Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Indian Journal of Medical Microbiology 40 (2022) 608–610

Contents lists available at ScienceDirect

Indian Journal of Medical Microbiology

journal homepage: www.journals.elsevier.com/indian-journal-of-medical-microbiology

Case Report

Three waves, three vaccines, three COVID-19 infections - Saga of a frontline health care worker during the pandemic

Darpanarayan Hazra [a,*], Ankita Chowdary Nekkanti [a], Mahesh Moorthy [b], Kundavaram Paul Prabhakar Abhilash [a]

[a] Department of Emergency Medicine, Christian Medical College and Hospital, Vellore, 632004, India
[b] Department of Clinical Virology, Christian Medical College and Hospital, Vellore, 632004, India

ARTICLE INFO

Keywords:
COVID-19 disease
Reinfection
COVID vaccination
ED physicians

ABSTRACT

The COVID-19 pandemic affected millions around the globe, with front line healthcare workers (HCW) amongst the most vulnerable. The Emergency Department (ED) was the first line of care for all patients infected with the virus, making HCWs in the ED one of the most exposed populations during the pandemic. We highlight the case of a 35-year-old ED physician who developed COVID-19 infections on three separate instances during the peaks of each wave despite the usage of personal protective equipment and being triple vaccinated.

1. Introduction

During the COVID-19 pandemic, the Emergency Department (ED) was the initial point of care for all infected patients. Frontline healthcare workers (HCW), though vaccinated early in the pandemic, had a high incidence of reinfection during subsequent waves [1]. Though a few cases of reinfections were reported amongst frontline HCW, none have been described in recipients of the booster dose [2–4]. We hereby report a case of a 35-year-old Emergency physician who developed a COVID-19 infection in each wave, despite three doses of the Oxford AstraZeneca (Covishield) vaccine.

2. Case report

During the third wave of the pandemic, in late December 2021, a 35-year-old ED physician developed symptoms of fever, myalgia, fatigue, loss of smell and acute shortness of breath and was diagnosed to have COVID-19 infection by a positive Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). He was not immunocompromised and had no comorbid illnesses but was a smoker with a history of 5 pack years. On auscultation, bilateral scattered wheeze and crepitations were noted. He was hemodynamically stable during his hospital stay but required low dose oxygen therapy for mild hypoxia along with prophylactic anticoagulants and symptomatic care. He was discharged stable on the 10th day after being asymptomatic for 3 days.

In the preceding 2 years, he had a history of two prior COVID-19 infections, during the peak of each wave of the pandemic in India. During his first infection (August 2020) confirmed by Rapid Antigen Test (RAT), he had predominant respiratory symptoms and required 5 days of hospitalization for oxygen therapy for hypoxemia. Reinfection during the peak of the second wave in May 2021 confirmed by RT-PCR, was however less severe and didn't warrant hospital admission. Details of all three infections, including radiological imaging findings and treatment required are summarized in Table 1.

He had been vaccinated with the Oxford AstraZeneca (Covishield) vaccine in January 2021, March 2021, and received a booster dose in August 2021 as part of a randomized control trial of a booster dose at Christian medical College, Vellore. At multiple times (April 2020, July 2020, October 2020, March 2021, June 2021, September 2021) during the pandemic, antibodies to the Nucleoprotein (anti-N) and Spike Receptor Binding Domain (anti-S) were performed using commercially available kits - Elecsys® SARS-CoV-2 and Elecsys® SARS-CoV-2 S, respectively, based the electro-chemiluminescence (ECLIA) assay principle on a Cobas e411 analyzer (Roche Diagnostics Pvt. Ltd) as per manufacturer's instructions. Numerical values of the cut-off index (COI) and Units/ml (U/ml) ≥ 1 and ≥ 1.0 were considered positive for anti-N and anti-S, respectively. Fig. 1 demonstrates a timeline graph depicting the chronology of the three infections, vaccinations, and antibody levels. At present, after recovering from three COVID-19 infections during each wave of the pandemic, he is asymptomatic and has returned to baseline functional status.

* Corresponding author.
E-mail addresses: drdarpahazra@gmail.com (D. Hazra), ankita.chowdary22@gmail.com (A.C. Nekkanti), maheshmoorthy@cmcvellore.ac.in (M. Moorthy), kppabhilash@gmail.com (K.P. Prabhakar Abhilash).

https://doi.org/10.1016/j.ijmmb.2022.07.001
Received 26 March 2022; Received in revised form 5 April 2022; Accepted 6 July 2022
Available online 20 July 2022

Table 1
Clinical course, imaging findings, treatment, and outcomes of the infections.

Variables	1st infection	2nd infection	3rd infection
Date of diagnosis	01.08.2020	05.05.2021	08.01.2022
Signs and symptoms	Fever, cough, myalgia, fatigue	Myalgia, fatigue, loss of smell	Fever, myalgia, fatigue, loss of smell, shortness of breath
Oxygen saturation (on room air) at admission	92%	96%	90%
Requirement of hospitalization	Yes	No	Yes
Requirement of respiratory support	Yes (oxygen therapy via nasal cannula)	No	Yes (oxygen therapy via mask)
Chest imaging findings	Chest X-ray showed features of bilateral minimal basal infiltrates	Not done	Computed Tomography Chest showed bilateral basal ground-glass opacities
Cortico-steroid usage	Yes	No	Yes
Antiviral usage	Yes (Inj. Remdesivir)	No	No
Anticoagulant usage	Yes (Inj. Enoxaparin)	No	Yes (Inj. Enoxaparin)
Duration of symptoms	5 days	3 days	7 days

3. Discussion

This case describes a frontline HCW, who developed symptomatic COVID-19 infection in each wave of the pandemic, highlighting the unrelenting threat of this virus, despite being triple vaccinated. Repeated COVID-19 infections, though relatively rare, are being reported more often, especially with the arrival of the Omicron variant, which partially evades the protection of the COVID-19 vaccines [5].

The first cases in India were reported in late March 2020, when frontline HCW bore the brunt of the impact during the early stages of the pandemic. Over the next two years, several vaccines were developed, and management protocols were instituted and continually optimized based on new data and evidence. While vaccines have been shown to reduce the severity of infection in affected patients, including adverse events such as hospitalization, oxygen requirement, intensive care unit (ICU) admission, and death, they do not mitigate the risk of the infection itself [6,7]. A case reported by Salhin S et al. showed the risk of pulmonary artery hypertension in patients with reinfections [8].

Reports of immunocompetent patients with three symptomatic COVID-19 infections are few and far between [2,3]. The case we have described is by no means the only one of its kind, but it is one of the few to be described in the form of a detailed medical report. We can certainly speculate about the factors that contributed to the reinfections in our colleague. No response to anti-N was seen during his infection in the first and second waves. Anti-S antibodies were undetectable until October 2020. After the first vaccination (28.01.2021) anti-S antibodies were 49 U/ml. During the Delta wave, the individual had reinfection (05.05.2021) tested by RT-PCR (Altona Realstar® SARS CoV-2) with a Ct value of 33.1 and 32.5 for the envelope (E) and Spike (S) genes. This infection resulted in the boosting of anti-S antibodies to >250 U/ml in June 2021. These results suggest that the individual had not mounted an immune response to SARS-CoV-2 (evidenced by the anti-N negativity), but after vaccination, he developed a modest response to anti-S which was further boosted during the Delta wave. In January 2022, the individual was reinfected with SARS-CoV-2 confirmed by an RT-PCR: Ct value - 29.47 (RNA-dependent RNA polymerase). However, no antibody results were available following this infection. The antibody response in our case was transient, with minimal protection against reinfection, similar to the case reported by Salhin S et al. [8] However, it is important to keep in mind that these factors alone would not have accounted for the multiple reinfections in this and other such reported cases. More research and study are required to determine what characteristics make these subjects more prone to reinfection, and what they can expect as the pandemic progresses. A limitation of our case is that RAT was used for confirmation of the first COVID-19 infection, specificity, and sensitivity of which remains lower than a RT-PCR. In the setting of a pandemic, etiological workup for other respiratory viruses was also not done to rule out other etiologies or co-infection.

4. Conclusion

This case highlights the perils of reinfection amongst frontline HCW. Multiple reinfections despite the booster dose of vaccination are possible; however, the disease severity is less. Serial antibody titres can be done to

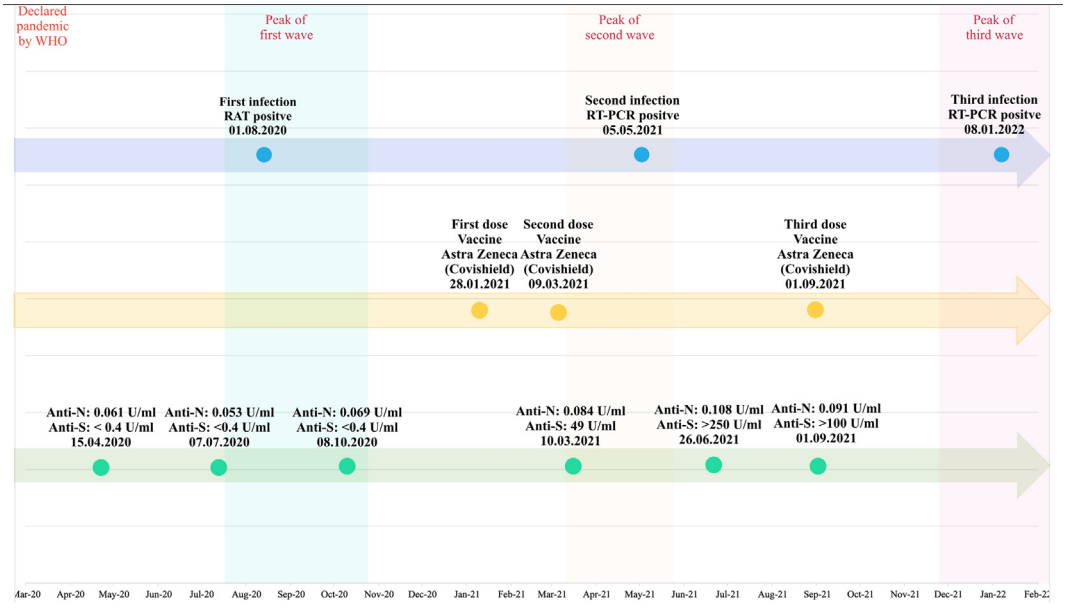

Fig. 1. Timeline graph representing the chronology of infections, vaccinations, and antibody titers during each peak of the pandemic.

monitor the immunity status of HCW; however, the antibody response can be transient.

CRediT author statement

Darpanarayan Hazra: Concept, design, definition of intellectual content, literature search, manuscript preparation and review.

Ankita Chowdary Nekkanti: Design, definition of intellectual content, manuscript preparation and review.

Mahesh Moorthy: Concept, design, manuscript review.

Kundavaram Paul Prabhakar Abhilash: Design, definition of intellectual content, manuscript preparation and review, guarantor.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has given their consent for their images and other clinical information to be reported in the journal. The patient's relative understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Presentation at a meeting

No.

Source of funding

None.

Declaration of competing interest

None.

Acknowledgements

None declared.

References

[1] Fernandes Valente Takeda C, Moura de Almeida M, Gonçalves de Aguiar Gomes R, Cisne Souza T, Alves de Lima Mota M, Pamplona de Góes Cavalcanti L, et al. Case report: recurrent clinical symptoms of COVID-19 in healthcare professionals: a series of cases from Brazil. Am J Trop Med Hyg 2020;103(5):1993–6. https://doi.org/10.4269/ajtmh.20-0893. PMID: 32888288; PMCID: PMC7646791.

[2] Coll B. One patient, three Covid-19 infections: An exception that's becoming more common in Spain. EL PAÍS English Edition; 2022 [cited 2022 Feb 8]. Available from: https://english.elpais.com/society/2022-01-12/one-patient-three-covid-19-infections-an-exception-thats-becoming-more-common-in-spain.html.

[3] Delhi doctor is first proven case of 3 Covid infections, 2 times after vax | Mumbai News - Times of India [cited 2022 Feb 8]. Available from: https://timesofindia.indiatimes.com/city/mumbai/delhi-doc-is-first-proven-case-of-3-covid-infections-2-times-after-vax/articleshow/84843796.cms.

[4] Two doctors in India get COVID-19 thrice, samples collected for study. The News Minute; 2021 [cited 2022 Feb 8]. Available from: https://www.thenewsminute.com/article/two-doctors-india-get-covid-19-thrice-samples-collected-study-153132.

[5] Roberts AT, Piani F, Longo B, Andreini R, Meini S. Reinfection of SARS-CoV-2 - analysis of 23 cases from the literature. Inf Disp 2021;53(7):479–85. https://doi.org/10.1080/23744235.2021.1905174. Epub 2021 Apr 13. PMID: 33849385; PMCID: PMC8054490.

[6] Moghadas SM, Vilches TN, Zhang K, Wells CR, Shoukat A, Singer BH, et al. The impact of vaccination on COVID-19 outbreaks in the United States. medRxiv 2021. https://doi.org/10.1101/2020.11.27.20240051 [Preprint] Update in: Clin Infect Dis. 2021;73(12):2257-2264. PMID: 33269359; PMCID: PMC7709178.

[7] Eyre DW, Taylor D, Purver M, Chapman D, Fowler T, Pouwels KB, et al. Effect of covid-19 vaccination on transmission of alpha and Delta variants. N Engl J Med 2022;386(8):744–56. https://doi.org/10.1056/NEJMoa2116597. Epub 2022 Jan 5. PMID: 34986294; PMCID: PMC8757571.

[8] Salcin S, Fontem F. Recurrent SARS-CoV-2 infection resulting in acute respiratory distress syndrome and development of pulmonary hypertension: a case report. Respir Med Case Rep 2021;33:101314. https://doi.org/10.1016/j.rmcr.2020.101314. Epub 2020 Dec 5. PMID: 33312856; PMCID: PMC7718582.