Original Research Article

Epidemiological Characteristics Of Cases Of COVID-19 Reinfection In Rivers State, Nigeria

Abstract

Background: The immune system's antibodies have been trained to deal with similar-looking pathogens through prior infection or vaccination. With the COVID-19 pandemic, the protection level of convalescents' antibodies against reinfections remains unclear. However, immunological solid evidence of antibodies protection against severity exists. Antibody levels are said to serve as a realistic stand-in for immune protection. How long these convalescent antibodies last in the body are still subject to research. Some findings document three months to eight months after infection to SARS-CoV-2. This study aimed to investigate the cases of COVID-19 reinfection in individuals who had recovered from an initial COVID-19 infection.

Methods: A case series of individuals with a second positive COVID-19 PCR test result in Rivers State between March 2020 to June 2021.

Result: Five cases were retested positive for COVID-19 with a median age of 46 (36-49) years, four males and a female. Four of the cases were found to have comorbidities of diabetes, hypertension, and human immunodeficiency virus (HIV). The median interval between the two episodes was 96 (37-196) days. Except for one asymptomatic case in the second episode, the convalescent participants had symptoms of COVID-19 in both the first and second episodes.

Conclusion: This study is illustrative of the possibility of COVID-19 reinfection. The longevity of circulating antibodies and the existence of other chronic disease conditions like HIV and diabetes in the individual may be related to this outcome. While further studies are recommended, full vaccination of all eligible persons, including COVID-19 convalescent persons with comorbidities is advised. Continued adherence to non-pharmaceutical interventions will enhance the chances of safety in the pandemic.

Keywords: COVID-19, antibodies, convalescents, comorbidities, reinfection, PCR test.

Introduction

SARS-CoV-2 stands for “severe acute respiratory syndrome coronavirus 2,” which is the virus that causes COVID-19 in humans.[1] The duration of immunity after COVID-19 infection remains unclear; however, studies report that COVID-19 convalescent cases are likely to develop immunity to the virus that lasts at least six to eight months.[2] Nevertheless, recent studies affirm the presence of memory plasma cells that can persist for several years and have the possibility of conferring life-long immunity in most individuals.[3] Interestingly, in about 10% of individuals, there could be the persistence of COVID-19 symptoms after the convalescence period for more than twelve weeks.[4] This circumstance should not be confused with a recurrence[5] when the individual is infected with the same variant and strain of a micro-organism that was present initially or reinfection, which is secondary infection with a different strain of the micro-organism.[4] The reported maximum shedding period for SARS-CoV-2 is 83 days in the upper respiratory tract and 56 days in the lower respiratory tract.[6] However, there is evidence of the non-existence of antibodies within three months of testing positive for the virus.[7] This seems to explain the plausibility of reinfection or recurrence of the COVID-19 virus after prior exposure.[7]

Reinfection with SARS-CoV-2, although considered rare[2] has been reported in several countries, including Hong Kong, Nevada, the USA, Belgium, India, and Ecuador.[8] This phenomenon necessitated an investigation by institutions like United States Center for Diseases Control and Prevention (CDC) and European Centre for Disease Prevention and Control (ECDC) through the project known as SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN).[9] An important factor for the effective definition for reinfection or recurrence is the time factor for the occurrence of the COVID-19 disease. Nevertheless, the time-lapse reported in the literature between clinical episodes is variable. However, some authors have defined a PCR positivity that occurred at least 28 days after a previous PCR-positive COVID-19 episode that was followed by clinical recovery and at least one negative PCR as reccurrence[6] while a positive COVID-19 testing and recurrent clinical symptoms occurring after 90 days should be required to diagnose true reinfection.[8,10] Also, reinfection, according to the interim guidelines on

detecting SARS-COV-2 is said to have occurred if a period occurred when a case had a negative PCR-test for COVID-19 (epidemiological criteria) and complete sequencing of genomic material of COVID-19 in both episodes showed evidence of different genetic clades or lineage irrespective of the number of single nucleotide variation (laboratory criteria).[9] This study investigated suspected cases of COVID-19 reinfection in individuals who had recovered from an initial COVID-19 infection.

Methods

Before the study was conducted and data collected, ethical approval was obtained from the Rivers State Ministry of Health, Nigeria.

The study considered some cases of recurrence and reinfection of COVID-19 in Rivers State. A case series of COVID-19 patients in Rivers State between March 2020 to June 2021 were reviewed and analyzed.

Naso-pharyngeal samples were collected as part of the state and national surveillance by the Rivers State Ministry of Health and the Nigeria Centre for Disease Control (NCDC) teams. Samples were collected from all symptomatic individuals and contacts of known COVID-19 cases. The gold standard test for COVID-19 was the Real-Time Polymerase Chain Reaction (RT-PCR) of SARS COV-2 specific viral gene sequencing. As part of the approved protocol, patients who test positive to COVID-19 were advised to home-isolate if the symptoms were mild or hospitalized if symptoms were severe. The WHO clinical progression scale for COVID-19 was used for classification and assessing disease severity. All patients with initial COVID-19 positive results were followed and discharged once they reached clinical recovery or achieved a negative COVID-19 PCR test result.

Definition of terms

For this study:

Recurrence is the clinical occurrence of symptoms compatible with COVID-19 accompanied by positive or persisting RT-PCR within 90 days of primary infection and

supported by the presence of epidemiological exposure or the absence of another cause illness.[10]

Reinfection - Is as any positive RT-PCR test (Ct values < 35) more than 90 days from the first episode, regardless of symptoms.[10] This takes into cognizance the definition by (Yahav et al) where reinfection is defined as clinical recurrence of symptoms compatible with COVID-19, accompanied by positive PCR test (Ct < 35), more than 90 days after the onset of the primary infection, supported by close-contact exposure or outbreak settings, and no evidence of another cause of infection. In addition, in the presence of epidemiological risk factors, a patient with two Negative RT-PCR results and similar clinical symptoms occurring within the first 90 days after the first episode had resolved will also be considered as reinfection on diagnosis (RT-PCR).[10]

Results

Between March 2020 and June 2021, 10947 cases of COVID-19 were observed. As shown in table 1, the distribution of the cases between 2020 and 2021, the highest number of cases were observed in Jan 2021, followed by Jun 2020, then Feb 2021. 75.89% (8,308) and 24.11% (2,639) were males and females respectively (Fig. 1a). As shown in the pie chart (Fig. 1b) below, the cases were distributed among the age groups: <18 years (414; 6%), 26-35 years (607; 8%), 36-59 years (1833; 25%), 60+ years (3981; 55%).

Table 1: COVID-19 cases in Rivers State March 2020 – June 2021

Monthly cases	Male	Female	<18 Yrs	18-25Yrs	26-35Yrs	36-59 Yrs	60+ Yrs
Mar-20	0	1	0	1	0	0	0
Apr-20	9	8	0	0	9	5	3
May-20	176	93	24	30	68	118	18
Jun-20	713	313	61	70	269	558	61
Jul-20	403	153	36	29	168	289	35
Aug-20	273	45	14	16	87	187	14

Sep-20	301	20	6	15	87	208	5
Oct-20	354	41	14	20	109	236	9
Nov-20	153	18	11	13	41	102	4
Dec-20	406	82	31	26	162	247	18
Jan-21	1497	630	208	295	438	1034	146
Feb-21	623	210	44	65	204	468	68
Mar-21	380	55	8	11	110	293	9
Apr-21	100	27	4	4	34	78	7
May-21	89	14	3	5	22	68	5
Jun-21	104	34	3	7	29	86	13

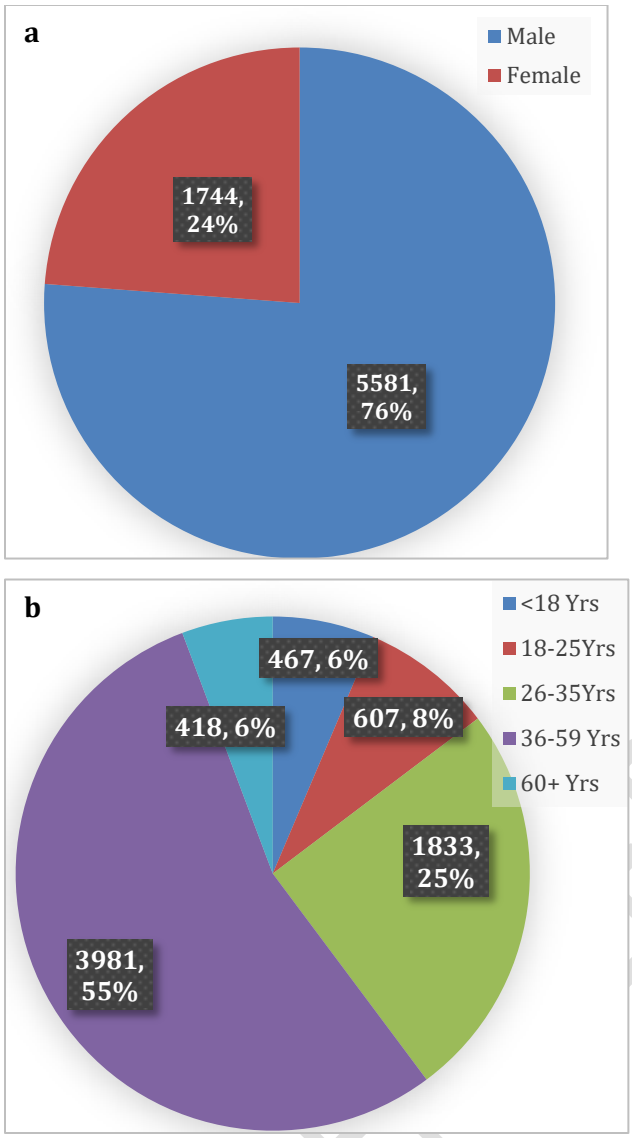

Figure 1: Distribution of (a) sex (b) age groups in the study

Of the 10,947 cases followed up, 204 of these cases had retesting, of which five cases were positive for COVID-19 with a median age of 46 (36-49) years. There were four males and a female. Four of the cases had comorbidities which were diabetes, hypertension, and human immunodeficiency virus (HIV). Four cases had negative COVID-19 PCR test results with complete recovery in between episodes, while one case had symptom-free periods with complete recovery between episodes. One case was a healthcare worker who had a COVID-19 re-exposure in the COVID unit. The median interval between the two episodes was 96 (37-196) days. All cases had symptoms of COVID-19 during the first episodes. These symptoms include difficulty in

breathing, headache, fever, sore throat, cough, fatigue, myalgia, anosmia, and malaise. Two of the cases were hospitalized, while three were managed as outpatients (at home). However, four patients were symptomatic during the second episode while one was asymptomatic. Of the four that had symptoms two were severe and were hospitalized, while two were managed as outpatients. The symptoms during the second episode include difficulty in breathing, chest pain, cough, dyspnoea, body weakness, anosmia, arthralgia, rhinorrhoea, fatigue, nausea, ageusia, and sneezing (Table 2).

Table 2: Demographic and Clinical Characteristics of Cases

	Patient A	**Patient B**	**Patient C**	**Patient D**	**Patient E**
Sex	Male	Male	Female	Male	Male
Age (year)	47	38	36	49	46
comorbidities	Hypertension, Diabetes	Diabetes	HIV	Hypertension	None
First infection					
Clinical presentation	Difficulty in breathing, headache, fever	Sore throat, cough, fever	Fever, fatigue, myalgia, headache, anosmia	Myalgia, weakness	Headache, fever, malaise
Date of RT PCR for COVID-19 (initial diagnosis)	1/5/2020	1/6/2020	18/6/2020	10/3/2020	8/1/2021
History of contact	No	Yes	No	No	No
Care intensity associated with initial positive test	Inpatient	Outpatient	Inpatient	Outpatient	Outpatient

Repeat testing	13/4/2020	22/6/2020	28/6/2020	Not done	23/1/2021
Criteria for discharge	Negative PCR test /clinical recovery	Negative PCR test/ clinical recovery	Negative PCR result / clinical recovery	Clinical recovery 24/3/2020	Negative PCR test/clinical recovery
Second infection					
Days to the recurrent positive result	37 days	196 days	96 days	49 days	150 days
Date of RT-PCR TEST	6/6/2020	23/12/2020	21/9/2020	27/4/2020	6/6/2021
History of contact	No	Yes	No	No	No
Disease indicator at repeat testing	Symptoms only	Symptoms and exposure	Symptoms only	Symptoms only	None
Clinical presentation	Difficulty in breathing, chest tightness	Fever, cough, anosmia, arthralgia	Cough, chest pain, fatigue, nausea, rhinorrhoea	Myalgia, Weakness	NONE
Care intensity associated with repeat positive test	Inpatient	outpatient	Inpatient	outpatient	Outpatient
Repeat testing	3/7/2020	30/12/2020	5/10/2020	16/5/2020	19/6/2021

Criteria for discharge	Negative PCR/clincal recovery	Negative PCR/clinical recovery	Negative PCR/clinical recovery	Clinical recovery	Negative PCR
Interpretation	Recurrence	Reinfection	Reinfection	Recurrence	reinfection

Discussion

The maximum duration of COVID-19 shedding in the upper respiratory tract has been reported to be 83 days,[11] positive RT-PCR results after 83 days could suggest the possibility of recurrence. Although the second episode may be asymptomatic, the time interval where the patient was symptom-free between both episodes is also important.[11] In these cases, the median time of positive RT-PCR results between the two episodes was 96 days. Although two of the cases had positive RT-PCR result intervals of fewer than 83 days, they were symptom-free between the two episodes. Furthermore, a case had diabetes and two negative PCR test results before discharge but became symptomatic, and the second episode was more severe than the first episode. However, the finding negates observation made in a previous study that noted that patients with diabetes, the elderly, and those who had a severe clinical episode were less likely to have a recurrent COVID-19 positivity[12]. False-negative PCR test may have resulted in the recurrent positivity but the presence of nucleic acid alone cannot be used to determine if viral shedding or infectiousness occurred[13]. Yet, a review done to determine the mechanism of underlying recurrent COVID-19 positivity could not state if it was attributable to false-negative results, reactivation, relapse, or reinfection[12]. Also, the fact that false-negative PCR tests may occur does not exclude the possibility that patients who had true negative PCR test results may have a re-occurrence or reinfection with other strains of COVID-19.[14]

It was found that all the patients who had a second episode of COVID-19 infection in this study were young. This agrees with documented observations of younger age being associated with an increased probability of having a second episode of COVID-19 infection[12]. The recurrence of COVID-19 occurred in two patients in this study with

varying degrees of symptoms between the first and second episodes, while the possibility of reinfection occurred in three patients. But to prove that these cases were reinfections, samples from both episodes of the illness should be sequenced genetically and the genomes compared[6]. Nevertheless, applying the clinical and epidemiological definition of reinfection set by Yahav et al, this study demonstrated three cases of reinfection; in one of the cases, there were epidemiological data of re-exposure, clinical symptoms, negative COVID-19 result, and a longer time interval of 196 days between the first and second episodes. This follows the clinical definition of reinfection[10] and the reinfection criteria set by the Pan American Health Organization and World Health Organization[9]. In another case, there were 150 days between the first and second infection, a negative PCR test result but there were no symptoms. This agrees with the epidemiological definition of reinfection as any positive RT-PCR result occurring more than 90 days from the first episode, regardless of symptoms.[10] Finally, the third reinfection case had an interval of 96 days although the patient was immunosuppressed and was discharged based on clinical recovery from symptoms and a negative COVID-19 result, the repeat positive PCR result exceeded 83 days which is the longest shedding period for COVID-19 in the upper respiratory tract[11]and it fits into the epidemiological definition of reinfection.[10]

The limitation of the study was that genomic sequencing of the virus was not done.

Conclusion

This study shows three cases of covid-19 reinfection and two cases of recurrence. Therefore, it is illustrative of the possibility of COVID-19 reinfection and recurrence. The longevity of circulating antibodies and the existence of other chronic disease conditions like HIV and diabetes in the individual may be related to this outcome. While further studies are recommended to fully comprehend the antibody-virus interplay in covid-9 infections, follow-up of convalescent cases and full vaccination of all eligible persons, including persons with comorbidities, is advised. Continued adherence to non-pharmaceutical interventions will enhance the chances of safety in the pandemic.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

References

1. Tillett RL, Sevinsky JR, Hartley PD, Kerwin H, Crawford N, Gorzalski A, Laverdure C, Verma SC, Rossetto CC, Jackson D, Farrell MJ. Genomic evidence for reinfection with SARS-CoV-2: a case study. The Lancet infectious diseases. 2021;21(1):52-8.
2. Liu W, Fontanet A, Zhang PH, Zhan L, Xin ZT, Baril L, Tang F, Lv H, Cao WC. Two-year prospective study of the humoral immune response of patients with severe acute respiratory syndrome. The Journal of infectious diseases. 2006;193(6):792-5.
3. Hall VJ, Foulkes S, Charlett A, Atti A, Monk EJM, Simmons R, et al. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). Lancet. 2021;397(10283):1459–69.
4. To KK, Hung IF, Ip JD, Chu AW, Chan WM, Tam AR, Fong CH, Yuan S, Tsoi HW, Ng AC, Lee LL. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2020
5. Hall VJ, Foulkes S, Charlett A, Atti A, Monk EJM, Simmons R, et al. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative healthcare workers in England: a large, multicentre, prospective cohort study (SIREN). Lancet. 2021;397(10283):1459–69.
6. Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J, Ho A. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. The lancet microbe. 2021 Jan 1;2(1):e13-22.
7. Liu A, Wang W, Zhao X, Zhou X, Yang D, Lu M, et al. Disappearance of antibodies to SARS-CoV-2 in a -COVID-19 patient after recovery. Clin Microbiol Infect. 2020 ; 26(12):1703–5.

8. European Centre for Disease Prevention and Control. Reinfection with SARS-CoV: considerations for public health response. ECDC. 2020 Sep 21.
9. Pan American Health Organization, & World Health Organization. (2020). Interim guidelines for detecting cases of reinfection by SARS-CoV-2. Paho/Who; accessed 2022 January 13, Available from: https://www.paho.org/en/documents/interim-guidelines-detecting-cases-reinfection-sars-cov-2
10. Yahav D, Yelin D, Eckerle I, Eberhardt CS, Wang J, Cao B, Kaiser L. Definitions for coronavirus disease 2019 reinfection, relapse and PCR re-positivity. Clinical Microbiology and Infection. 2021 Mar 1;27(3):315-8.
11. Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J, Ho A. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. The lancet microbe. 2021;2(1):e13-22.
12. Azam M, Sulistiana R, Ratnawati M, Fibriana AI, Bahrudin U, Widyaningrum D, Aljunid SM. Recurrent SARS-CoV-2 RNA positivity after COVID-19: a systematic review and meta-analysis. Scientific reports. 2020;10(1):1-2.
13. Chen Z, Li Y, Wu B, Hou Y, Bao J, Deng X. A patient with COVID-19 presenting a false-negative reverse transcriptase polymerase chain reaction result. Korean journal of radiology. 2020;21(5):623.
14. Dao T L, Hoang V T, Gautret P. Recurrence of SARS-CoV-2 viral RNA in recovered COVID-19 patients : a narrative review. Euro J of Clin Microbiol Infect Dis.2020;1–13.