immunomodulatory and regenerative properties (1,2).

MSCs have been shown to attenuate immune hyperactivation by reducing pro-inflammatory cytokines such as IL-6, TNF-α, and IL-1β, while upregulating anti-inflammatory cytokines including IL-10 and IL-4 (3,4). These effects are particularly relevant in managing the cytokine storm characteristic of severe COVID-19 cases. Preclinical models and early-phase clinical studies have demonstrated that MSCs can decrease lung inflammation, promote epithelial repair, and improve oxygenation (2,5).

To date, over 80 clinical trials have been registered globally investigating MSC therapy in COVID-19 patients. Results from several small-scale studies suggest that intravenous administration of MSCs is safe and may lead to improvements in pulmonary function, radiological imaging, and systemic inflammation without serious adverse events (1,6). Among various sources, umbilical cord-derived MSCs (UC-MSCs) have been particularly favored due to their low immunogenicity and high proliferative capacity (7).

However, several limitations must be addressed before routine clinical use. The variability in MSC products, including differences in source, donor age, culture methods, and ACE2 expression levels, may influence safety and efficacy (2,8). Although some studies suggest that MSCs express low levels of ACE2 and TMPRSS2 and are therefore resistant to SARS-CoV-2 infection, other reports highlight potential susceptibility under certain conditions (8).

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To overcome such challenges, genetic engineering of MSCs has been proposed to enhance their antiviral resilience and immunomodulatory performance. For example, MSCs can be engineered to secrete higher levels of IL-10 or to resist viral entry by downregulating ACE2 expression (2,9). These approaches may prolong MSC survival in the inflamed microenvironment and improve their therapeutic potential in severe COVID-19.

In conclusion, MSC therapy holds considerable promise as an adjunctive treatment for severe COVID-19. Yet, further large-scale, randomized controlled trials are urgently needed. Standardization of MSC manufacturing, careful patient selection, and integration of advanced bioengineering tools will be essential to fully realize the therapeutic potential of stem cells in combating COVID-19 and its complications.resistance-related conditions.

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References

1. Xu R, Feng Z, Wang FS. Mesenchymal stem cell treatment for COVID-19. eBioMedicine. 2022;77:103920.

2. Karakaş N, Üçüncüoğlu S, Uludağ D, Karaoğlan BS, Shah K, Öztürk G. Mesenchymal stem cell-based COVID-19 therapy: bioengineering perspectives. Cells. 2022;11(3):465.

3. Li Z, Niu S, Guo B, Gao T, Wang L, Wang Y, et al. Stem cell therapy for COVID-19, ARDS and pulmonary fibrosis. Cell Prolif. 2020;53(12):e12939.

4. Choudhery MS, Harris DT. Stem cell therapy for COVID-19: possibilities and challenges. Cell Biol Int. 2020;44(10):2182–2191.

5. Bhaskar S, Sinha A, Banach M, Mittoo S, Weissert R, Kass JS, et al. Cytokine Storm in COVID-19-Immunopathological Mechanisms, Clinical Considerations, and Therapeutic Approaches: The REPROGRAM Consortium Position Paper. Front Immunol. 2020;11:1648.

6. Liang B, Chen J, Li T, Wu H, Yang W, Li Y, et al. Clinical remission of a critically ill COVID-19 patient treated by human umbilical cord mesenchymal stem cells: A case report. Medicine (Baltimore). 2020;99(31):e21429.

7. Golchin A, Seyedjafari E, Ardeshirylajimi A. Mesenchymal stem cell therapy for COVID-19: present or future. Stem Cell Rev Rep. 2020;16(3):427–433.

8. Li YR, Dunn ZS, Garcia G Jr, Carmona C, Zhou Y, Lee D, et al. Development of off-the-shelf hematopoietic stem cell-engineered invariant natural killer T cells for COVID-19 therapeutic intervention. Stem Cell Res Ther. 2022;13(1):112.

9. Harrell CR, Sadikot R, Pascual J, Fellabaum C, Jankovic MG, Jovicic N, et al. Mesenchymal Stem Cell-Based Therapy of Inflammatory Lung Diseases: Current Understanding and Future Perspectives. Stem Cells Int. 2019;2019:4236973.