ISSN 2220-3249 (online)

World Journal of *Virology*

World J Virol 2022 March 25; 11(2): 90-112

Published by Baishideng Publishing Group Inc

World Journal of Virology

Contents

Bimonthly Volume 11 Number 2 March 25, 2022

OPINION REVIEW

MINIREVIEWS

LETTER TO THE EDITOR

World Journal of Virology

Bimonthly Volume 11 Number 2 March 25, 2022

Contents

ABOUT COVER

AIMS AND SCOPE

The primary aim of *World Journal of Virology* (*WJV*, *World J Virol*) is to provide scholars and readers from various fields of virology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJV mainly publishes articles reporting research results obtained in the field of virology and covering a wide range of topics including arbovirus infections, viral bronchiolitis, central nervous system viral diseases, coinfection, DNA virus infections, viral encephalitis, viral eye infections, chronic fatigue syndrome, animal viral hepatitis, human viral hepatitis, viral meningitis, opportunistic infections, viral pneumonia, RNA virus infections, sexually transmitted diseases, viral skin diseases, slow virus diseases, tumor virus infections, viremia, and zoonoses.

INDEXING/ABSTRACTING

The *WJV* is now abstracted and indexed in PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Virology

ISSN
ISSN 2220-3249 (online)

LAUNCH DATE
February 12, 2012

FREQUENCY
Bimonthly

EDITORS-IN-CHIEF
Mahmoud El-Bendary, En-Qiang Chen

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2220-3249/editorialboard.htm

PUBLICATION DATE
March 25, 2022

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Virology

Submit a Manuscript: https://www.f6publishing.com

World J Virol 2022 March 25; 11(2): 107-110

DOI: 10.5501/wjv.v11.i2.107

ISSN 2220-3249 (online)

LETTER TO THE EDITOR

Bacterial and fungal co-infection is a major barrier in COVID-19 patients: A specific management and therapeutic strategy is required

Tarun Sahu, Henu Kumar Verma, Lakkakula V K S Bhaskar

Specialty type: Virology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Lozada-Martinez I

Received: August 14, 2021
Peer-review started: August 14, 2021
First decision: September 2, 2021
Revised: September 8, 2021
Accepted: February 10, 2022
Article in press: February 10, 2022
Published online: March 25, 2022

Tarun Sahu, Department of Physiology, All India Institute of Medical Science, Raipur 492001, Chhattisgarh, India

Henu Kumar Verma, Department of Immunopathology, Institute of Lung Health and Immunity, Comprehensive Pneumology Center, Helmholtz Zentrum, Munich 85764, Germany

Lakkakula V K S Bhaskar, Department of Zoology, Guru Ghasidas Vishwavidyalaya, Bilaspur 495001, Chhattisgarh, India

Corresponding author: Henu Kumar Verma, PhD, Research Scientist, Senior Researcher, Department of Immunopathology, Institute of Lung Health and Immunity, Comprehensive Pneumology Center, Helmholtz Zentrum, Neuherberg Inglostäder Landstrapβe 1, Munich 85764, Germany. henu.verma@yahoo.com

Abstract

Microbial co-infections are another primary concern in patients with coronavirus disease 2019 (COVID-19), yet it is an untouched area among researchers. Preliminary data and systematic reviews only show the type of pathogens responsible for that, but its pathophysiology is still unknown. Studies show that these microbial co-infections are hospital-acquired/nosocomial infections, and patients admitted to intensive care units with invasive mechanical ventilation are highly susceptible to it. Patients with COVID-19 had elevated inflammatory cytokines and a weakened cell-mediated immune response, with lower $CD4^+$ T and $CD8^+$ T cell counts, indicating vulnerability to various co-infections. Despite this, there are only a few studies that recommend the management of co-infections.

Key Words: COVID-19; Co-infection; Bacterial co-infection; Fungal co-infection

Core Tip: The immune systems of coronavirus disease 2019 patients are already compromised, making them vulnerable to bacterial, fungal, and viral co-infections. These secondary infections, also known as co-infections, are hospital-acquired/nosocomial infections, and mechanically ventilated patients are especially vulnerable. There are no specific guidelines or treatment options for these types of co-infections at the moment, which is contributing to an increase in morbidity and mortality among these patients.

Citation: Sahu T, Verma HK, Bhaskar LVKS. Bacterial and fungal co-infection is a major barrier in COVID-19 patients: A specific management and therapeutic strategy is required. *World J Virol* 2022; 11(2): 107-110
URL: https://www.wjgnet.com/2220-3249/full/v11/i2/107.htm
DOI: https://dx.doi.org/10.5501/wjv.v11.i2.107

TO THE EDITOR

The first case of coronavirus disease 2019 (COVID-19) was reported in Wuhan, China, in December 2019, and the World Health Organization declared it a pandemic in March 2019. Approximately one-third of patients experienced severe complications of COVID-19 and required hospitalization[1]. Recently, secondary bacterial/fungal infections or co-infections are another major concern in COVID-19 patients, impacting mortality but lacking attention. Less evidence of bacterial and fungal infection was documented in earlier coronavirus pandemics and epidemics, such as severe acute respiratory syndrome (SARS)-1 and Middle East respiratory syndrome[2]. Recently, we have seen a paper by Saeed *et al*[3] entitled "Bacterial co-infection in patients with SARS-CoV-2 in the Kingdom of Bahrain"[3] in your well-regarded journal *World J Virol*. We appreciate the work done by Saeed *et al*[3] as they reported the microbial infections in patients with COVID-19 in the Kingdom of Bahrain.

The most common bacterial species they reported were *K. pneumonia, P. aeruginosa, A. baumannii, E. coli, S. aureus, E. faecalis,* and *E. faecium*. Among all of these, hospital-acquired (HAI)/nosocomial infection was higher (73.8%) than community-acquired infection. Similar results were reported by Mahmoudi[4] and Sharifipour *et al*[5] in the neighboring country Iran. Both authors reported the same species of bacterial strains, which are the most common. Later on, a descriptive study conducted in the United Arab Emirates found bacterial co-infection in patients with COVID-19 and especially *Klebsiella pneumonia, Escherichia coli, Staphylococcus aureus,* and *Acinetobacter baumannii* were most predominant strains[6]. The recent reviews and meta-analysis also show that *Klebsiella pneumonia, Haemophiles influenzae, Streptococcus pneumoniae,* and *Staphylococcus aureus* are the most frequently identified bacteria among co-infected patients[7,8]. A unique case series from Saudi Arabia reported Middle East respiratory syndrome coronavirus co-infection in 12% of patients already suffering from severe acute respiratory syndrome coronavirus 2[9]. At the same time, another case series from Saudi Arabia by Shabrawishi *et al*[10] reported 7 cases of COVID-19 and tuberculosis co-infection[10]. The interesting results of Hashemi *et al*[11] showed influenza A (H1N1) virus, human metapneumovirus, bocavirus, adenovirus, respiratory syncytial virus (RSV), and parainfluenza viruses in 105 dead patients with COVID-19 in northeastern Iran[11].

Other than bacteria, fungal and viral co-infections are also severe issues with COVID-19 patients. In the present article, the authors reported fungal co-infection in about 10% of total microbial co-infection. The most common isolated fungi were *Candida galabrata, Candida tropicalis, Candida albicans,* and *Aspergillus fumigatus*. They also found that the death rates in patients with fungal co-infection were very high (70.4%)[3]. Studies from other different regions found aspergillosis or invasive candidiasis as the common fungal co-infections[12]. In contrast, influenza type A, type B, and RSV were the most common viral co-infections in patients with COVID-19[7]. These co-infections are associated with an increased probability of death. Most of the articles reported that microbial co-infections were HAI/nosocomial infections, similar to Saeed *et al*[3], who found 71% were HAI.

Further, the authors have described well different microbial co-infections in patients of COVID-19. Furthermore, the study has some limitations, such as the authors not providing any treatment or management options for COVID-19 infected patients. That is the most crucial concern for the patient's benefit. In this context, we would like to draw your attention to the management and recommendations for the infection. Chedid *et al*[13] reviewed the most common antibiotics used by COVID-19 hospitalized patients, primarily in an intensive situation, by analyzing the use of antibiotics in different types of bacterial secondary and co-infection[13].

On the other hand, Sieswerda *et al*[14] gave evidence-based recommendations for antibacterial therapy for secondary microbial and co-infection[14]. Wu *et al*[15] described the management of respiratory co-infection and secondary bacterial pneumonia in patients with COVID-19[15]. For the treatment of fungal co-infections, Song *et al*[16] suggested the regimen, which is currently in an induction phase and includes amphotericin B deoxycholate and flucytosine, followed by (1) Fluconazole; alternative options for fluconazole + flucytosine or amphotericin B deoxycholate +

fluconazole; (2) Consolidation phase for fluconazole; and (3) Maintenance (or secondary prophylaxis) phase for fluconazole[16].

Depending upon disease severity, patients with influenza A or B viral co-infection should be treated with oseltamivir or its substitute[17]. Treatment options for other viral co-infection, such as RSV, are restricted and beneficial only in specific circumstances, such as immunosuppression or hypogammaglobulinemia[18,19].

Patients with COVID-19 had elevated levels of inflammatory cytokines and a debilitated cell-mediated immune response, with lower $CD4^+$ T and $CD8^+$ T cell counts, indicating vulnerability to various co-infections. Furthermore, COVID-19 patients who are immunocompromised, such as those with extended neutropenia, hematopoietic stem cell transplantation, hereditary or acquired immunodeficiencies, or tumor, are more likely to develop co-infection. Co-infection and superinfection of pathogens in COVID-19 patients is a critical issue as it is difficult to distinguish the associated complications. Specific diagnostic tests should be recommended for proper treatment and management of these infections to reduce morbidity and mortality.

FOOTNOTES

Author contributions: Sahu T, Verma HK, and Bhaskar LVKS wrote and revised the letter.

Conflict-of-interest statement: The authors declare no conflict of interest.

Country/Territory of origin: Germany

ORCID number: Tarun Sahu 0000-0002-2721-7432; Henu Kumar Verma 0000-0003-1130-8783; Lakkakula V K S Bhaskar 0000-0003-2977-6454.

S-Editor: Fan JR
L-Editor: Filipodia
P-Editor: Fan JR

REFERENCES

1 **Sahu T**, Mehta A, Ratre YK, Jaiswal A, Vishvakarma NK, Bhaskar LVKS, Verma HK. Current understanding of the impact of COVID-19 on gastrointestinal disease: Challenges and openings. *World J Gastroenterol* 2021; **27**: 449-469 [PMID: 33642821 DOI: 10.3748/wjg.v27.i6.449]

2 **Rawson TM**, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M, Satta G, Cooke G, Holmes A. Bacterial and Fungal Coinfection in Individuals With Coronavirus: A Rapid Review To Support COVID-19 Antimicrobial Prescribing. *Clin Infect Dis* 2020; **71**: 2459-2468 [PMID: 32358954 DOI: 10.1093/cid/ciaa530]

3 **Saeed NK**, Al-Khawaja S, Alsalman J, Almusawi S, Albalooshi NA, Al-Biltagi M. Bacterial co-infection in patients with SARS-CoV-2 in the Kingdom of Bahrain. *World J Virol* 2021; **10**: 168-181 [PMID: 34367932 DOI: 10.5501/wjv.v10.i4.168]

4 **Mahmoudi H**. Bacterial co-infections and antibiotic resistance in patients with COVID-19. *GMS Hyg Infect Control* 2020; **15**: Doc35 [PMID: 33391970 DOI: 10.3205/dgkh000370]

5 **Sharifipour E**, Shams S, Esmkhani M, Khodadadi J, Fotouhi-Ardakani R, Koohpaei A, Doosti Z, Ej Golzari S. Evaluation of bacterial co-infections of the respiratory tract in COVID-19 patients admitted to ICU. *BMC Infect Dis* 2020; **20**: 646 [PMID: 32873235 DOI: 10.1186/s12879-020-05374-z]

6 **Senok A**, Alfaresi M, Khansaheb H, Nassar R, Hachim M, Al Suwaidi H, Almansoori M, Alqaydi F, Afaneh Z, Mohamed A, Qureshi S, Ali A, Alkhajeh A, Alsheikh-Ali A. Coinfections in Patients Hospitalized with COVID-19: A Descriptive Study from the United Arab Emirates. *Infect Drug Resist* 2021; **14**: 2289-2296 [PMID: 34188495 DOI: 10.2147/IDR.S314029]

7 **Musuuza JS**, Watson L, Parmasad V, Putman-Buehler N, Christensen L, Safdar N. Prevalence and outcomes of co-infection and superinfection with SARS-CoV-2 and other pathogens: A systematic review and meta-analysis. *PLoS One* 2021; **16**: e0251170 [PMID: 33956882 DOI: 10.1371/journal.pone.0251170]

8 **Westblade LF**, Simon MS, Satlin MJ. Bacterial Coinfections in Coronavirus Disease 2019. *Trends Microbiol* 2021; **29**: 930-941 [PMID: 33934980 DOI: 10.1016/j.tim.2021.03.018]

9 **Elhazmi A**, Al-Tawfiq JA, Sallam H, Al-Omari A, Alhumaid S, Mady A, Al Mutair A. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) coinfection: A unique case series. *Travel Med Infect Dis* 2021; **41**: 102026 [PMID: 33727175 DOI: 10.1016/j.tmaid.2021.102026]

10 **Shabrawishi M**, AlQarni A, Ghazawi M, Melibari B, Baljoon T, Alwafi H, Samannodi M. New disease and old threats: A case series of COVID-19 and tuberculosis coinfection in Saudi Arabia. *Clin Case Rep* 2021; **9**: e04233 [PMID: 34084515 DOI: 10.1002/ccr3.4233]

11 **Hashemi SA**, Safamanesh S, Ghasemzadeh-Moghaddam H, Ghafouri M, Azimian A. High prevalence of SARS-CoV-2 and influenza A virus (H1N1) coinfection in dead patients in Northeastern Iran. *J Med Virol* 2021; **93**: 1008-1012 [PMID: 32720703 DOI: 10.1002/jmv.26364]

12 **Fungal Diseases and COVID-19**. Coronavirus disease-19: The First 7,755 Cases in the Republic of Korea. 2021 Preprint. Available from: medRxiv2020.03.15.20036368

13 **Chedid M**, Waked R, Haddad E, Chetata N, Saliba G, Choucair J. Antibiotics in treatment of COVID-19 complications: a review of frequency, indications, and efficacy. *J Infect Public Health* 2021; **14**: 570-576 [PMID: 33848886 DOI: 10.1016/j.jiph.2021.02.001]

14 **Sieswerda E**, de Boer MGJ, Bonten MMJ, Boersma WG, Jonkers RE, Aleva RM, Kullberg BJ, Schouten JA, van de Garde EMW, Verheij TJ, van der Eerden MM, Prins JM, Wiersinga WJ. Recommendations for antibacterial therapy in adults with COVID-19 - an evidence based guideline. *Clin Microbiol Infect* 2021; **27**: 61-66 [PMID: 33010444 DOI: 10.1016/j.cmi.2020.09.041]

15 **Wu CP**, Adhi F, Highland K. Recognition and management of respiratory co-infection and secondary bacterial pneumonia in patients with COVID-19. *Cleve Clin J Med* 2020; **87**: 659-663 [PMID: 32393593 DOI: 10.3949/ccjm.87a.ccc015]

16 **Song G**, Liang G, Liu W. Fungal Co-infections Associated with Global COVID-19 Pandemic: A Clinical and Diagnostic Perspective from China. *Mycopathologia* 2020; **185**: 599-606 [PMID: 32737747 DOI: 10.1007/s11046-020-00462-9]

17 **Uyeki TM**, Bernstein HH, Bradley JS, Englund JA, File TM, Fry AM, Gravenstein S, Hayden FG, Harper SA, Hirshon JM, Ison MG, Johnston BL, Knight SL, McGeer A, Riley LE, Wolfe CR, Alexander PE, Pavia AT. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenzaa. *Clin Infect Dis* 2019; **68**: 895-902 [PMID: 30834445 DOI: 10.1093/cid/ciy874]

18 **Beigel JH**, Nam HH, Adams PL, Krafft A, Ince WL, El-Kamary SS, Sims AC. Advances in respiratory virus therapeutics - A meeting report from the 6th isirv Antiviral Group conference. *Antiviral Res* 2019; **167**: 45-67 [PMID: 30974127 DOI: 10.1016/j.antiviral.2019.04.006]

19 **Ruan Q**, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* 2020; **46**: 846-848 [PMID: 32125452 DOI: 10.1007/s00134-020-05991-x]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com