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Investigation of Microbial Biofilms during COVID-19 Pandemic: A Bibliometric Analysis

Ali Salehinasab[1], Adel Rezvani Sichani[1], Maryam Mousavi[2], Zeynab Bayat[1], Ali Pezhhan[3], Beneen M. Hussien[4], Muhja Ahmed[5], Mehdi Hassanshahian[1*]

[1]Department of Biology, Faculty of Science, Shahid Bahonar University of Kerman, Kerman, Iran
[2]Departments of Biology, Faculty of Science, Shahrekord University, Shahrekord, Iran
[3]Department of Social Sciences, Faculty of Demography, Islamic Azad University Central Tehran Branch, Tehran, Iran
[4]Medical Laboratory Technology Department, College of Medical Technology, Islamic University, Najaf, Iraq
[5]Medical Technical College, Al-Farahidi University, Baghdad, Iraq

* ***Corresponding author:*** Mehdi Hassanshahian, Biology Department, Faculty of Science, Shahid Bahonar University of Kerman, Kerman, Iran. Email: mshahi@uk.ac.ir

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Abstract

Background: The Corona pandemic caused by the COVID-19 disease has become a trending topic in recent years. Moreover, microbial biofilms have received a lot of attention due to the problems they cause in industry and medicine.
Objectives: The present study aimed to examine the published documents concerning the Corona pandemic and microbial biofilms.
Methods: Document review was performed in Web of Science Core Collection, Scopus, and PubMed databases; then, due to the publication of more documents in the Scopus database, information from this database was used for bibliographic analysis by VOSviewer and Rstudio.
Results: The obtained results showed that the process of publishing documents increased during 2005-2022, and the type of documents mostly were articles (49%) and reviews (38%). Most published cases were in the field of medicine, immunology, and microbiology.
Conclusion: Studies can be examined from three medical, environmental, and engineering perspectives. The structure and composition of biofilm, the interaction of microorganisms in biofilm, the investigation of the dental biofilm infection in the infected people and waste systems, as well as the use of engineered biofilms for virus isolation are among the recommended topics for further research.

Keywords: Bibliometric, Biofilm, Coronavirus, COVID-19, SARS-CoV-2

1. Background

COVID-19, a viral lung infection caused by the SARS-CoV-2 virus, was first observed in China in 2019 and spread until recognized as a pandemic in 2020. Five worrying variants of alpha, beta, gamma, delta, and omicron of this RNA virus were reported. COVID-19 was included in the group of zoonotic diseases due to the common disease between humans and bats (1, 2).

Some oral and injectable drugs, such as Paxlovid, molnupiravir, and remdesivir, were used to treat COVID-19 disease (3), and then various vaccines were produced and offered to control the disease. Despite extensive research and reports around the world that led to increased knowledge and awareness of this disease, many issues surrounding this disease remain unknown and unclear. The nature of the genome of this virus has the potential to cause genetic mutations and the emergence of new substrains. In addition to increasing mortality, widespread disease outbreaks cause great economic losses to societies.

Microbial biofilms are microorganism communities of bacteria, fungi, or viruses in the form of monomicrobial or polymicrobial. At the beginning of the biofilm formation stage, microbial signals in the process of quorum sensing cause the accumulation of microorganisms. In the next step, it is connected to the surface. Attachment to both living and non-living surfaces is possible. The formation of biofilm microcolony in a matrix containing protein, nucleic acid, and polysaccharide is done after the attachment stage. The transformation of a microcolony into an adult colony and then the destruction of an adult colony lead to the spread of microorganisms inside the biofilm. In addition to being a rich environment for the nutrition of microorganisms, the microbial biofilm protects them from the harmful effects of the environment, such as antimicrobial compounds (4, 5). Microbial biofilms are resistant structures that can be problematic in medicine, industry, and the environment.

Due to the importance of raising awareness about the latest viral pandemic and microbial biofilms, present study was conducted on this topic. Bibliometric analyses provide information on how and the process of conducting research. In addition to clarifying the research path for other researchers, this information also identifies new topics and unanswered research questions (6).

The present study examined the published documents concerning the Corona pandemic and microbial biofilms.

1.1. Examining different approaches of biofilm and Corona pandemic

Although COVID-19 is known as a respiratory disease, gastrointestinal symptoms were also observed in some patients. According to a hypothesis by Besharati et al., biofilm formation is possible in the gastrointestinal system. As it is clear, the cells in bacterial biofilms are more stable than the planktonic form, and they cause chronic infections through the protection of the immune system (7).

The way of intercellular transmission of human T cell leukemia virus type 1 (HTLV-1) and some of its similarities with bacterial biofilms can probably be an example of viral biofilms. Infected T cells cover the virus in a matrix containing carbohydrates and proteins, which in addition to protecting the viral particle, this extracellular matrix is also responsible for attaching it to another cell. The matrix of microbial and viral biofilms may be similar in composition and function. However, the production of this matrix in HTLV-1 is by T cells and in microbial biofilms by the microorganisms forming the biofilm (8, 9).

Microbial co-infection in patients with COVID-19 was investigated by Chen et al. (10). Fungi such as *Aspergillus* (11) and *Candida* (12), viruses such as Metapneumovirus (13), and bacteria such as *Acinetobacter baumannii* (13), *Klebsiella pneumoniae* and *Legionella pneumophila* (14) have been reported by other researchers in COVID-19 patients.

Some researchers have investigated the formation of *Aspergillus fumigatus* biofilm *in vivo* and *in vitro* (15, 16). The results of a study by Mowat et al. indicated that the formation of *A. fumigatus* biofilm is inhibited in the presence of *Pseudomonas aeruginosa* (17). While the study by Phuengmaung et al. showed the opposite result in *Candida albicans* fungus. *P. aeruginosa* biofilm formation is intensified in the presence of *Candida* (18). *P. aeruginosa* is present in most lung infections, especially in patients with cystic fibrosis.

The *A. baumannii* is another bacterial strain that, similar to *P. aeruginosa*, causes nosocomial infections. *A. baumannii* can be attached to respiratory epithelial cells and form biofilm, especially in patients hospitalized in the intensive care unit (ICU). The percentages reported from several countries regarding the co-infection of this bacterium and COVID-19 patients have been different, which requires further investigations (19-21).

K. pneumoniae, a bacterium capable of forming biofilms in urinary and respiratory catheters, is often responsible for ventilator-associated pneumonia (22). The prevalence of *K. pneumoniae* resistant to carbapenem in patients with COVID-19 was determined to be 0.35–53%, according to the findings by Mędrzycka-Dąbrowska et al. (23).

L. pneumophila, the causative agent of Legionellosis disease, binds to surfaces through sulfated glycosaminoglycans (GAGs) in the process of biofilm formation and leads to severe lung disease (24). The co-infection rate of this bacterium in COVID-19 patients was reported to be 1.1%, according to a study conducted in Germany (25). Furthermore, Chao et al. announced an increase in Legionella contamination in the hospital water network during the Corona pandemic (26). The relationship between SARS-CoV-2 and biofilms in sewage systems can be discussed and investigated from the two aspects of accumulation, preservation, and spread of the virus in the biofilm, as well as the accumulation of the virus genome in the biofilm (27, 28).

A part of the virome is dedicated to phages, especially in the lungs of healthy people. Bacteriophages can transfer genes for antibiotic resistance and adaptation of the host to the environment of the respiratory system (29). The possibility of the presence of the virus or its components in the dental biofilm of patients can also be considered, which has been discussed by some researchers (30, 31).

In addition to medical and environmental approaches, in the field of engineering, engineered microbial biofilms can be investigated to capture and isolate SARS-CoV-2. Özkul et al. have achieved this goal by using a hybrid recombinant protein from an *Escherichia coli* species (32).

2. Objectives

The present study aimed to examine the published documents concerning the Corona pandemic and microbial biofilms.

3. Methods

3.1. Methods and Materials

Bibliometric analysis was performed on April 13, 2023, in three databases, Web of Science Core Collection (https://www.webofscience.com/), Scopus (https://www.scopus.com/) and PubMed (https://pubmed.ncbi.nlm.nih.gov/), using the search term (TITLE-ABS-KEY ("COVID-19" OR "Coronavirus Disease 2019" OR "SARS-CoV-2" OR "Severe Acute Respiratory Syndrome Coronavirus 2" OR "Coronavirus" OR "Betacoronavirus") AND TITLE-ABS-KEY ("Biofilm*")).

Considering that the largest number of documents is published in the Scopus database, the documents of this database were analyzed using VOSviewer (https://www.vosviewer.com/) version 1.6.16 (33) and Bibliometrix-package (http://www.bibliometrix.org/) in Rstudio (34). Keywords in Scopus include the author's keywords and indexed keywords.

4. Results

The number of documents published without a time limit in Scopus, Web of Science, and PubMed databases is 346, 187, and 152, respectively. The start of publication of documents in the Scopus database in 2005 (3 documents), 2008 to 2010 (1 document each year), 2020 (41 documents), 2021 (96 documents), 2022 (154 documents), and 2023 (49 documents) show an increasing trend. Based on this, the annual growth rate was determined to be 49.04%.

The main information of the examined documents is reported in Table 1, as well as the type of documents and subject area in Figure 1. Most types of documents are in the category of articles and reviews. Additionally, most studies are in the fields of medicine, immunology and microbiology, biochemistry, genetics and molecular biology.

The co-occurrence of keywords was checked with the minimum number of occurrences of a keyword (10 times), and the result is shown in Figure 2. A total of 209 selected keywords were grouped into four clusters with the color of cluster 1 red, cluster 2 green, cluster 3 blue, and cluster 4 yellow. The number of items in clusters 1 to 4 is 61, 55, 49, and 44, respectively.

Ten documents with the most cited global documents based on total citations (TC) per year are listed in Table 2.

The results of examining the relationship of authors, keywords and sources are shown in a three-column design in Figure 3. The keywords of COVID-19, *Pseudomonas aeruginosa* and biofilm are mentioned more.

Table 1. Main information of documents published in the Scopus database

Documents		Authors		Authors Collaboration	
Average years from publication	1.63	Authors	1896	Single-authored documents	24
Average citations per documents	9.26	Author Appearances	2035	Documents per Author	0.182
Average citations per year per doc	2.598	Authors of single-authored documents	20	Authors per Document	5.48
Keywords Plus	5407	Authors of multi-authored documents	1876	Co-Authors per Documents	5.88
Author's Keywords	1176			Collaboration Index	5.83

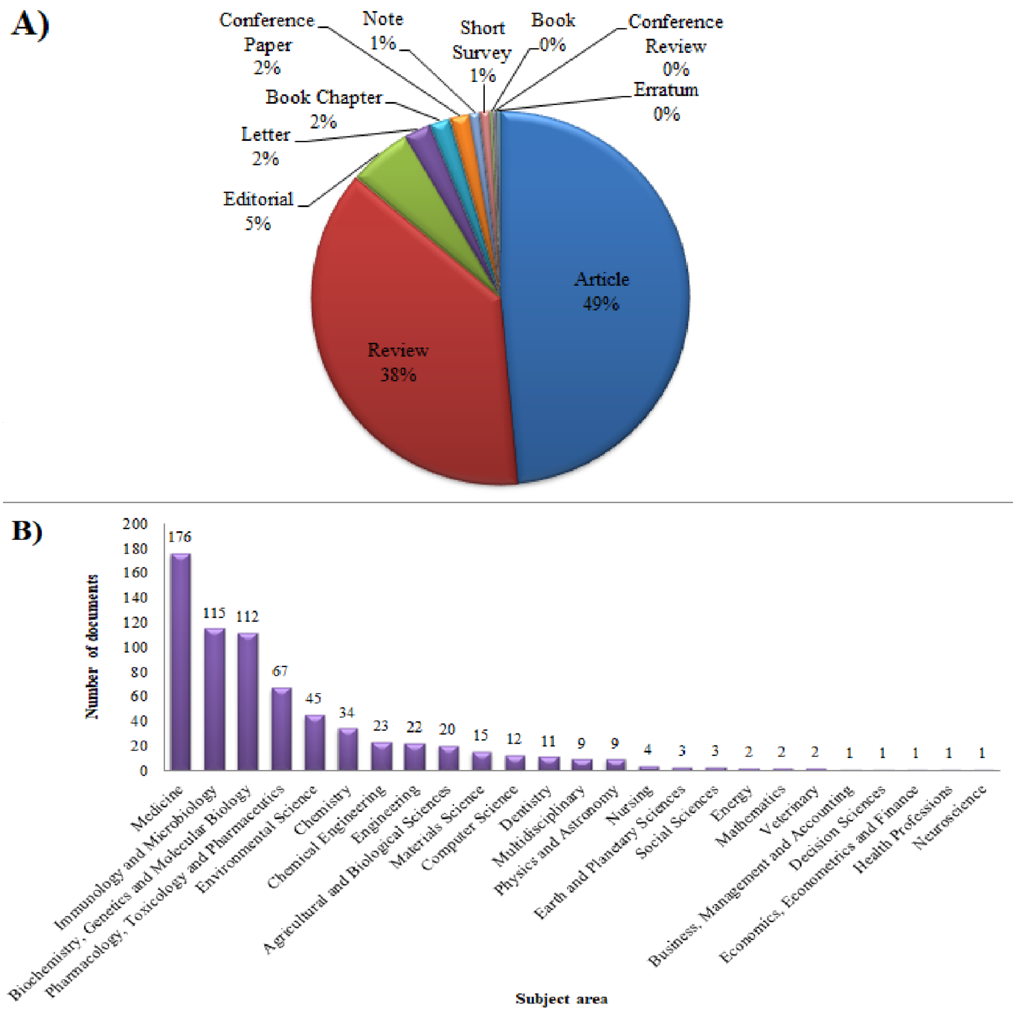

Figure 1. Analysis of documents published in the Scopus database A) Type of documents, B) Subject area

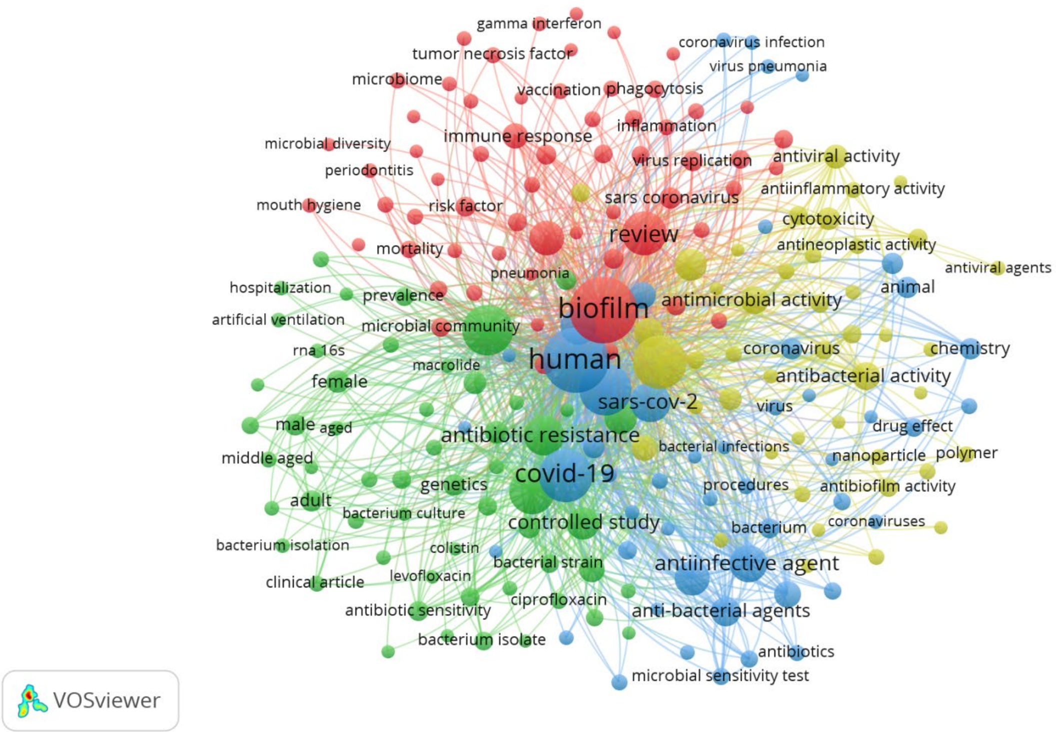

Figure 2. Co-occurrence of keywords

Table 2. Most cited global documents based on total citations (TC) per year

#	Paper (Author, Year, Source)	Title	TC	TC per Year	Normalized TC	Ref
1	HUAN Y, 2020, FRONT MICROBIOL	Antimicrobial peptides: classification, design, application and research progress in multiple fields	340	85	11.5973	(35)
2	BALASUBRAMANIAM B, 2021, ACS PHARM TRANSL SCI	Antibacterial and Antiviral Functional Materials: Chemistry and Biological Activity toward Tackling COVID-19-like Pandemics	104	34.667	9.7691	(36)
3	NAYAK V, 2021, NEW J CHEM	Potentialities of selenium nanoparticles in biomedical science	66	22	6.1996	(37)
45	BLOCK MS, 2020, J ORAL MAXILLOFAC SURG	Hypochlorous Acid: A Review	84	21	2.8652	(38)
5	CARROUEL F, 2020, J CLIN MED	COVID-19: A Recommendation to Examine the Effect of Mouthrinses with β-Cyclodextrin Combined with Citrox in Preventing Infection and Progression	84	21	2.8652	(39)
6	VENUGOPAL A, 2020, CURR OPIN ENVIRON SCI HEALTH	Novel wastewater surveillance strategy for early detection of Coronavirus disease 2019 hotspots	80	20	2.7288	(40)
7	TRAN TV, 2022, ENVIRON CHEM LETT	Green synthesis of ZrO_2 nanoparticles and nanocomposites for biomedical and environmental applications: a review	39	19.5	13.7437	(41)
8	KUMARAVEL V, 2021, CHEM ENG J	Antimicrobial TiO_2 nanocomposite coatings for surfaces, dental and orthopaedic implants	57	19	5.3542	(42)
9	ALMEIDA A, 2020, ANTIBIOTICS	Antimicrobial Photodynamic Therapy in the Control of COVID-19	67	16.75	2.2854	(43)
10	SAFDAR N, 2005, RESPIR CARE	The pathogenesis of ventilator-associated pneumonia: Its relevance to developing effective strategies for prevention	309	16.263	2.6186	(44)

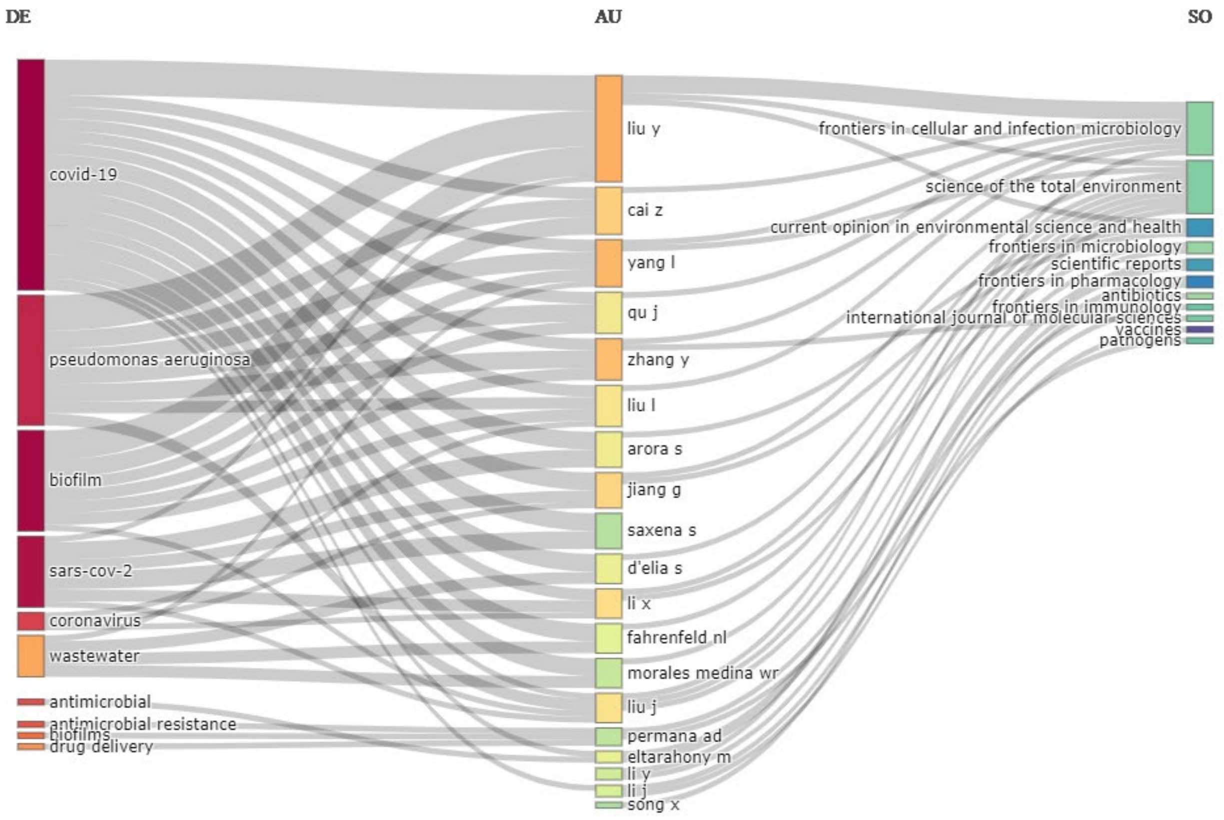

Figure 3. Three-field plot. DE: Author's Keywords, AU: Authors, SO: Sources

5. Discussion

Although the Corona pandemic began from 2020, only six documents have been published from 2005 to 2010. Three cases were related to otitis media (45-47), one case was related to dentistry (48), and two cases were related to respiratory system infections (49, 50). The possible explanation for this result is that some of the keywords used in the search term have been identified as EMTREE medical terms in the Scopus indexed keywords. However, some keywords are also clearly mentioned in the abstract or authors' keywords.

The microbial biofilms role during the Corona pandemic can be investigated from several aspects. In the medical field, the importance of the presence of Coronavirus or viral components or in interaction with other bacterial, fungal and viral microorganisms in a polymicrobial form in biofilm is debatable. Microbe-microbe and microbe-host interactions can be extremely significant. The formation of biofilm in medical equipment used to treat these patients and dental biofilms in terms of structure and prevalence, needs further investigation. In environmental microbiology, the presence of Coronavirus or its components in urban and hospital sewage systems in the form of biofilm can be further investigated to help manage the disease during a pandemic. In the field of engineering, investigating and manipulating some characteristics of microbial biofilms can increase the sensitivity of Coronavirus diagnostic methods. Moreover, the ability to connect to different surfaces, which is one of the initial stages of biofilm formation, is of special importance.

6. Conclusion

Studies can often be examined from three medical, environmental, and engineering perspectives. The structure and composition of biofilm, the interaction of microorganisms in biofilm, the investigation of biofilm in the dental of infected people and waste systems, and the use of engineered biofilms for virus isolation are among the recommended topics for further research.

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Footnotes

Conflicts of Interest: There was no conflict of interest between the authors.

Author Contribution:

Funding: This research was supported by no funding.

Ethical Statements: This study was not performed on humans or animals; therefore, no ethical consideration was needed.

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