

Application of Stem Cell Therapy (SCT) to Covid-19: A Scientometric Assessment of Global Publications during 2020-21

B M Gupta^{1,*}, Mallikarjun Kappi², K K Mueen Ahmed³

ABSTRACT

Objectives: The study makes a bibliometric evaluation of global publications on "Application of Stem Cell Therapy to Covid-19" during 2020-22. **Methods:** The published publications on this theme were searched, retrieved, and downloaded from the Elsevier's Scopus international database and analyzed using bibliometric techniques based on select bibliometric indicators. The VOSviewer software and Biblioshiny application were used to construct and visualize bibliometric networks. **Results:** In all 1413 publications were indexed on "Application of Stem Cell Therapy to Covid-19" in the Scopus database till 30 December 2021. These publications registered an average of 18.03 citations per paper. Of these, the funded publications were 452(31.99%). In all, 91 countries, 690 organizations, and 1068 authors participated in global research and published in 317 journals. Among participating countries, China, the U.K., Italy, and India lead in publications output (with 185, 148, 127, and 110 papers) and China (58.38 and 3.24), France (47.0 and 2.61), Netherlands (46.63 and 2.59) and the U.K. (41.84 and 2.32) leads in citation impact. Among participating organizations, Tehran University of Medical Sciences, Iran (37 papers), Harvard Medical School, USA (36 papers), Memorial Sloan Kettering Cancer Center, USA (29 papers) and Shahid Beheshti University of Medical Sciences, Iran (26 papers) leads in publications productivity (with 37, 36, 29 and 26 papers) and Brigham and Women's Hospital, USA (110.78 and 6.14), Massachusetts General Hospital, USA (81.35 and 4.51), Icahn School of Medicine at Mount Sinai, USA (78.95 and 4.38) and Harvard Medical School, USA (75.42 and 4.18) leads in citation impact. Among participating authors, K.K.Sahu (9 papers), J. Cerny (7 papers), M.A. Perales and M.Z. Ratajzak (7 papers each) leads in publication productivity and M. Mohty (37.0 and 2.05), P.R.M. Rocco (35.8 and 1.99), D.J. Weiss (33.5 and 1.86) and M.A. Perales (32.86 and 1.82) leads in citation impact. *Stem Cell Reviews and Reports* (35 papers), *Frontiers in Immunology* (32 papers), *Bone Marrow Transplantation* (30 papers) leads in publication productivity and *Journal of Medical Virology* (132.10), *American Journal of Hematology* (75.20), *Aging and Disease* (55.46) and *Cell Stem Cell* (33.14) leads in citation impact. **Conclusion:** The research is mainly dominated by North America and Western Europe, but with some contribution from China, India, Iran, and Brazil playing also an important role. The developing countries need to prioritize their research in this area and increase their collaboration with North America and Western Europe countries. The analysis will help scholars and policy-makers to take stock of the present situation and decide the future course of action on the "Application of Stem Cells in Covid-19"

Keywords: Covid-19, Coronavirus 19, Cell Therapy, Stem Cell Applications, Global Publications, Bibliometrics, Scientometrics.

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INTRODUCTION

Covid-19 caused by the novel severe acute respiratory coronavirus-2 is currently spreading throughout the world with a high rate of infection and mortality and poses a huge threat to global public health. Covid-19 primarily manifests as hypoxic respiratory failure and acute respiratory distress syndrome, which can lead to multiple organ failures. The main target cells for SARS-CoV-2 infection are ACE2-positive cells, such as type II alveolar epithelial (AT2) cells and resident alveolar macrophages in the lung, and the endothelial cells in the liver, kidney, hearts, and intestines.

Despite advances in supportive care approaches, there is still a lack of clinically effective therapies. Among

available therapies, vaccination is undoubtedly the best choice to fight against the Covid-19 pandemic. However, data from current clinical studies cannot determine the duration of Covid-19 vaccine protection, and no vaccine can achieve 100% protection. To complement the role of vaccines, there is an urgent need to develop and explore novel alternate strategies for the treatment of Covid-19.

Of late, cell therapies have received extensive attention as a new treatment method in a variety of diseases, including lung,^{1,2} cardiovascular,^{3,4} liver,⁵ kidney,⁶ etc. Currently, stem cell therapy has become a promising therapeutic field, in which many

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scholars see opportunities to cure incurable diseases.⁷ Among these, Mesenchymal Stem Cell Therapy (MSCs) in particular has attracted the widest attention due to source potential, a high proliferation rate, low invasive procedure, and being free of ethical issues. There is much superiority in using MSC therapy in comparison with other treatments:⁸ (i) They are easily accessible and can be isolated from various tissues, etc.; (ii) They are multi-potent stem cells; (iii) MSCs can easily expand to clinical volume in a suitable period of time; and (iv) MSCs can be stored for repetitive therapeutic usage.

Currently, many applications and studies for experimental stem cell therapy in critically ill patients with Covid-19, especially MSC therapy⁹ are available. MSCs are derived from the mesoderm and ectoderm at the early stage of embryonic development and have attracted increasing attention due to their multidirectional differentiation potential, immunomodulatory properties, and lack of ethical controversy.⁹⁻¹¹ MSCs have been isolated from different tissues and used for specific tissue repair and regeneration.¹² To date, MSCs can be obtained from a variety of adult tissues, mainly bone marrow, umbilical cord blood, adipose tissue, endometrium, umbilical cord blood, embryos, etc.¹²⁻¹⁴ The umbilical cord is different from the bone marrow and contains a high concentration of MSCs. It is one of the most abundant sources of MSC. MSCs derived from the human umbilical cord can be extracted non-invasively, and the cells proliferate rapidly, making them the most suitable stem cells for the treatment of Covid-19. Covid-19 patients treated with MSCs derived from adipose tissue were also reported.¹⁵ MSCs derived from menstrual blood have typical MSC characteristics such as self-cloning, rapid proliferation, and pluripotency.¹⁶ They can be easily obtained from discarded menstrual blood in a non-invasive way and can be obtained periodically and transplanted without trauma or ethical risk.

Recent studies suggest that the therapeutic effects of MSCs, especially those that are immune-modulatory, can be largely attributed to paracrine effectors.¹⁷ Exosomes (EXOs) released by MSCs are one of the important components of paracrine factors. Thanks to its remote targeting and stability, some EXOs can replace MSCs from which they are derived to perform similar therapeutic functions. Compared with MSCs, MSC-EXOs can be isolated from patients in a non-invasive manner. They present the composition, physiological state and characteristics of original MSCs and contain unique bioactive molecules.^{18,19}

According to the US National Institutes of Health (NIH) ClinicalTrials.gov database, 417 clinical investigations of cell therapies against SARS-CoV-2 have been conducted²⁰ till March 2021, which indicates that this cell therapy has been suggested as a beneficial alternative to treating Covid-19 and its complications ARDS. Among the 417 registered trials, 203 were recruiting participants, five were enrolling participants by invitation, 32 were active, having already passed the recruitment phase, and 63 were completed. Of these 63, six trials already presented results. The remaining 114 trials were not in progress or had an unknown status.

LITERATURE REVIEW

Many previous bibliometric studies²¹⁻²⁴ were carried out which aimed to analyze the global and national research output on stem cells - focusing either on examining the research strengths or depicting research trends or on its applications in Parkinson's disease²⁵ and diabetes syndrome.^{26,27} There is, however, only one extensive review,²⁸ which has studied its applications in relation to Covid-19, identifying existing clinical case studies, case reports, clinical trials, pilot studies, *in vitro* and *in vivo* studies. The data collected for each type of study were analyzed on several studies ($n=39$). Of the total studies, 22 focused on *in vitro* investigations and 17 on human studies (clinical cases=9), case series (2), pilot clinical trials (5), clinical trials (1). *In vitro* studies that induced pluripotent stem cells were the most used ($n=12$), and in clinical studies, the umbilical

stem cells derived were the most reported ($n=11$). The study concludes that the use of stem cells is a highly relevant therapeutic option as shown in both *in vitro* studies and clinical trials.

Keeping the above research purview in mind and the non-availability of any comprehensive bibliometric study in this area, the present study by the authors was planned to provide a comprehensive evaluation of the global research output on the application of stem cell therapy in the treatment of Covid-19 patients. The study aimed to evaluate the overall global output and its citation impact, contribution, and impact of top 10 countries, the subject focus of research, and the role of organizations and authors and journals in global output.

METHODS

The publications on "Application of Stem Cell Therapy to Covid-19" was first identified and then downloaded from the Elsevier international bibliographical and citation Scopus database. For this purpose, the authors developed a comprehensive search strategy (shown below) that used different keywords related to "Covid-19" and "stem cell", which are tagged to "Keywords" and "Title" (Article Title) confining the search to period 2020-21. The search yielded 1413 records, which were further analyzed using additional features in the Scopus database.

The study used a number of quantitative and qualitative indicators on one hand and raw and relative indicators on the other hand. Among qualitative indicators, the publication in a peer-reviewed journal is a good indicator of output. The publication count of authors, organizations, and countries is driven by the complete count approach, where each actor received full credit or score irrespective of its occurrence in first or last position in the byline of addresses of authors in a paper. Among qualitative indicators, citation per paper, relative citation index, and share in high cited papers are mainly used. The VOSviewer and Biblioshing applications were used for evaluating and visualizing the interactions among countries, organizations, authors, and keywords. The citations were counted from the data of publications till 30 December 2021.

TITLE ("COVID 19" OR "2019 novel coronavirus" OR "coronavirus 2019" OR "coronavirus disease 2019" OR "2019-novel CoV" OR "2019 ncov" OR covid 2019 OR covid19 OR "corona virus 2019" OR ncov-2019 OR ncov2019 OR "nCoV 2019" OR 2019-ncov OR covid-19 OR "Severe acute respiratory syndrome coronavirus 2" OR "SARS-CoV-2") OR KEY ("COVID 19" OR "2019 novel coronavirus" OR "coronavirus 2019" OR "coronavirus disease 2019" OR "2019-novel CoV" OR "2019 ncov" OR covid 2019 OR covid19 OR "corona virus 2019" OR ncov-2019 OR ncov2019 OR "nCoV 2019" OR 2019-ncov OR covid-19 OR "Severe acute respiratory syndrome coronavirus 2" OR "SARS-CoV-2") and Key (stem cell*)

ANALYSIS AND RESULTS

Overall Overview

The global research on "Application of Stem Cell Therapy to Covid-19" accumulated a total of 1413 publications (2020=606; 2021=806; 2022=1) during 2020-22. These publications received 25480 citations, averaging 18.03 citations per paper. Of the 1413 publications, 452 (31.99%) received external funding support from 100+ research agencies and received 10929 citations, averaging 24.18 citations per paper. Among major funding agencies supporting research in this area, the National Institute of Health supported research contributed the largest number of papers (124 papers), followed by the National Natural Foundation of China (71 papers), National Heart, Lung, and Blood Institute (41 papers), National Cancer Institute (35 papers), National Institute of Allergy and Infectious Diseases (29 papers), Deutsche Forschungsgemeinschaft (23 papers), National Key Research and Development Program of China

(22 papers), Pfizer (22 papers), Janssen Pharmaceuticals (19 papers), Novartis (19 papers), etc.

The majority of publications appeared as articles and reviews (40.55% and 34.18%) among total publications and the remaining output appeared as letters (12.53%), editorials (6.09%), notes (5.02%), book chapters (0.78%), short surveys (0.71%) and conference papers (0.14%). The English language (1397 publications) constitute the major share in among total output, followed by Chinese (7), French (5), Russian (4), Portuguese (3), German (2), Persian (2), Spanish (2), Italian (1) and Japanese (1).

Among publications by population, 838 publications focused on humans and 419 on non-humans. The 366 publications involve adults, 229 aged, 227 middle-aged, 113 children, and 86, adolescents.

The 247 publications were controlled studies among total output, followed by 213 clinical trials (53 were phased 2 clinical trials and 59 randomized controlled), 157 case reports, 75 systematic reviews, and 74 retro-specific studies. Only 44 publications reported *in-vitro* studies and 29 *in-vivo* studies among the total publications.

Among the type of research, clinical studies account for the largest number of publications (422), followed by pathophysiology (416 papers), epidemiology (190 papers), risk factors (153 papers), genetics (141 papers), and complications (111 papers).

Hematopoietic Stem Cells reported the largest publications output (467 papers) among types of Mesenchymal stem cell studies, followed by Allogeneic Stem Cells (294 papers), Pluripotent Stem Cell (170 papers), Mesenchymal Stem Cell-Organoid (164 papers), Mesenchymal Stem Cell- Bone Marrows (80 papers), Umbilical Cord Mesenchymal Stem Cell (61 papers), Mesenchymal Stem Cell – Adipose Tissue-Derived (46 papers), Mesenchymal Stem Cell--Cord Blood (28 papers) and Dental Pulp Stem Cell (7 papers).

Profile of Top 15 Countries

In all 91 countries participated in global research on “Application of Stem Cell Therapy (SCT) to Covid-19”: 67 countries contributed 1-10 papers each, 24 countries 11-50 papers each, 4 countries 51-100 papers each, and 6 countries 102-447 papers each. The top 15 countries individually contributed 38 to 447 papers each and together contributed 1613 papers and 47356 citations, constituting more than 100.0% share each in total global publications and citations. On further analysis, it was observed that: (i) Six countries contributed above the group publication average (94.2) of top 15 countries: USA (447 papers), China (185 papers), U.K. (148 papers), Italy (127 papers), India (110 papers) and Germany (102 papers); and (ii) Seven countries registered citations per paper and relative citation index more than the group average (29.36 and 1.63) of top 15 countries: China (58.38 and 3.24), France (47.0 and 2.61), Netherlands (46.63 and 2.59), U.K. (41.84 AND 2.32), Australia (39.24 and 2.18), Japan (37.5 and 2.08) and Italy (31.52 and 1.75).

Figure 1-2 shows the co-authorship network of the top 50 countries distributed in 5 clusters with 644 links and 2321 total link strength. Cluster 1 (red colour) includes 16 countries like India, USA, Japan, etc., Cluster 2 (Green colour) includes 16 countries like the UK, Germany, France, and others. Cluster 3 (Blue colour) includes 8 countries like Iran, Russia, and others. Cluster 4 (Yellow color) and cluster 5 (Purple colour) include 5 countries each. The clusters are categorized according to the number of collaborations that each country represents. Countries of the same color mean that they are close to each other and are grouped together. Figure 2 shows the countries' citations collaboration networks. Here a minimum of 10 citations was counted for analysis and the countries are scattered in 7 clusters.

The total collaborative links among the top 15 countries varied from 37 to 360 and individual country to country links varied from 1 to 52. The top three countries with the largest collaborative links (360, 282 and 218) were depicted by the USA, U.K., and Italy. In terms of the individual country to country collaboration links, the largest number of links (52)

Table 1: Bibliometric Profile of Top 15 Most Productive Countries.

Sl. No.	Name of the country	TP	TC	CPP	HI	ICP	%ICP	RCI
1	USA	447	9536	21.33	41	192	42.95	1.18
2	China	185	10801	58.38	32	59	31.89	3.24
3	U.K.	148	6193	41.84	20	91	61.49	2.32
4	Italy	127	4003	31.52	24	67	52.76	1.75
5	India	110	1243	11.30	14	47	42.73	0.63
6	Germany	102	2663	26.11	21	64	62.75	1.45
7	Iran	92	900	9.78	17	33	35.87	0.54
8	France	65	3055	47.00	18	38	58.46	2.61
9	Spain	62	1558	25.13	18	30	48.39	1.39
10	Canada	59	1630	27.63	14	46	77.97	1.53
11	Brazil	51	621	12.18	14	20	39.22	0.68
12	Turkey	46	272	5.91	9	9	19.57	0.33
13	Australia	41	1609	39.24	15	33	80.49	2.18
14	Japan	40	1500	37.50	10	24	60.00	2.08
15	Netherlands	38	1772	46.63	17	31	81.58	2.59
	Total of 15 countries	1613	47356	29.36	284	784	48.61	1.63
	Global total	1413	25480	18.03	19.00			1.00

TP=Total papers; TC=Total citations; CPP=Citations per paper; ICP=International collaborative papers; RCI=Relative citation index

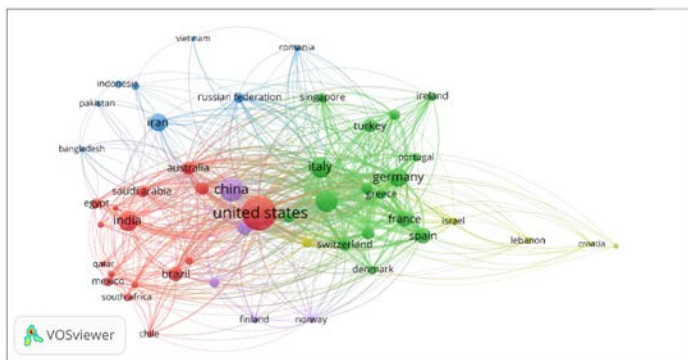


Figure 1: Authorship-countries collaboration network.

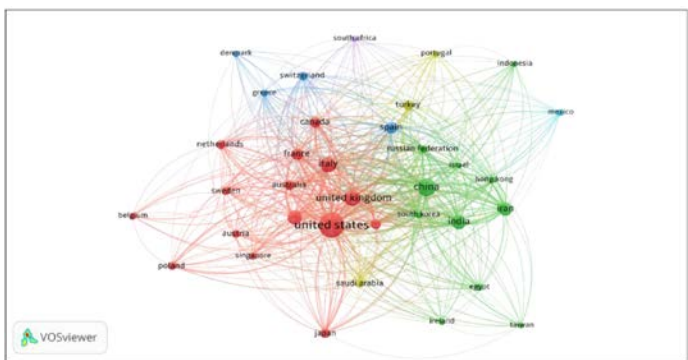


Figure 2: Citations – countries.

Table 2: Broad Subject-Wise Distribution of Global Papers.

Sl. No	Name of the subject	TP	TC	CPP	%TP
1	Medicine	1004	17738	17.67	71.05
2	Biochemistry, Genetics and Molecular Biology	576	9721	16.88	40.76
3	Immunology and Microbiology	206	5881	28.55	14.58
4	Pharmacology, Toxicology and Pharmaceutics	136	1168	8.59	9.62
5	Neuroscience	54	623	11.54	3.82
	Global total	1413	25480	18.03	100.00

were between USA-U.K., followed by USA-Italy (45), USA-China (42), U.K.-Italy, USA-India and USA-Germany (36 each), U.K. –Germany (33), USA-Australia (25), U.K.-Netherlands (24), U.K.-France (23), China-U.K., USA-France and USA-Spain (20 each), Italy-Netherlands (16), etc.

Broad Subject-Wise Distribution

According to the subject classification of Scopus, Medicine journals account for the largest publication share (71.05%) in global output, followed by biochemistry, genetics and molecular biology (40.76%), immunology and microbiology (14.58%), pharmacology, toxicology and pharmaceutics (9.62%) and neuroscience (3.82%). Immunology and microbiology registered the highest citation impact per paper (28.55) and pharmacology, toxicology and pharmaceutics the least (8.59 (Table 2)).

Significant Keywords

The keywords indicate independently or in combination convey important developments in a research field and their frequency of appearance indicates the extent of importance. As a result, we have identified 53 important keywords in the literature on “Application of Stem Cell Therapy (SCT) to Covid-19” with the frequency of appearance varying from 66 to 1392. The most significant keywords are Covid-19 (1392), Coronavirus 2019 (1201), SARS-CoV-2 (1063), Mesenchymal Stem Cell (394), Hematopoietic Stem Cell Transplantation (332), Mesenchymal Stem Cell Transplantation (325), Adult Respiratory Distress Syndrome (232), Hydroxychloroquine (231), Cytokine Storm (207) and Stem Cell Transplantation (223) and Cytokine Storm (222) (Table 3).

Figure 3 shows the density of keyword occurrence in the study. For analysis of 11974 keywords, the minimum occurrence of the keyword was 50 or more times selected. Among the 11974 keywords, 207 keywords connected each other. The generated bibliographic network consists of nodes and edges that are weighted according to the frequency of the terms and the strength of the interrelationships. Such an analysis could provide important insights into the Covid-19 and Stem Cells research areas. In the keyword frequency network visualization, the size of the keywords reflects the number of papers the keyword appears in, and the distance between the keywords gives the approximate correlation of the keywords. The all-keywords map spread over 4 clusters, 20125 links, and 286353 total link strengths.

Profile of Top 25 Most Productive Organizations

In all 690 organizations unevenly participated in global research on “Application of Stem Cell Therapy (SCT) to Covid-19”: 435 organizations contributed 1-5 papers each, 211 organizations 6-10 papers each, and 44 organizations 11-37 papers each. The top 25 most productive organizations individually contributed 15 to 37 papers each and together contributed 504 papers and 19104 citations, constituting 35.67% and 74.98% share of global publications and citations. On further analysis, it was observed that: (i) Nine organizations contributed papers more than the group average (20.16) of top 25 organizations: Tehran University of Medical Sciences, Iran (37 papers), Harvard Medical School, USA (36 papers), Memorial Sloan Kettering Cancer Center, USA (29 papers), Shahid Beheshti University of Medical Sciences, Iran (26 papers), Weill Cornell Medicine, New York, USA, Karolinska Institute, Sweden and Icahn School of Medicine at Mount Sinai, USA (22 papers each) and Imperial College London, U.K. and University of Washington, USA (21 papers each) and (ii) Nine organizations reported citations per paper and relative citation index more than the group average (37.90 and 2.10) of top 15 organizations: Brigham and Women’s Hospital, USA (110.78 and 6.14), Massachusetts General Hospital, USA (81.35 and 4.51), Icahn School of Medicine at Mount Sinai, USA (78.95 and 4.38), Harvard Medical School, USA (75.42 and 4.18), Imperial College London, U.K. (69.1 and 1.83), Sorbonne University, France (58.87 and 3.26), Memorial Sloan Kettering Cancer Center, USA (58.38 and 3.24), University of Washington, USA (57.62 and 3.20) and Karolinska Institute, Sweden (56.91 and 3.16) (Table 4).

Figure 4 shows the institutional collaboration network for the global publication on Covid-19 and stem cell research. To analyze the organizational collaboration network, the researchers used a partial method and selected 25 organizations as the maximum number of organizations.

The total individual collaborative links of the top 25 organizations varied from 9 to 70 and organization to organization links varied from 1 to 20. The three organizations depicting the largest collaborative links (70, 65,

Table 3: List of Most Important Keywords along with their Frequency of Appearance in Global Literature on “Application of Stem Cells to Covid-19”.

Sl. No	Name of the keyword	Frequency	Sl. No	Name of the keyword	Frequency
1	Covid-19	1392	28	Antiviral Agents	109
2	Coronavirus 2019	1201	29	Convalescent Plasma	108
3	SARC-CoV-2	1063	30	Favipiravir	98
4	Mesenchymal Stem Cell	394	31	Gene Expression	97
5	Hematopoietic Stem Cell Transplantation	332	32	SARS-CoV-2 Vaccine	97
6	Mesenchymal Stem Cell Transplantation	325	33	Hematopoietic Stem Cells	93
7	Adult Respiratory Distress Syndrome	232	34	Cytokines	90
8	Hydroxychloroquine	231	35	Signal Transduction	90
9	Stem Cell Transplantation	223	36	Lymphocytopenia	88
10	Cytokine Storm	222	37	Monoclonal Antibodies	88
11	Remdesivir	187	38	Acute Myeloid Leukemia	85
12	Tocilizumab	182	39	Thorax Radiography	85
13	Immunomodulation	178	40	Cancer Chemotherapy	84
14	Exosome	161	41	Hematologic Malignancy	82
15	Genetics	138	42	Neoplasms	82
16	Chloroquine	137	43	Multiple Myeloma	79
17	Immunosuppressive Treatment	137	44	Hypertension	79
18	Computer-Assisted Tomography	129	45	Organoid	65
19	Cell Therapy	127	46	Mesenchymal Storma Cells	55
20	Lopinavir Plus Ritonavir	127	47	Bone Marrow Transplantation	47
21	Immunoglobulin	126	48	Acute Lymphoblastic Leukemia	44
22	Corticosteroid	124	49	Allogeneic Stem Cell Transplantation	35
23	Dexamethasone	122	50	Umbilical Cord	35
24	Azithromycin	120	51	Mesenchymal Stromal Cell Therapy	23
25	Induced Pluripotent	120	52	Umbilical Cord Mesenchymal Stem Therapy	23
26	Immunotherapy	111	53	Adipose Derived Stem Cells	22
27	Allogeneic Hematopoietic Stem Cell Transplantation	109			

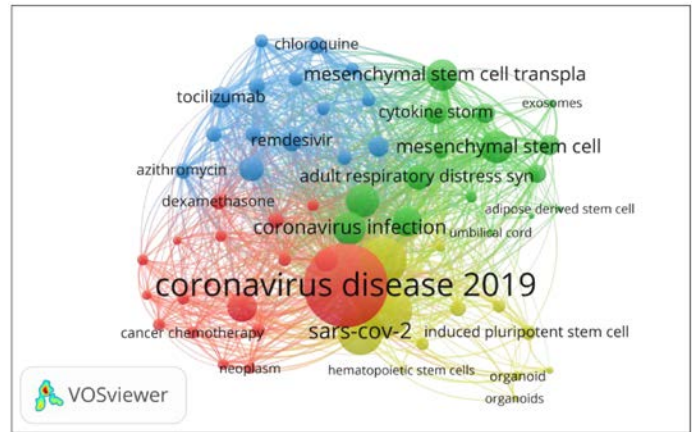


Figure 3: Most significant keywords co-occurrence network.

and 59) were: Harvard Medical School, USA, Memorial Sloan Kettering Cancer Center, USA, and Massachusetts General Hospital, USA.

Harvard Medical School, USA – Massachusetts General Hospital, USA and Tongji Medical College, China – Huazhong University of Science and Technology, China together registered the highest number of collaborative Links (20 each), followed by Karolinska Institute, Sweden - Karolinska Universitetssjukhuset, Sweden (17 links), Harvard Medical School, USA - Brigham and Women’s Hospital, USA, Memorial Sloan Kettering Cancer Center, USA - Weill Cornell Medicine, New York, USA and - University of Washington, USA - Fred Hutchinson Cancer Research Center, USA (16 links each), Tehran University of Medical Sciences, Iran - Shahid Beheshti University of Medical Sciences, Iran (11 links), Harvard Medical School, USA - Dana-Farber-Cancer Institute, USA and AP-HP Assistance Publique-Hopitaux de Paris, France - Sorbonne University, France (10 links each).

Profile of Top 25 Most Productive Authors

In all 1068 authors unevenly participated in global research on “Application of Stem Cell Therapy (SCT) to Covid-19”: 587 authors contributed 1 paper each, 311 authors 2 papers each, 110 authors 3 papers each, 35 authors 4 papers each and 25 authors 5-9 papers each. The top 25 most productive authors individually contributed 5 to 9 papers each and together contributed 145 papers and 2430 citations, constituting 10.26% and 9.54% share of global publications and citations. On further analysis, it was observed that: (i) Thirteen authors contributed papers more than the group average (5.8) of top 25 authors: K.K.Sahu (9 papers), J. Cerny (7 papers), M.A. Perales, M.Z. Ratajczak and S.N. Rezaei (7 papers each), S. Chhabra, R. Ciccocioppo, F. Ciceri, R.P. Gale, R. Ljungman, M.Mohty, D.J. Weiss and A.Zumla (6 papers each); and (ii) Thirteen authors reported citations per paper and relative citation index more than the group average (16.96 and 0.93) of top 25 authors: M. Mohty (37.0 and 2.05), P.R.M. Rocco (35.8 and 1.99), D.J. Weiss (33.5 and 1.86), M.A. Perales (32.86 and 1.82), M. Maeuer (12.6 and 1.81), M. Kamboj (12.4 and 1.8), A. Zumla (27.5 and 1.53), D.N. Kotton (24.6 and 1.36), R. Ljungman (20.5 and 1.14), S.N. Rezaei (19.71 and 1.09) and M.Z. Ratajczak (15.71 and 0.87) (Table 5).

The co-authorship analysis examines the interactions between authors in the field of research. Since co-authorship is a formal way of academic collaboration among researchers, it is important to understand how researchers interact with one another. Figure 5 shows the co-authorship network. Of 1068 authors for 1413 papers in the Scopus database, the minimum number of documents of a researcher was 5, of which 64 were

Table 4: Bibliometric Profile of Top 25 Organizations.

SI. No	Name of the organization	TP	TC	CPP	HI	ICP	%ICP	RCI
1	Tehran University of Medical Sciences, Iran	37	338	9.14	10	11	29.73	0.51
2	Harvard Medical School, USA	36	2715	75.42	16	22	61.11	4.18
3	Memorial Sloan Kettering Cancer Center, USA	29	1693	58.38	13	10	34.48	3.24
4	Shahid Beheshti University of Medical Sciences, Iran	26	297	11.42	7	6	23.08	0.63
5	Weill Cornell Medicine, New York, USA	22	800	36.36	13	6	27.27	2.02
6	Karolinska Institute, Sweden	22	1252	56.91	8	17	77.27	3.16
7	Icahn School of Medicine at Mount Sinai, USA	22	1737	78.95	11	11	50.00	4.38
8	Imperial College London, U.K.	21	1451	69.10	9	15	71.43	3.83
9	University of Washington, USA	21	1210	57.62	8	11	52.38	3.20
10	Fred Hutchinson Cancer Research Center, USA	20	207	10.35	7	7	35.00	0.57
11	University of Texas MD Anderson Cancer Center, USA	20	217	10.85	8	7	35.00	0.60
12	Brigham and Women's Hospital, USA	18	1994	110.78	7	9	50.00	6.14
13	AP-HP Assistance Publique-Hopitaux de Paris, France	18	222	12.33	9	9	50.00	0.68
14	Tongji Medical College, China	17	348	20.47	8	7	41.18	1.14
15	Dana-Farber-Cancer Institute, USA	17	486	28.59	10	9	52.94	1.59
16	University of Toronto, Canada	17	161	9.47	7	12	70.59	0.53
17	Huazhong University of Science and Technology, China	17	348	20.47	8	7	41.18	1.14
18	Massachusetts General Hospital, USA	17	1383	81.35	9	10	58.82	4.51
19	University College London, U.K.	16	96	6.00	8	11	68.75	0.33
20	University of Oxford, U.K.	16	96	6.00	4	8	50.00	0.33
21	Univ. Federal do Rio de Janeiro, Brazil	15	234	15.60	6	7	46.67	0.87
22	INSERM, France	15	245	16.33	6	8	53.33	0.91
23	Sorbonne University, France	15	883	58.87	9	7	46.67	3.26
24	Albert Einstein College of Medicine of Yeshive University, USA	15	485	32.33	9	5	33.33	1.79
25	Karolinska Universitetssjukhuset, Sweden	15	206	13.73	6	10	66.67	0.76
	Total of 25 organizations	504	19104	37.90	8.64	242	48.02	2.10
	Global total	1413	25480	18.03				1.00
	Share of top 25 organizations in global total	35.67	74.98					

TP=Total papers; TC=Total citations; CPP=Citations per paper; ICP=International collaborative papers; RCI=Relative citation index

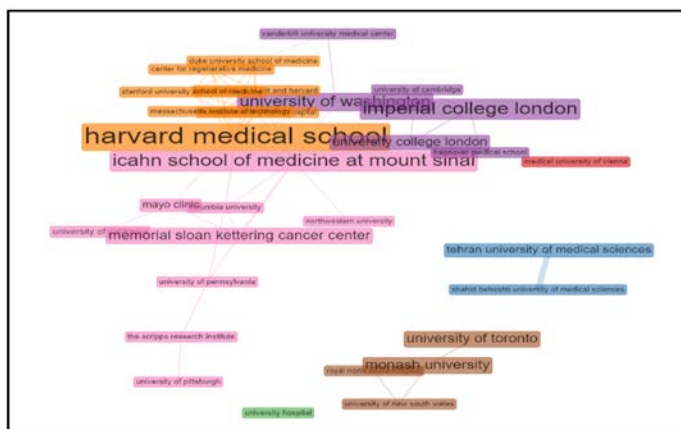


Figure 4: Visualization of institutions collaboration Network.

meet the threshold. In this network 52 authors were connected to each other's in 7 clusters, having 244 links and 309 total link strengths. Cluster 1 consists of the highest number (12 authors), cluster 2 consists of 10 authors, cluster 3 consist of 7 authors, cluster 4 consists of 7 authors, cluster 5 and 6 consist of 6 authors each, and cluster 7 consists of 4 authors respectively.

Among individual author-to-author links, the largest number of collaborative links (7) were between K.K. Sahu and J. Cerny, followed by A. Zumla - M. Maeuer (5 links), M.A. Perales - M. Kamboj (4 links), S. Chhabra - M. Hamadani (4 links), etc.

Profile of Top 25 Most Productive Journals

Of the 1413 papers on "Application of Stem Cells to Covid-19", 1397 appear in 317 journals, 14 in book series, and 1 each as book and conference paper. Of the 317 journals, 271 journals contributed 1-5 papers each, 27 journals 6-10 papers each, 11 journals 11-20 papers each, and 8

Table 5: Bibliometric Profile of Top 25 Most Productive Authors.

S.No	Name of the author	Affiliation of the author	TP	TC	CPP	HI	ICP	%ICP	RCI
1	K.K. Sahu	Saint Vincent Hospital, Worcester, U.K.	9	71	7.89	5	1	11.11	0.44
2	J. Cerny	University of Massachusetts Medical School, USA	7	68	9.71	5	0	0.00	0.54
3	M.A. Perales	Memorial Sloan Kettering Cancer Center, USA	7	230	32.86	5	1	14.29	1.82
4	M.Z. Ratajczak	University of Louisville, USA	7	110	15.71	2	4	57.14	0.87
5	S.N. Rezaei	Tehran University of Medical Sciences, Iran	7	138	19.71	4	2	28.57	1.09
6	S. Chhabra	Medical College of Wisconsin, USA	6	68	11.33	4	0	0.00	0.63
7	R. Ciccocioppo	Universita degli Studu di Verona, Italy	6	22	3.67	2	2	33.33	0.20
8	F. Ciceri	Universita Vita-Salute San Raffaele, Italy	6	27	4.50	3	2	33.33	0.25
9	R.P. Gale	Imperial College, London, U.K.	6	18	3.00	2	4	66.67	0.17
10	R. Ljungman	Karolinska Institute, Sweden	6	123	20.50	3	5	83.33	1.14
11	M. Mohty	Hospital Saint Antonine, France	6	222	37.00	5	4	66.67	2.05
12	D.J. Weiss	University of Vermont, USA	6	201	33.50	4	6	100.00	1.86
13	A. Zumla	University College London, U.K.	6	165	27.50	4	6	100.00	1.53
14	M. Aljurf	King Faisal Specialist Hospital and Research Center, Saudi Arabia	5	42	8.40	3	4	80.00	0.47
15	S.M. Devine	National Marrow Donor Program, Minnespolis, USA	5	45	9.00	3	0	0.00	0.50
16	M. Dominici	AZIenda Ospedaliere Universita di Modena, Italy	5	69	13.80	4	3	60.00	0.77
17	N. Hamad	St, Vincent Hospital, Sydney	5	31	6.20	2	3	60.00	0.34
18	M. Hamadani	Medical Colege of Wisconsin, USA	5	71	14.20	4	1	20.00	0.79
19	M. Kamboj	Memorial Sloan Kettering Cancer Center, USA	5	162	32.40	4	0	0.00	1.80
20	D.N. Kotton	Boston University School of Medicine, USA	5	123	24.60	4	3	60.00	1.36
21	B. Larijani	Endocrinology and Metabolism Research Institute, Iran	5	11	2.20	1	1	20.00	0.12
22	M. Maeuer	University College London, U.K.	5	163	32.60	4	5	100.00	1.81
23	C. Mc Omish	Boston Biomedical Research Institute, USA	5	0	0.00	0	0	0.00	0.00
24	P.R.M. Rocco	Univ. Fed. Di Rio Janeiro, Brazil	5	179	35.80	4	4	80.00	1.99
25	D. Weisdorf	University of Minnesota Twin Cities, USA	5	71	14.20	4	3	60.00	0.79
		Total of 25 authors	145	2430	16.76	3.4	64	44.14	0.93
		Global total	1413	25480	18.03				1.00
		Share of top 20 authors in global total	10.26	9.54	0.93				

TP=Total papers; TC=Total citations; CPP=Citations per paper; ICP=International collaborative papers; RCI=Relative citation index

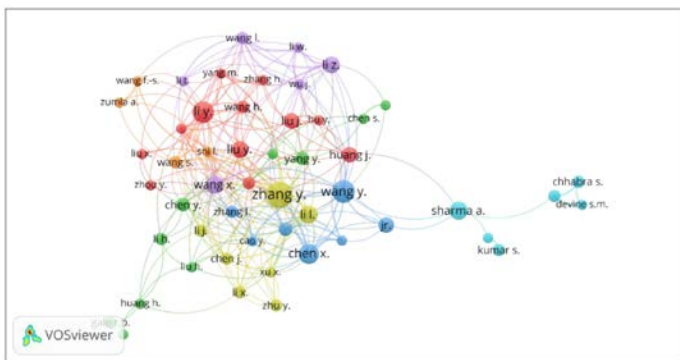


Figure 5: Authors co-authorship network.

journals 31-35 papers each. The top 25 journals individually contributed 9-35 papers and together contributed 428 papers, constituting a 29.99% share of global journal output. The top 8 most productive journals were: *Stem Cell Reviews and Reports* (35 papers), *Frontiers in Immunology* (32 papers), *Bone Marrow Transplantation* (30 papers), *Pediatric Blood and*

Cancer and Stem Cell Research and Therapy (23 papers each), *British Journal of Haematology* and *Cell Stem Cell* (22 papers each). The top 8 most impactful journals in terms of citations per paper were: *Journal of Medical Virology* (132.10), *American Journal of Hematology* (75.20), *Aging and Disease* (55.46), *Cell Stem Cell* (33.14), *Leukemia* (19.90), *Stem Cells and Developments* (18.67), *Stem Cell Reviews and Reports* (17.77) and *Stem Cell Research and Therapy* (17.22) (Table 6).

The VOSviewer Visualization of sources identified journals on “Application of Stem Cell Therapy (SCT) to Covid-19”. Out of a total of 630 journals reported by researchers on this topic, the 25 most important journals, their articles and citations are listed in Table 6. The citations network for all top journals is shown in Figure 6. These journals also have the highest level of link strength. This makes these journals the most important channel for further publications in this area.

High-Cited papers

The 34 papers (assumed as high-cited) out of a total of 1413 on “Application of Stem Cells to Covid-19” have received 100 to 1560 citations. They together received 14819 citations, averaging 435.85 citations per paper. Out of 34 high-cited papers, 15 are in citation range

Table 6: Bibliographical Profile of Top 25 Journals.

Sl. No	Name of the journal	TP	TC	CPP	%TP
1	Stem Cell Reviews and Reports	35	622	17.77	2.51
2	Frontiers in Immunology	32	261	8.16	2.29
3	Bone Marrow Transplantation	30	357	11.90	2.15
4	Pediatric Blood and Cancer	23	197	8.57	1.65
5	Stem Cell Research and Therapy	23	396	17.22	1.65
6	British Journal of Haematology	22	187	8.50	1.57
7	Cell Stem Cell	22	729	33.14	1.57
8	Cells	21	103	4.90	1.50
9	International Journal of Molecular Sciences	19	116	6.11	1.36
10	Stem Cell Translational Medicine	19	197	10.37	1.36
11	Lancet Haematology	17	238	14.00	1.22
12	Stem Cell Reports	17	118	6.94	1.22
13	Transplantation and Cellular Therapy	16	29	1.81	1.15
14	Aging and Disease	13	721	55.46	0.93
15	Frontiers in Oncology	13	66	5.08	0.93
16	International Immunoharmaceuticals	13	57	4.38	0.93
17	Frontiers in Cell and Development Biology	12	35	2.92	0.86
18	Stem Cells and Developments	12	224	18.67	0.86
19	World Journal of Stem Cells	11	34	3.09	0.79
20	American Journal of Hematology	10	752	75.20	0.72
21	Biology of Blood and Marrow Transplantation	10	124	12.40	0.72
22	Journal of Medical Virology	10	1321	132.10	0.72
23	Leukemia	10	199	19.90	0.72
24	Journal of Translational Medicine	9	69	7.67	0.64
25	Leukemia and Lymphoma	9	15	1.67	0.64
	Total of top 25 journals	428	7167	16.75	30.64
	Global total in journals	1397		0.00	100.00
	Share of top 25 journals in global total in journals	29.99			

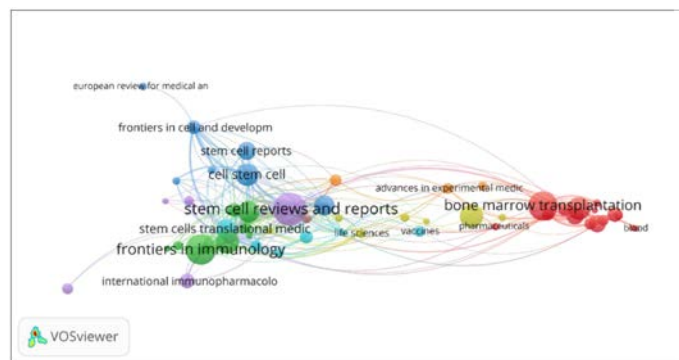


Figure 6: Citation network of Most preferred journals.

organization (zero collaborative papers) in 4 papers and 30 involve the participation of 2 or more organizations (19 nationally collaborative and 11 international collaboratives),

About 246 organizations and 385 authors participated in 34 high-cited papers, with 4 papers from Harvard Medical School, USA, 3 papers from Icahn School of Medicine at Mount Sinai, USA, 2 papers each from Brigham and Women’s Hospital, USA, Huazhong University of Science and Technology, China, Imperial College, London, U.K., Massachusetts General Hospital, USA, Memorial Sloan Kettering Cancer Center, USA, Tongji Medical College, China, and Weill Cornell Medicine, USA.

The 34 high cited papers are published in 29 journals, of which 2 papers each is contributed by *International Journal of Microbial Agents*, *Journal of Medical Virology*, *Nature Medicine*, *Nature Reviews Immunology* and *Stem Cell Review and Reports* and 1 paper each by *Acta Physiologica*, *Aging and Disease*, *American Journal of Hematology*, *Brain Behavior and Immunity*, *Cell Death and Differentiation*, *Cell Stem Cell*, *Current Oncology Reports*, *Engineering*, *European Respiratory Journal*, *JAMA Cardiology*, *Journal of Infection*, *Journal of Internal Medicine*, *Journal of Leukocyte Biology*, *Lancet Digital Health*, *Lancet Neurology*, *Lancet Rheumatology*, *Medicine*, *Nature*, *New England Journal of Medicine*, *Pain Physician*, *Science Advances*, *Stem Cell and Developments and Trends in Pharmaceutical Sciences*.

SUMMARY AND CONCLUSION

The 1413 global papers were published on “Application of Stem Cells to Covid-19”, as reflected in indexed documents in Scopus international database, receiving 25480 citations, with an average of 18.03 citations per paper. 31.99% (452) of the total global papers received external funding support and attracted 10929 citations, with an average of 24.18 citations per paper.

The 91 countries participated in global research on this theme with China (185 papers), the U.K. (148 papers), Italy (127 papers) and India (110 papers) leading in publication productivity and China (58.38 and 3.24), France (47.0 and 2.61), Netherlands (46.63 and 2.59) and U.K. (41.84 and 2.32) leading in citation impact in terms of citations per paper and relative citation index.

In all 690 organizations and 1068 authors unevenly participated in global research on “Covid-19 and Stem Cells”, of which the top 25 most productive organizations and authors contributed 35.67% and 10.26% and 74.98% and 9.54% share of global publications and citations.

The top six organizations in terms of publication productivity were: Tehran University of Medical Sciences, Iran (37 papers), Harvard Medical School, USA (36 papers), Memorial Sloan Kettering Cancer Center, USA (29 papers), Shahid Beheshti University of Medical Sciences, Iran

100-195, 7 in citation range 202-427, 7 in citation range 572-918, and 5 in citation range 1060-1560.

The 23 countries participated in 34 high-cited papers, with the largest number of papers (17) from China, followed by the USA (13 papers), the U.K. (7 papers), Italy (5 papers), France (3 papers), Brazil, Canada, Chile, Germany, Greece, Hong Kong, Japan, Macau, South Korea and Spain (2 papers each), Australia, India, Iran, Laos, Netherlands, Singapore, Slovenia, and Sweden

The 34 high-cited papers (15 articles, 14 reviews, 2 letters, and 1 each as editorial, note, and short survey) involve the participation of one

(26 papers), Weill Cornell Medicine, New York, USA and Karolinska Institute, Sweden. The top six organizations in terms of citation impact were: Brigham and Women's Hospital, USA (110.78 and 6.14), Massachusetts General Hospital, USA (81.35 and 4.51), Icahn School of Medicine at Mount Sinai, USA (78.95 and 4.38), Harvard Medical School, USA (75.42 and 4.18), Imperial College London, U.K. (69.1 and 1.83) and Sorbonne University, France (58.87 and 3.26). The top six most productive authors were K.K.Sahu (9 papers), J. Cerny (7 papers), M.A. Perales, M.Z. Ratajzak and S.N. Rezaei (7 papers each) and S. Chhabra (6 papers). The six most impactful authors in terms of citations per paper and relative citation index were M. Mohty (37.0 and 2.05), P.R.M. Rocco (35.8 and 1.99), D.J. Weiss (33.5 and 1.86), M.A. Perales (32.86 and 1.82), M. Maeuer (12.6 and 1.81) and M. Kamboj (12.4 and 1.8).

The 317 journals participated in research on this theme, of which the top 25 journals contributed 29.99% share in global journal output. The top 6 most productive journals were: *Stem Cell Reviews and Reports* (35 papers), *Frontiers in Immunology* (32 papers), *Bone Marrow Transplantation* (30 papers), *Pediatric Blood and Cancer*, and *Stem Cell Research and Therapy* (23 papers each) and *British Journal of Haematology*. The top 6 journals in terms of citations impact per paper were *Journal of Medical Virology* (132.10), *American Journal of Hematology* (75.20), *Aging and Disease* (55.46), *Cell Stem Cell* (33.14), *Leukemia* (19.90), *Stem Cells and Developments* (18.67), *Stem Cell Reviews and Reports* (17.77) and *Stem Cell Research and Therapy* (17.22).

The research is mainly dominated by North America and Western Europe. Among other countries, China, India, Iran, and Brazil play also an important role. These four countries need to prioritize their research in this area and increase their collaboration with North America and Western Europe countries.

Conclude that the above presentation gives an overview of the field and help the scholars and policy-makers to take stock of the present situation and decide the future course of action on the "Application of Stem Cells in Covid-19"

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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