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Review Article

The Progress and Research Trends in Coronavirus (COVID-19) Research Publications: Epidemiological and Bibliometrical Approaches

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ABSTRACT

The main objective of the present study is to summarize the research output about COVID-19. The search was conducted in *Scopus*, the *largest* abstract and citation database of peer-reviewed literature, and later it was analyzed on VOSviewer. Total 34716 research documents have been published about COVID-19 till September 2020. We focused on three parameters, i.e., co-authorship pattern, citations, and co-words analysis. Based on the total number of publications, h-index, total citations, and citations per document, we provided the list of the top ten authors, institutes, and countries. Based on the total number of publications, the top-ranked author is Wiwanitkit, V., and the top institute is Harvard Medical School, USA. It is worthy to note that more than 150 countries have contributed to research output. Based on the total publications, citations, and h-index, we provided details for each continent. Later, we provided the list of the top ten countries. The highest documents are published by the USA (25.35%). We analyzed the 343682 keywords from all publications to provide a general overview or the common trends in publications. We also analyzed the top 2000 most cited documents and provided the details of the top ten authors, institutes, and countries. Based on the VOSviewer' analysis, the information on the co-occurrence of words in titles, abstracts, and keywords is provided. This may help to depict the common trends in research publications. Based on the bibliometrics results, significant work has been published on pathogenesis, diagnosis, treatment, and prevention of this pandemic.

Epidemiological Characteristics of COVID-19

Due to the COVID-19 rapid spread and upward trend of the outbreak, the epidemiological data is updated weekly [1]. According to the WHO reports, the globally recorded new cases of the pandemic are still increasing [1, 2]. Based on the updated statistics (on 25th Oct, 2020), WHO declared more than 42 million cumulative cases and 1.1 million deaths [1]. From 18th to 24th Oct, 2020, on average, 2,552 new daily cases and 25 daily deaths were recorded in Canada, indicating a 14% increase compared with previous weeks [3]. Similarly, until October 30th, 2020, the center for disease control and prevalence (CDC) reported in the U.S. the total cases and deaths were 8,924,548 and 228,100, respectively [4]. However, the number of infected cases underestimated the real burden of disease due to the partial diagnoses and reported acute infections. According to the extracted data from seroprevalence surveys in the U.S. and Europe, it has been suggested that the rate of prior exposure to the virus exceeds the incidence by 10-fold or even more with considering the possible false positive/negative results [5-7]. It has also been well-established that the primary transmission route mainly refers to the person-to-person spread through the respiratory transmission. While, WHO jointly with China reported that fecal-oral and blood-borne routes appear to be no risk factors in virus transmission and subsequent infection spread [8, 9].

Shedding of Viral RNA

In terms of virus shedding, it should be considered that viral RNA shedding directly depends on the age and the severity of illness. However, the potency of virus transmission is higher in the early stage of the disease before the onset of symptoms progression (the highest load of viral RNA in the upper respiratory). The levels of viral RNA in asymptomatic patients are similar to those with overt manifestations of the disease [10].

It is worthy to note that the viral RNA can be detected in respiratory specimen several months after the infections. Still, the level of viral RNA is below that which can induce infectiousness ($<10^6$ copies/mL), particularly in non-severe patients or in whom with resolved symptoms [11, 12]. Therefore, the detection of viral RNA does not necessarily designate the presence of active infectious [11].. Based on the reports of sporadic cases, the reinfection has also been reported with distinct strains in patients with the positive RT-PCR genomic and laboratory-confirmed COVID-19 tests following the recovery and two consecutive negative results [13-16].

Virology

To our knowledge, the coronaviruses strains are large, lipid-enveloped, positive-stranded RNA viruses that belong to the Coronaviridae family. They can be classified into four genera including, alpha-coronavirus, beta-coronavirus, gamma-coronavirus, and delta-coronavirus. Based on the genome sequencing analysis, it has been revealed that SARS-CoV-2 belongs to the beta-coronavirus [17]. Overall, the coronavirus genome is comprised of approximately 30000 nucleotides, which replicate in the human-cell cytoplasm [17]. Despite the severe acute respiratory syndrome (SARS) subgenus is responsible for COVID-19 pathogenicity, the International Committee on Taxonomy of Viruses (ICTV) has also designated the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) for this virus [18].

The Coronavirus Structure

The genome of coronavirus encodes the variety of functional and structural proteins including nucleocapsid (N), membrane (M), and envelop (E) proteins, which participate in virus assembling.

The structural protein named spike (S) protein, which mediates the virus attachment as well as entry into the host cells and is known as a target for the neutralizing antibodies. S-protein with two subunits of S1, and S2 is defined as a surface spike glycoprotein leading virulence by binding to the human angiotensin-converting enzyme 2 (ACE-II) receptors. Previous literature also revealed two strains of coronavirus consisting of type S and L, which directly involved disease severity [19]. In addition, hemagglutinin-esterase dimer (HE) has been located on the surface of the virus that presumably participates in virus entry and appears to be important for conferring infectivity.

Immune Responses Following the Infection

SARS-CoV-2-specific antibodies (Abs), as well as cell-mediated responses, are stimulated following the infection. Previous evidence suggested that these humoral immune responses are partially protective. However, it is not established that whether all infected patients acquired enough immunity or not. Nevertheless, the detectable serum antibodies against the receptor-binding domain of the viral spike protein in the large portion of recovered patients were developed [20], which drop over several months [21]. Of note, detectable neutralizing antibodies are most likely associated with the disease severity and could not identify in mild infection [22, 23]. However, it has been estimated that cell-mediated immunity such as T cells subsets (CD4 and CD8) appear to have more stability in convalescent patients [24].

SARS-CoV-2 Mechanism of Action

The infection of COVID-19 primarily depends on cell entry by specific receptors. As mentioned above, the main host receptor for SARS-CoV-2 internalization refers to the angiotensin-converting enzyme 2 (ACE2) receptors as a membrane-associated zinc metalloprotease [25]. ACE2 related gene is ubiquitously expressed in various human tissues, e.g., lung, kidney, vascular endothelium, gastrointestinal track, and cardiac muscle [26]. Besides, the cellular transmembrane protease serine 2 (TMPRSS2) appears to be critical for virus conferring infectivity [27]. In detail, SARS-CoV-2 binds to the ACE2 receptor through the receptor-binding domain of its spike protein and subsequently enters into the cell through the plasma membrane fusion or endocytosis [27]. In this regard, after screening the amino acid changes in spike protein among a large sequence database, it has been surprisingly found that D614G substitution, as a glycine for aspartic acid, causes a dominant polymorphism [28]. Viral genome replication commonly occurs in the cytoplasm via the double-membrane vesicles from the endoplasmic reticulum (ER). Pp1a and pp1ab termed as two imperative polyproteins also play a pivotal role in viral replication and transcription [29, 30] and simultaneously propagate the release of functional polypeptides of a spike, envelop, membrane, nucleoprotein, replicas, and polymerase. After that, newly synthesized viral RNA packs are incorporated into the virions. Following the vesicular transportation, the matured virions can export from the host cells through the exocytosis process [31]. In lung tissue, SARS-CoV-2 is transmitted by respiratory aerosols to cause a presumable infection in upper or lower respiratory tract. Some respiratory complications induced by coronaviruses include tracheobronchial lymphadenopathy, multifocal pulmonary atelectasis, lymphocytic bronchiolitis, type II pneumocyte hyperplasia, edema and consolidation [32].

Therapeutic Interventions for COVID-19 Treatment

The understanding of COVID-19 is evolving moment by moment**,** leading us to achieve an effective therapeutic approach besides the vaccines. The common symptoms of COVID-19 include headache, dry cough, dizziness, myalgia, fever, sore throat, dyspnea, which can progress to the ARDS [33]. Many clinical trials are also being carried out to pre- and post-exposure prophylaxis to determine the drug's safety and efficacy against the COVID-19. In this regard, hydroxychloroquine (HCQ) and anti-malaria drug were considered as a candidate therapeutic agent in both pre- or post-exposure prophylactic settings. However, further available data suggested that HCQ could not be effective in terms of the COVID-19 treatment and preventing the SARS-CoV-2 infection [34]. Recently, an anti-viral drug named remdesivir (Veklury) revealed clinically desirable impacts against the diseases, especially in the complicated form of the disease, and makes it the first officially FDA-approved therapeutic agent once received the authorization of emergency application in May 2020, for all adult patients and pediatrics (12 years and older) with diagnosed COVID-19. Remdesivir is known as a prodrug of adenosine analogue with the potential to inhibit RNA polymerase activity [35]. Similarly, favipiravir, another antiviral drug with a broad spectrum inhibitory effects of viral RNA polymerase, is commonly prescribed for outpatients [36, 37]. Furthermore, it has been proposed that lopinavir/ritonavir (Kaletra), as a protease inhibitor, has therapeutic potential for COVID-19 treatment. The recent literature clarified that lopinavir/ritonavir significantly improved the outcomes in hospitalized patients; In contrast, according to the results of the recovery clinical trial, it has been suggested that monotherapy with lopinavir/ritonavir is not to be an effective therapeutic candidate, while the combination with interferon-beta would be remarkably more effective [38]. Notably, the recovery trial provided evidence for the administration of dexamethasone in ill patients admitted to IUC. The results of this comprehensive study established that the use of dexamethasone can significantly drop the 28-day mortality in those under invasive mechanical ventilation conditions [39]. The development of monoclonal antibodies is also being evaluated to neutralize SARS-CoC-2 in the post-exposure manner [40]. For example, tocilizumab (TCZ), a monoclonal antibody against interleukin-6 (IL-6), was recommended as an alternative treatment to quench the cytokine storm in ill patients with COVID-19 [40]. Besides, the stimulated non-specific immune responses against the SARS-CoV-2 infection following the Bacille-Calmette-Guerin (BCG) vaccine have also recently attracted researchers' attention in this era [41].

Bibliometric Analysis

Bibliometric analysis can be defined as a statistical evaluation of published scientific articles, books, chapters of a book, journals, broad research areas, institutions, and any specific country. The literature analysis is a very important means of sharing data information about the quantity and quality of scientific work [42, 43]. Various parameters like citation, co-citation, co-words analysis, H- index, impact factors are used for analysis purposes. These analytical tools can help researchers to understand the regularities and patterns in their specialized domain. The field of bibliometric was first introduced in information and library sciences, but now every field of study, either social science, physical or biological sciences, can implement it to evaluate trends and expansion in respective domains [42, 43]. It is a reliable method for studying the intellectual structure of every field. This technique helps evaluate individual authors, institutes, and countries in the scientific

literature. It also provides a guideline for quick survey among inter-disciplinary researchers [42, 43].

It is worthy to note that several articles are published about bibliometric analysis of COVID-19; however, they covered a comparatively smaller number of publications [7-10]. For example, Chahrour M. et al. conducted a bibliometric analysis of 564 documents on COVID-19 published until March 18, 2020. Similarly, Hossain M. compiled bibliometric analysis results of 422 COVID-19 research documents indexed in the Web of Science (WoS) core collection until April 1, 2020. Comparatively, a more comprehensive study was conducted by Hojat et al., which studied the publication pattern of 923 documents published until 1st April 2020 [44-47]. The present study was designed to perform the bibliometric analysis of COVID-19 publications. The following three basic parameters will be covered: Co-authorships, and Citations and Co-words analysis. We will precisely focus on the most productive scientists, institutes, and countries. The graphical overview of the bibliographic data will be provided by using visualization of similarities (VOSviewer) software.

Material and Method

Source of Information

Scopus (Elsevier BV Company, USA) is the largest database of scientific literature. The data was retrieved between 1st and 10th September 2020 using the code name (COVID-19). It is worthy to note that only those documents were considered for analysis that contained the word "COVID-19" in the titles of the publications. The data was collected by all authors and downloaded in CSV format. Later, it was quantitatively and qualitatively analyzed in Microsoft Excel 2013 for access type, year, author name, document type, keywords, affiliations, and country.

VOSviewer Analysis or Visualization Maps

Considerable literature is available which confirms the importance of analysis of co-authorship, bibliographic coupling, and co-citation networks. It has a long history, with early work dating back to the 1960s [48]. We used VOSviewer version 1.6.9 for viewing and creating the desired bibliometric maps. The software was developed by Van Eck and Waltman [49] for constructing and visualizing bibliometric networks [49]. For more information, please see http://www.vosviewer.com/. By default, at most, 1,000 lines are displayed and represent the 1,000 strongest links between items. The distance between two items in the visualization approximately indicates the relatedness of the items. The results are presented as network visualization maps.

Results and Discussion

Analysis of Publication Outputs

On 7th September, we retrieved the publication data from Scopus. We kept the search strategy very strict. Only those documents were considered for analysis that contained the words "Covid-19" in the titles of publications. Total 34716 research documents have been published about Covid-19. Only twenty-three were published in 2019. The most frequently published documents were articles (n = 16954/48.84 &), followed by letters (n = 7528/21.68%), reviews (n =3586/10.33%), notes (n = 3068/8.84%), editorials (n = 2835/8.17%), short surveys (n =362/1.04%), errata (202/0.58%), conference papers (n = 132/0.38%), data papers (n = 43/0.12%), and six (6/0.02%) book chapters. One document was retracted.

Scopus also categorized the publications in different subject areas. For example, most of the publications were in added in medicine (n = 27381), followed by biochemistry, genetics and molecular biology (n = 3045), social sciences (n = 2690), immunology and microbiology (n = 2084), nursing (n = 1522), neuroscience (n = 1257), psychology (n = 1225), environmental science (n = 1168), pharmacology, toxicology and pharmaceutics (1165), and health professions (n = 703).

We also highlighted the details of the top ten (10) sources. The highest documents are published in BMJ Clinical Research Ed (n = 455), followed by BMJ (n = 364), Journal of Medical Virology (n = 337), International Journal of Environmental Research and Public Health (n = 281), Lancet (n = 239), Medical Hypotheses (n = 213), Dermatologic Therapy (n = 212), JAMA Journal of the American Medical Association (n = 181), Critical Care (n = 180), and International Journal of Infectious Diseases (n = 179).

Co-Authorship Analysis for Researchers, Institutions, and Countries

As scientific research has grown, a significant increase in the productivity rate (total publications) has been observed. H-index is an authentic parameter for the analysis of the productivity index. Hirsch introduced the parameter in 2005. This indicator measures the productivity and impact factor of researchers as well as of scientific journals. Total citation is another important indicator used for the evaluation of the author's output. This parameter acknowledges the quality of the work of authors, institutes, and countries. It is important to note that this parameter is effective in a comparative study. Self-citation is the reference given to a document from the same journal or the same work. Self-citation has some limitations as it affects the impact of both author and a journal. Citation per paper/document is also used to indicate the citation received per document in a journal. Based on the number of total publications, h-index, total citations, and self-citations, we provided the lists of top-rank authors, institutes, and countries.

The Top Ranked Authors

Based on the total number of publications, the top-ranked authors are Wiwanitkit, V. (n = 93) followed by Mahase, E. (n = 75), Iacobucci, G. (n = 53), Lippi, G. (n = 47), and Goldust, M. (n = 41). However, we observed some changes in rankings based on the h-index. Thus, the top slot is occupied by Lippi, G. (n = 16), followed by Rodriguez-Morales, A.J. (n = 10), Mahase, E. (n = 9), Buonsenso, D. (n = 9), Dhama, K. (n = 8), and Goldust, M. (n = 7). Based on total citation, Lippi, G. (n = 1143) was found to be top rank author, followed by Rodriguez-Morales, A.J. (n = 528), Dhama, K. (n = 436), Buonsenso, D. (n = 429), Mahase, E. (n = 361), and Wiwanitkit, V. (n = 221). While, based on the citation per document indicator, Lippi, G. (n = 24) was found to be the top rank author, followed by Rodriguez-Morales, A.J. (n = 17), Dhama, K. (n = 14), Buonsenso, D. (n = 13), Joob, B. (n = 5), and Mahase, E. (n = 5), respectively. The overall list is provided in Table 1.

Table 1

The List of Top Ten Authors with Total Publications (TP), H-index, Total Citations (TC), H-index Withoutself Citations (WSC), WSC and Citations per Documents (CPD)

S#	Author Name	TP	H-Index	TC	H- Index (WSC)	WSC	Citation Per Document
1.	Wiwanitkit, V.	93	6	221	6	196	2
2.	Mahase, E.	75	9	361	9	359	5
3.	Iacobucci, G.	53	5	122	5	122	2
4.	Lippi, G.	47	16	1143	16	1045	24
5.	Goldust, M.	41	7	124	5	63	3
6.	Rimmer, A.	40	5	47	5	47	1
7.	Joob, B.	34	5	174	5	152	5
8.	Buonsenso, D.	33	9	429	8	324	13
9.	Rodriguez-Morales, A.J.	32	10	528	8	408	17
10.	Dhama, K.	31	8	436	6	356	14

The Top Ranked Institutes

Based on the number of publications, the top five universities are Harvard Medical School (n = 705), Huazhong University of Science and Technology (n = 558), Tongji Medical College (n = 535), Inserm (n = 481), and University of Toronto (n = 413). Similarly, Huazhong University of Science and Technology can be ranked as the top university with the highest total citations (n = 10540), followed by Tongji Medical College (n = 10399), Harvard Medical School (n = 5859), Inserm (n = 4612), and University of Oxford (n = 3921). We also extended the idea and determined the top-ranked institutes based on the h-index. In this series, Tongji Medical College was noted as the top institute with the highest h-index (n = 50), followed by Huazhong University of Science and Technology (n = 49), Harvard Medical School (n = 36), Inserm (n = 30), and Universit Ãdegli Studi di Milano (n = 26). While the highest citations per document were obtained for Tongji Medical College (n = 19), Huazhong University of Science and Technology (n = 19), the University of Oxford (n = 12), University College London (n = 11), and Inserm (n = 10). The overall list is provided in Table 2.

Table 2

The List of Top Ten Institutes with Total Publications (TP), H-index, Total Citations (TC), H-index Withoutself Citations (WSC), WSC and Citations per Documents (CPD)

S#	Affiliation	TP	H-Index	TC	H- Index (WSC)	WSC	Citation Per Document
11.	Harvard Medical School	705	36	5859	34	5530	8
12.	Huazhong University of Science and Technology	558	49	10540	48	10317	19
13.	Tongji Medical College	535	50	10399	49	10197	19
14.	Inserm	481	30	4612	29	4396	10
15.	University of Toronto	413	23	2610	23	2407	6
16.	UniversitÃ degli Studi di Milano	389	26	3607	26	3363	9
17.	UniversitÃ degli Studi di Roma La Sapienza	377	20	1795	19	1534	5
18.	Massachusetts General Hospital	338	22	2060	20	1907	6
19.	University College London	336	23	3542	23	3397	11
20.	University of Oxford	318	23	3921	23	3814	12

The Top Ranked Countries

In a short span of only eight months, in all COVID-19 publications (n = 34716), more than 150 countries from different geographies have contributed. The data is provided in Table 3. Based on the number of publications, Europe can be declared as the top continent. More than 35 different

countries have contributed in (n = 12769/ 37.16%) publications. The top five European countries are; United Kingdom (n = 4012), Italy (n = 3758), France (n = 1510), Spain (n = 1457) and Germany (n = 1279). The 2nd dominant region is North America, with 9847 publications. This constitutes 28.66% of total publications. United States is the top-ranked country in this region (n = 8623), followed by Canada (n = 1488) and Mexico (n = 340). Asia has significantly contributed to 26% of publications (or n = 8911). In total, 26 different countries are involved in publications. The top five countries from this region are China (n = 4137), India (n = 2207), Singapore (n = 602), Japan (n = 474), and Hong Kong (n = 396). Australia and New Zealand (Ociana region) collectively contributed in 2112 publications. From the Middle East, 15 countries were directly involved in research output. In total, 2112 documents were published by this region. The top five countries are Iran (n = 948), followed by Saudi Arabia (n =387), Israel (n = 283), United Arab Emirates (n = 120), and Morocco (n = 86). Twenty countries (20) from South America have contributed in 1711 (or app. 5%) publications. Brazil (1045), Colombia (n = 215), Argentina (n = 181), Chile (n = 155), and Peru (n = 133) are the top five productive countries. While from the Africa region, 53 countries have contributed to 1207 research publications. The top five countries from this region are South Africa (n = 35), Egypt (n = 229), Nigeria (n = 149), Tunisia (n = 58), and Ghana (n = 51).

Table 3

The Number of Publications, %, H-Index and Total Citations of Different Continents

S#	Continent	No of Countries	No of Pub	% Collectively	H-Index	Total Citations
1.	Europe	40	12769	37.16	90	58460
2.	North America	3	9847	28.66	93	53582
3.	Asia	26	8911	25.93	121	73516
4.	Ociana	2	2112	6.15	37	6115
5.	Middle East	15	2112	6.15	37	7154
6.	South America	20	1711	4.98	27	4394
7.	Africa	53	1207	3.51	25	3081

Irrespective of the region, the list of the top 10 countries is described in Appendix 1. Based on the number of publications, USA is the top country with 8711 (or 25.35 %) publications, followed by China (n = 4164/ 12.12%), United Kingdom (n = 4051/11.79%), Italy (n = 3806/11.08%), and India (n = 2238/6.51%). While, based on total citations, China is the top-ranked country (n = 56606), followed by USA (n = 50736), United Kingdom (n = 23725), Italy (n = 21382) and France (n = 9486). On the basis of H-index, China (n = 107), USA (n = 93), UK (n = 67), Italy (n = 60) and France (n = 43) can also be ranked as top five countries. Similarly, we can also depict the publications and citation data as citation per document (CPD). In this way, China can be termed as the top-ranked country (CPD = 14). France, Germany, UK, the USA, and Italy have a CPD score of six (n = 6), while the CPD for Canada, Australia, Spain, and India are four (4), four (4), and two (2), respectively.

The Analysis of Top-Ranked Author, University and Country

We also quantitatively analyzed the top-ranked author, university, and country. This may help in explaining that a single author, university, and country can affect collaboration and networking. For this purpose, we focused on three fundamental factors, i.e., the total number of co-authors, institutes and collaborations with international countries were elucidated. As stated earlier, based on the total number of publications, the top-ranked author is Wiwanitkit, V. (n = 93). In all of his

publications, ten authors have collectively contributed. Similarly, 69 different institutes of departments have contributed to publications.

In Harvard Medical School publications (n = 705), more than 3500 authors have contributed. However, 50 authors have published at least five or more than five publications. The names of all authors are provided in Figure 1.

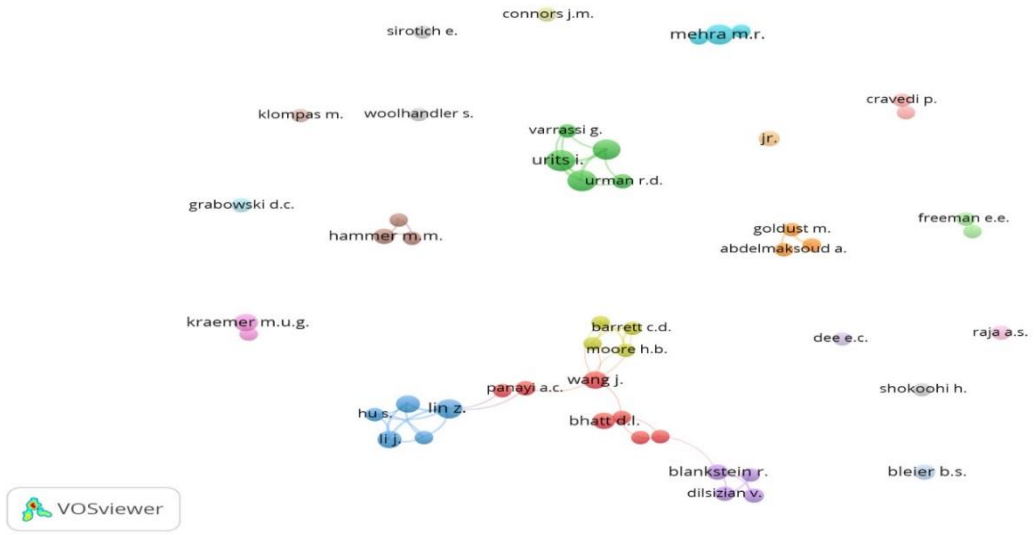

Figure 1. The co-authorship network for Harvard University. The clusters represent different authors.

Based on the number of publications, Urits, I. (16) was the top-ranked authors, followed by Mehra, M. R. (15), Viswanath, O. (15), and Kaye, A. D. (14). However, based on the citations, the top three authors from this school are Mehra M. R. (n = 978), Ruschitzka F. (n = 642), and Schuepbach R. A. (n = 453). Institutionally, more than 3000 different institutional affiliations were recorded in all publications (n = 705). Twenty-nine institutes have published at least five or more than five documents. The details are depicted in Figure 2.

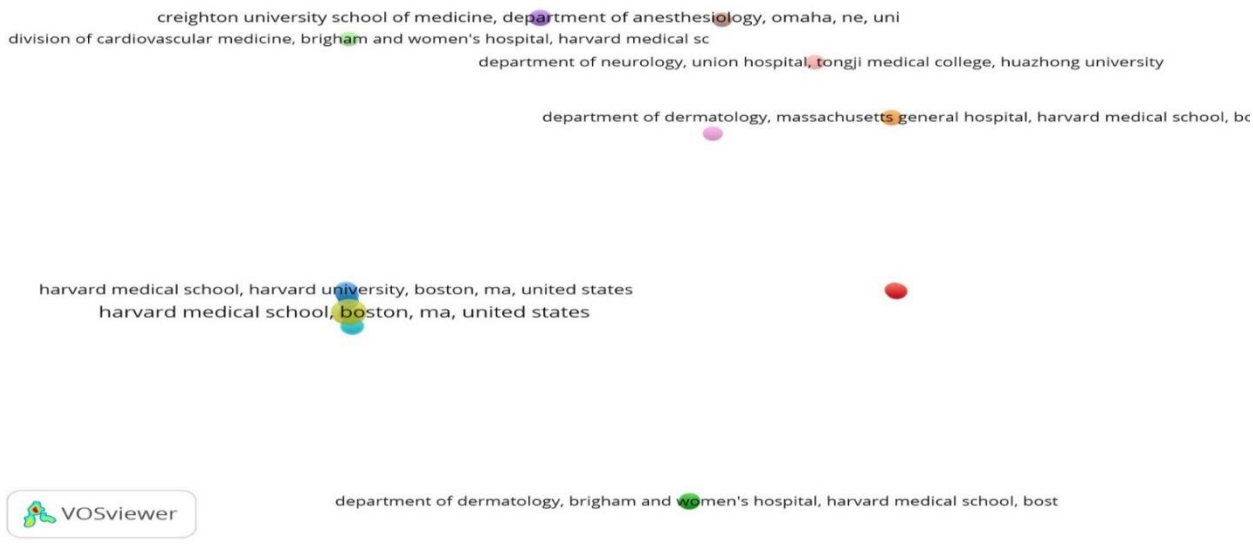

Figure 2. The co-authorship network for Harvard University. The clusters represent different institutes and/or departments.

In all Harvard-affiliated publications, more than 90 countries have contributed. At least 39 countries were directly involved in at least five publications. While the top three sources are the New England Journal of Medicine (n = 18), JAMA Journal of the American Medical Association (n = 13), and Journal of the American Academy of Dermatology (n = 13). The USA was found to be top-ranked with the highest number of publications (n = 8763). The top five authors were determined to be Lippi, G. (n = 33), Goldust, M. (n = 27), Henry, B. M. (n = 26), Sahu, K. K. (n = 26), and Jafferany, M. (n = 22). Most of the publications were contributed by Harvard Medical School (n = 661), Massachusetts General Hospital (n = 311), Brigham and Women's Hospital (n = 296), Icahn School of Medicine at Mount Sinai (n = 268), and the University of California, San Francisco (n = 233). While, the top five sources are JAMA Journal of the American Medical Association (n =132), Journal of The American Academy of Dermatology (n = 85), Otolaryngology Head and Neck Surgery United States (n = 82), Lancet (n = 75), and Journal of Medical Virology (n = 74). More than 150 countries also showed collaborations. The top five in this series were United Kingdom (n = 693), China (n = 598), Italy (n = 578), Canada (n = 501) and Australia (n = 376).

Co-Words Analysis of the COVID-19 Literature

The study of the co-occurrence of at least two technical words in research documents is termed as co-words analysis. It indicates the topics addressed in research articles and helps to explore the overall trend. With the help of this tool, researchers would better understand the hotspots and disciplinary structures of their research. It can also help to understand the progress and existing regularities in research output. To explore the major focus of COVID-19 related studies, we retrieved data consisting of 343682 keywords from more than 34000 research documents using the Scopus database. After a critical analysis, we categorized the collected data under different themes. The exact number and percentage of each group is depicted in Appendix 2.

COVID-19 Pandemic (152896 / 44%)

SARS-Cov-19 was diagnosed as a novel strain of Coronavirus declared a pandemic by WHO on January 30, 2020. Now the viral infection is named severe acute respiratory syndrome corona virus-2 (SARS-COV-2). These are RNA positive strain of the Corona family. The symptom of this virus *looks like* the common flu. Structurally, this virus has crown-like structures attached to ACE 2 (Angiotensin-converting enzyme 2) of the epithelium cells and cause severe respiratory disease. Researchers proposed several mechanisms for a viral invasion to CNS, most acceptable is via the olfactory route, thus leading to cause different neurological manifestations in patients.

This class covered 44% of the total keywords. Under this title, we collected relevant words like Pandemic, Coronavirus Disease 2019, Coronavirus Infection, Virus Pneumonia, Coronavirus Infections, Pandemics, Pneumonia, Viral, COVID-19, Betacoronavirus, Severe Acute Respiratory Syndrome Coronavirus 2, Coronavirus, SARS-CoV-2, Epidemic, Virology, Disease Severity, Adult Respiratory Distress Syndrome, Angiotensin-Converting Enzyme 2, Coronavirinae, Covid-19, SARS Coronavirus, and Viral Diseases.

Subject (56850 / 16%)

Medical experts and scientists mostly studied COVID-19 related research that has been analyzed mostly on humans of different age groups. This group consists of 16% of the total keywords. We compiled similar words that highlighted the trend in this field. The following words are Human,

Humans, Nonhuman, Female, Male, Adult, Child, Young Adult, Adolescent, Very Elderly, Middle Aged, Aged, Aged 80 and over, and Age. A total of 16% covered this domain.

Study (29794 / 9%)

This category covered 9% of the total retrieved keywords. In addition, considerable literature is reported on currently emerged pandemic COVID-19 in the form of review, Case report, Letter, Editorial, Note, Questionnaire, Article, Clinical Article, Retrospective Studies, Controlled Study, Major Clinical Study, Clinical Feature, Clinical Practice, and Priority Journal. The above-mentioned categories are considered constant as they are the major focus of every research publication. However, we further categorized the remaining 104142 keywords into different categories to understand the broader focus of researchers. The exact frequency and percentage are depicted in Appendix 2.

Health Care Access (33057 / 32%)

The emergence of fatal infection in the world emphasized the health authorities take a protective measurement for COVID 19. Different health policies and guidelines were planned to minimize the spread of the Coronavirus. The health worker restricts the movement of patients with different comorbidities to the hospitals by introducing telemedicine. Patients with different pathological manifestations communicate with a medical specialist by using electronic media (such as video calls, emailing, web conferences, phones, WhatsApp) for their assistance, such as supportive therapies and treatments that are interrupted during the lockdown.

In this category, we compiled different words like Health Care Access, Health Care Delivery, Health Care Planning, Health Care Policy, Risk Assessment, Risk Factors, Patient Safety, Global Health, Government, Hospital Discharge, Intensive Care, Organization And Management, Telemedicine, Hospitalization, Patient Care, Mortality Rate, Hospital Admission, Infection Prevention, Health Care System, Artificial Ventilation, Complication, Health Care Personnel, Risk Factor, Procedures, Mortality, Practice Guideline, Intensive Care Unit, and Comorbidity.

Symptomatology (21018 / 20%)

Medical experts and researchers determined several symptoms shown by COVID-19 patients. The most visible symptoms are related to the respiratory system. COVID-19 virus has the potential to invade the CNS and cause different neurological complications like encephalitis, multiple sclerosis, epilepsy, seizure, and myelitis. COVID-19 also causes secondary complications like depression, anxiety, Dyspnea, fever, headache. Researchers studied these disorders to propose the mechanism of viral invasion.

Following pathological complications associated with COVID-19 were compiled to depict the general trend of research in this domain. The most relevant words are Coughing, Pneumonia, Mental Health, Hypertension, Immunology, Diabetes Mellitus, Anxiety, Pregnancy, Diarrhea, Throat Culture, Depression, Cardiovascular Disease, Severe Acute Respiratory Syndrome, Immune Response, Respiratory Failure, Critically Ill Patient, Disease Association, Disease Course, Disease Exacerbation, and Disease Outbreaks.

Prevalence Factors (12990 / 12%)

This category covered 12% of the total keywords. The researchers and medical experts determined different measuring parameters like Quarantine, Social Distance, Social Isolation to stop or

minimize the prevalence of virus transmission. The local communities are made aware of public health about disease transmission, isolation, purification, medical education, education, infection risk, and communicable disease control via social media.

Prevention Parameters (12990 / 10%)

Under this theme, 10% of keywords are compiled that elaborate the prevention factors taken by medical specialists to minimize the erupt effects of COVID-19 infection. For this purpose, we collected a group of relevant words like emergency health service, follow up, incidence, isolation, hand washing, metabolism, personal protective equipment, prevalence, prevention, and control, prognosis, protective equipment, tocilizumab, treatment outcome, unclassified drug, and World Health Organization.

Pathophysiology (10004 / 10%)

Under this title, 10% of the retrieved keywords are collected that reflect several Laboratory Technique, Clinical Laboratory Techniques for the diagnosis of infection. The elevation observed in the cytokine storm, D Dimer accelerates the invasion of pathophysiological disorders. C Reactive Protein, Reverse Transcription Polymerase Chain Reaction, Interleukin 6, Blood, Polymerase Chain Reaction, Pathology, Pathogenicity, Epidemiology, Epidemiology were also added to this class.

Treatment (5932 / 6%)

The appearance of the deadly virus in human beings triggered many complicated pathologies. With the help of medical specialists, researchers collectively proposed treatment and/ or therapies to overcome the infection by synthesizing drugs/ medicines, effectively contributing to the recovery of COVID-19 patients. This class comprised 6% of the total retrieved keywords. The words like Drug Effect, Antiviral Agents, Antivirus Agent, Azithromycin, Remdesivir, Chloroquine, Lopinavir Plus Ritonavir, and Hydroxychloroquine were compiled under this title to understand the trend in this domain.

Diagnostic Techniques (5362 / 5%)

Five (5%) of the keywords highlighted the trend of research on the COVID-19 pandemic. Scientists used different instrumental tools like Diagnostic Imaging, Computer Assisted Tomography, Retrospective Study, X-ray Computed Tomography, Tomography, and X-Ray Computed to examine the internal damage caused by the virus. Thorax Radiography is a sensitive technique to identify the early symptoms of viral infection that could be useful for the prognosis of COVID-19.

Countries (5359 / 5 %)

The viral wave affects different countries of the world. However, about 5% of research highlighted the most affected countries such as China, Italy, the United States, and the United Kingdom (to name a few).

The VOSviewer Analysis of the Top Two Thousand (2000) Most Cited Documents

In all 2000 publications, more than 9300 authors have contributed. However, fifty-nine (n = 59) authors have published at least ten research documents. The details are provided in Table 4. Based on the number of publications, the top three authors are Wang Y. (n = 40), Liu Y. (n = 31), and Wang J. (n = 31). Based on total citations, Wang Y. (n = 6341) remains at the top, followed by Liu Y. N = 5320) and Zhang Y. (n = 4884). Furthermore, we also calculated the CPD for the top three

authors. As a result, Liu Z. can be declared the top-ranked author with CPD (CPD = 288), followed by Chen H. (CPD = 4021) and Li H. (CPD = 3249).

Table 4

List of Top Ten Authors (Based on Total Publications, Citations, and Citations per Document/CPD). The Data is for the Top 2000 most Cited Documents

S#	Author	Documents	Author	Citations	Author	CPD
1)	Wang y.	40	Wang y.	6341	Liu z.	288
2)	Liu y.	31	Liu y.	5320	Chen h.	287
3)	Wang j.	31	Zhang y.	4884	Li h.	217
4)	Chen y.	27	Chen h.	4021	Zhang c.	196
5)	Zhang l.	27	Liu z.	3451	Zhang y.	188
6)	Li y.	26	Li h.	3249	Liu s.	188
7)	Zhang y.	26	Zhang c.	2741	Liu y.	172
8)	Wang x.	25	Wang j.	2635	Liu h.	168
9)	Wang l.	23	Liu h.	2181	Wang y.	159
10)	Zhang s.	23	Zhang l.	2125	Wang c.	139

More than 8000 institutional affiliations were noted in the top 2000 most cited publications (based on the VOSviewer analysis). However, only 89 institutes have published at least three documents. The top ten list is provided in Table 5. Section of Clinical Biochemistry, Department of Neuroscience, Biomedicine and Movement, University of Verona, Verona, Italy has published the highest number of publications (n = 9), followed by London School of Hygiene and Tropical Medicine, London, United Kingdom (n = 8) and Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan (n = 7). However, based on total citations, the top three ranked institutes are as follow; Ihu-Méditerranée Infection, Marseille, France (n = 1129), Department of Radiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (n = 785) and Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan (n = 780). While based on CPD, the top three institutes are Ihu-Méditerranée Infection, Marseille, France (CPD = 1129), Department of Respiratory and Critical Care Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (CPD = 666), and Department of Internal Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Ma, United States (CPD = 618). Similarly, more than 100 countries have been directly involved in research output.

Table 5

List of Top Ten Institutes (Based on Total Publications, Citations and Citations per Document/CPD). The Data is for The Top 2000 most Cited Documents

S#	Organization	Documents	Organization	Citations	Organization	CPD
1)	Section Of Clinical Biochemistry, Department of Neuroscience, Biomedicine and Movement, University of Verona, Verona, Italy	9	Ihu-Méditerranée Infection, Marseille, France	1129	Ihu-Méditerranée Infection, Marseille, France	376
2)	London School of Hygiene and Tropical Medicine, London, United Kingdom	8	Department Of Radiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China	785	Department Of Respiratory and Critical Care Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China	222
3)	Department Of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan	7	Department Of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan	780	Department Of Internal Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Ma, United States	206

4)	Department Of Laboratory Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan	6	Department Of Laboratory Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan	724	Department Of Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan	203
5)	Department Of Experimental and Clinical Medicine, University of Florence, Florence, Italy	5	Department Of Respiratory and Critical Care Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China	666	Department Of Radiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China	196
6)	Department Of Laboratory Medicine, University Hospital of Padova, Padova, Italy	5	Department Of Internal Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Ma, United States	618	Barts And the London School of Medicine and Dentistry, Queen Mary University of London, United Kingdom	167
7)	Department Of Zoology, University of Oxford, Oxford, United Kingdom	5	Department Of Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan	608	Barts Health Nhs Trust, London, United Kingdom	167
8)	Massachusetts General Hospital, Boston, MA, United States	5	Department Of Zoology, University of Oxford, Oxford, United Kingdom	581	Department Of Cardiology, Renmin Hospital of Wuhan University, Wuhan, China	130
9)	National Centre for Infectious Diseases, Singapore	5	Section Of Clinical Biochemistry, Department of Neuroscience, Biomedicine and Movement, University of Verona, Verona, Italy	521	Department Of Population Health Sciences, School of Public Health, Georgia State University, Atlanta, GA, United States	121
10)	National Diabetes, Obesity and Cholesterol Foundation, New Delhi, India	5	Department Of Cardiology, Renmin Hospital of Wuhan University, Wuhan, China	520	Department Of Laboratory Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan	121

The USA publishes the highest documents (n = 664), followed by China (n = 552) and Italy (n = 304). One the basis of citations, China (n = 49566) overtakes USA (n = 37915), followed by UK (n = 17914). While based on CPD, Vietnam holds the top position (CPD = 165), followed by Peru (n = 96) and United Arab Emirates (n = 92). The top ten list is provided in the Table 6.

Table 6

List of Top Ten Countries (based on Total Publications, Citations and Citations per Document/CPD). The Data is for the Top 2000 most Cited Documents

S#	Country	Documents	Country	Citations	Country	CPD
1)	United states	664	China	49566	Vietnam	165
2)	China	552	United states	37915	Peru	96
3)	Italy	304	United Kingdom	17914	United Arab Emirates	92
4)	United Kingdom	303	Italy	14989	China	90
5)	France	123	France	7201	Thailand	85
6)	Germany	106	Germany	5809	Hong Kong	80
7)	Canada	103	Canada	5701	Netherlands	78
8)	Australia	90	Netherlands	4685	Japan	78
9)	Spain	86	Switzerland	4466	Greece	72

Co-Occurrence of Words in Titles, Abstracts and Keywords in the Top 2000 Cited Documents

In this part, we focused on the co-occurrence of words in titles, abstracts, and keywords of the publications. In titles, total terms or words were found to be 3859. Furthermore, 80 of them repeated at least ten times, as shown in Figure 3.

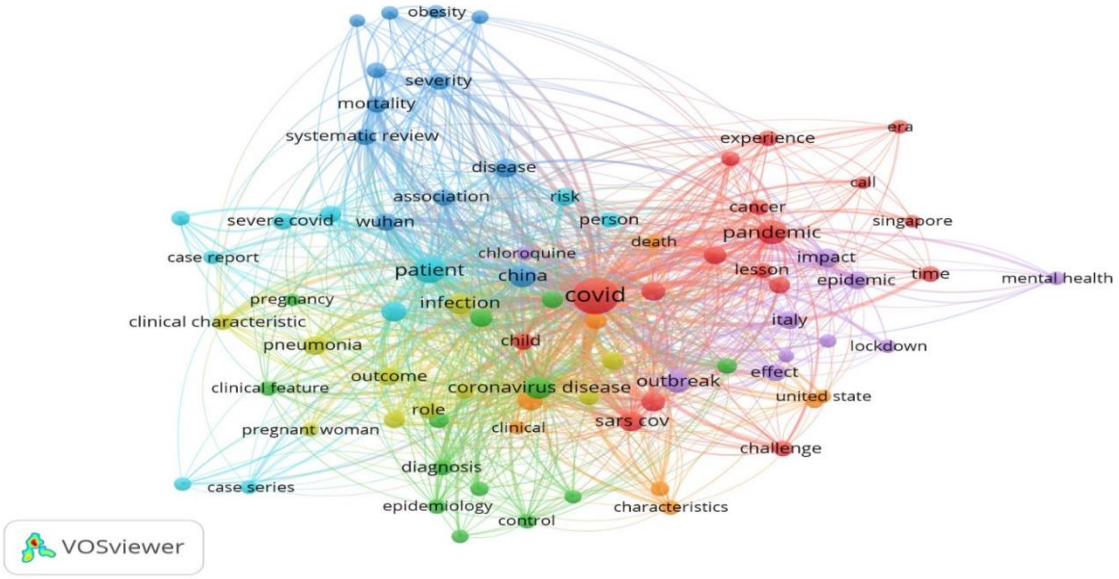

Figure 3. The most common co words in titles of the top 2000 cited documents.

Based on the words co-occurrence, we can describe the general tendency or broader aspects of these publications. First of all, we will state that different words such asacute respiratory distress syndrome, coronavirus, coronavirus disease, covid, novel coronavirus, novel coronavirus disease, and severe coronavirus disease were used in titles to represent the COVID-19 pandemic. Different cases, case reports, case series, challenges, clinical characteristics, and clinical features were described, with the main focus on detection, diagnosis, risks factors, spread, severity, transmission, implications, and prevention in the patients. Furthermore, the authors tried to provide an association of COVID-19 with cancer, infection, mental health, pneumonia, pregnancy, and obesity. Different measures like lockdown, control on the pandemic, management, lesson learned, or outcome are also described. Other words also appeared to represent countries and the time frame of the pandemic, such as February, Wuhan, China, India, Italy, the USA, and Singapore.

A total of 19766 words were appeared in all (n = 2000) abstracts, of which101 appeared at least 50 times (Figure 4). It can be stated that the overall pattern or tendency of co-words was similar with titles. For example, the authors majorly elaborated on different symptoms and association of COVID 19 with other complications like cough, diabetes, fever, hypertension, illness, infection, intensive care unit, pneumonia, mortality, death, etc. Other months, areas, and countries also appeared, such as December, January, February, March, April, Hubei Province, China, Italy, the USA, and India. Different words were also found in the abstract, which can provide direct information of the hospital admission, to diagnosis and data interpretations. Some examples of the words used in the abstract are admission, hospitalization, disease, diagnosis, knowledge, laboratory, data, and interpretation.

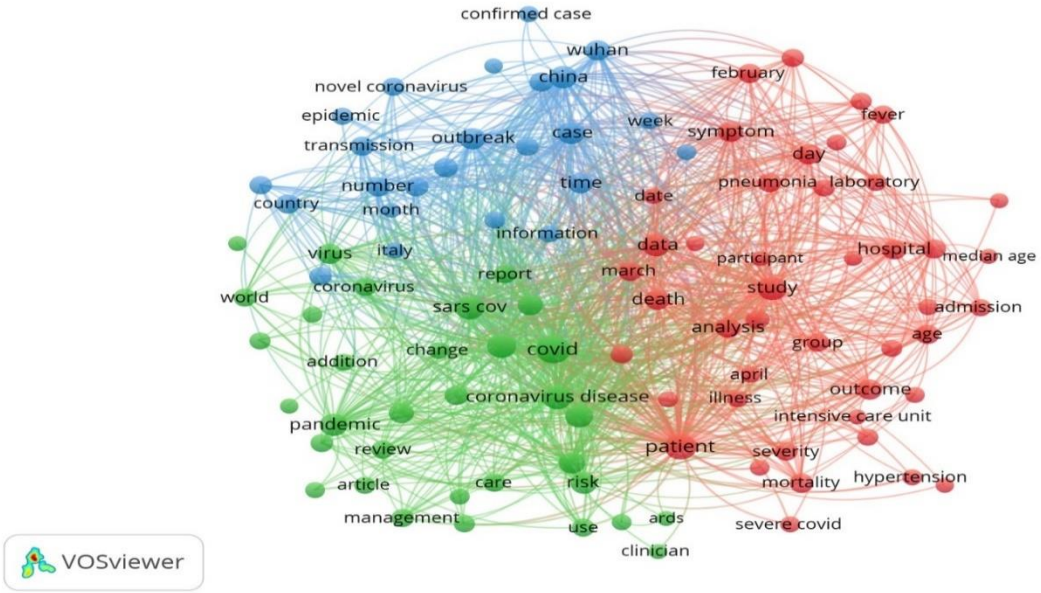

Figure 4. The most common co words in abstracts of the top 2000 cited documents.

While the total authors' keywords in 2000 documents were found to be 9280, of which 50 were repeated at least 103 times or 100 words were repeated at least 103 times (Figure 5). To further explore the broader trend in these documents (n = 2000), we also retrieved 42645 keywords to understand.

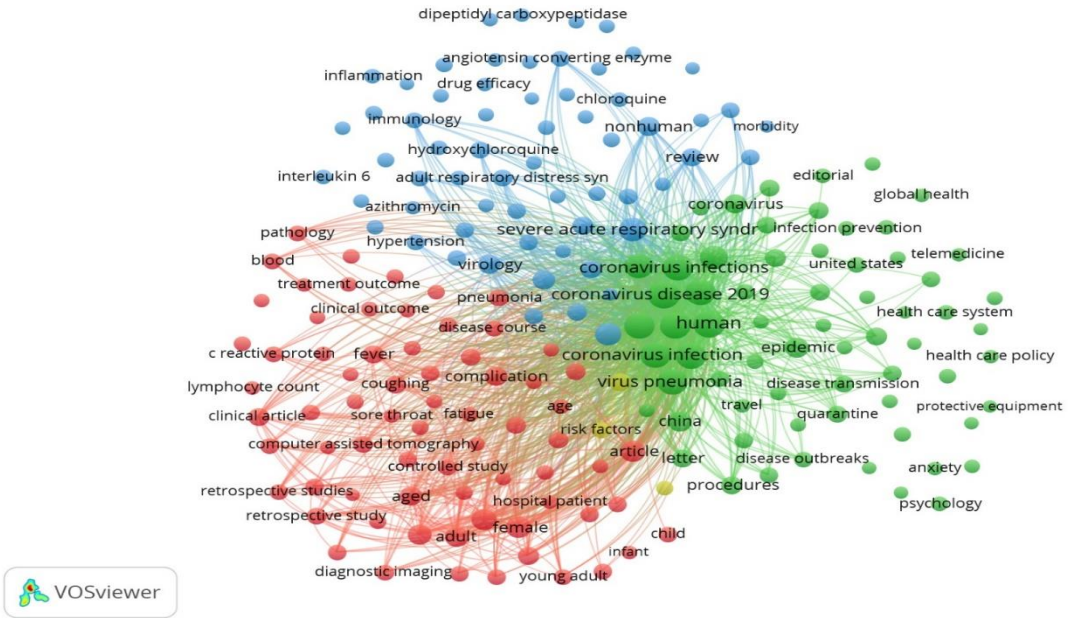

Figure 5. The most common co words in keywords of the top 2000 cited documents.

After a critical analysis, it was observed that the authors used different terminology for the virus such as coronavirinae, coronavirus, coronavirus disease 2019, coronavirus infection, COVID-, adult respiratory distress syndrome, *SARS-CoV-2*, SARS virus, SARScoronavirus. They also highlighted the viral association with different receptors or enzymes like angiotensin-converting enzyme 2, angiotensin II receptor antagonists that accelerate cytokine, cytokine storm, D dimer in

the patient's body. Other words like anxiety, cardiovascular disease, comorbidity, depression, diabetes mellitus, diarrhea, fatigue, fever, headache, hypertension, mental health, myalgia, pneumonia, severity of illness index, sore throat, disease association, disease course, disease outbreaks, disease progression, disease severity, disease surveillance, and disease transmission indicate that the authors tried to elucidate the possible association of these disorders with COVID 19 infections. In addition, hydroxychloroquine, corticosteroid, chloroquine are the effective drugs suggested for the patients. Similarly, different laboratory techniques for diagnosis and/or therapies were described in detail. For example, x-ray computed tomography, tomography, x-ray computed, thorax radiography, and oxygen therapy. In addition, the authors focused on quarantine, social distance, risk factors, and prevalence of COVID 19 in patients in different types of studies and reports like articles, case reports, controlled studies, and letters.

Conclusion

Although SARS-CoV-2 infected more than 10 million people, many aspects of the COVID-19 pathophysiology remain unclear. Therefore, the comprehensive bibliometric analysis on basic and clinical investigations and public health and clinical interventions can promote advances in COVID-19 management. Since COVID-19 emerged as a severe threat to public health, the number of publications on different aspects of this infection, such as epidemiology, pathogenesis, transmission, and prevention, etc., has dramatically increased. In-country analysis sections, it was found that more than 150 countries are vastly working and producing scientific documents to find a solution for this pandemic.

Competing Interests

The authors declared that they have no conflicts of interest.

Authors' Contributions

Waseem Hassan collected the data, Seyed Mohammad Nabavi interpreted the findings, Aysa Rezabakhshc designed, prepared, and revised the manuscript. Finally, all authors have read and approved the manuscript.

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Appendix 1

The list of top ten countries with total publications (TP), h-index, total citations (TC) and citations per documents (CPD)

S#	Country	TP	H-Index	TC	Citation Per Document
1)	United States	8711	93	50736	6
2)	China	4164	107	56606	14
3)	United Kingdom	4051	67	23725	6
4)	Italy	3806	60	21382	6
5)	India	2238	32	5510	2
6)	France	1529	43	9486	6
7)	Canada	1503	39	7955	5
8)	Spain	1495	35	5769	4
9)	Australia	1305	35	5762	4
10)	Germany	1293	40	7638	6

Appendix 2

List of the most common co-words in all publications

COVID-19 Pandemic	**#**	**Subject**	**#**	**Health Care Access**	**#**
Pandemic	17077	Human	19434	**Health Care Access**	**#**
Coronavirus Disease 2019	16506	Humans	13809	Health Care Access	554
Coronavirus Infection	14181	Female	4169	Health Care Delivery	942
Virus Pneumonia	14149	Male	4074	Health Care Planning	555
Coronavirus Infections	13990	Adult	3610	Health Care Policy	627
Pandemics	13939	Middle Aged	2429	Risk Assessment	946
Pneumonia, Viral	13897	Aged	2428	Risk Factors	887
COVID-19	12041	Child	976	Patient Safety	544
Betacoronavirus	11649	Nonhuman	2157	Global Health	611
Severe Acute Respiratory Syndrome Coronavirus 2	6068	Aged, 80 And Over	677	Government	674
Coronavirus	3821	Age	659	Hospital Discharge	502
SARS-CoV-2	3151	Young Adult	822	Intensive Care	727
Epidemic	2676	Adolescent	807	Organization And Management	1503
Virology	2300	Very Elderly	799	Telemedicine	1290
Disease Severity	2142	Total	56850	Hospitalization	1276
Adult Respiratory Distress Syndrome	1081	**Diagnostic techniques**	**#**	Patient Care	1174
Angiotensin Converting Enzyme 2	1072	Diagnostic Imaging	843	Mortality Rate	1152
Coronavirinae	955	Thorax Radiography	988	Hospital Admission	1102
Covid-19	839	Computer Assisted Tomography	1236	Infection Prevention	1066
SARS Coronavirus	685	Retrospective Study	971	Health Care System	1031
Viral Disease	677	X-ray Computed Tomography	739	Artificial Ventilation	1016
Total	152896	Tomography, X-Ray Computed	585	Complication	2117
		Total	5362	Health Care Personnel	1882
Pathophysiology	**#**	**Prevalence factors**	**#**	Risk Factor	1867
Laboratory Technique	730	Virus Transmission	1788	Procedures	2559
Clinical Laboratory Techniques	729	Quarantine	1810	Mortality	1829
Pathology	743	Public Health	1600	Practice Guideline	1827
Pathophysiology	911	Disease Transmission	1569	Intensive Care Unit	1456
Pathogenicity	803	Infection Risk	1413	Comorbidity	1341
Epidemiology	798	Isolation And Purification	1191	Total	33057
Inflammation	742	Social Distance	957		
C Reactive Protein	819	Social Isolation	641	**Symptomatology**	**#**
Reverse Transcription Polymerase Chain Reaction	720	Social Media	499	Fever	1678
Interleukin 6	699	Communicable Disease Control	513	Coughing	1370
Blood	609	Education	503	Psychology	1136
Cytokine Storm	652	Medical Education	506	Pneumonia	1126

Polymerase Chain Reaction	545		12990	Dyspnea	1057
D Dimer	504			Infection Control	2022
Total	10004	**Treatment**	#	Mental Health	990
		Drug Effect	563	Hypertension	897
Prevention parameters	#	Antiviral Agents	510	Immunology	886
Emergency Health Service	734	Antivirus Agent	771	Diabetes Mellitus	828
Follow Up	790	Azithromycin	665	Anxiety	797
Incidence	718	Remdesivir	641	Pregnancy	509
Isolation	595	Chloroquine	711	Diarrhea	504
Hand Washing	569	Lopinavir Plus Ritonavir	667	Throat Culture	687
Metabolism	540	Hydroxychloroquine	1404	Depression	633
Personal Protective Equipment	707	Total	5932	Cardiovascular Disease	627
Prevalence	871			Severe Acute Respiratory Syndrome	621
Prevention And Control	858	**Study**	#	Immune Response	609
Prognosis	826	Priority Journal	7442	Respiratory Failure	551
Protective Equipment	593	Article	5687	Critically Ill Patient	526
Tocilizumab	617	Letter	3929	Disease Association	897
Treatment Outcome	784	Review	1853	Disease Course	748
Unclassified Drug	535	Clinical Article	1631	Disease Exacerbation	524
World Health Organization	683	Editorial	1446	Disease Outbreaks	795
Total	10420	Case Report	1465	Total	21018
		Note	1393		
		Retrospective Studies	629	**Countries**	#
		Questionnaire	599	China	2391
		Controlled Study	893	Italy	1090
		Major Clinical Study	1384	United States	1266
		Clinical Feature	928	United Kingdom	612
		Clinical Practice	515	Total	5359
		Total	29794		