CASE SERIES

REPEATED COVID-19 INFECTION EXISTS: A CASE SERIES FROM PAKISTAN

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Background: Protection against SARS-CoV-2 in infected individuals of COVID-19 is lacking. We report a case series of repeated infections of SARS-CoV-2. **Methods:** A total of 12 patients were identified with repeated infections for SARS-CoV-2 from 25 April 2020 to 16 March 2021 from Pakistan. Repeated infection was defined as diagnosis of the SARS-CoV-2 with real-time reverse transcriptase–polymerase chain reaction (RT-PCR) tests in the first and second phase of infection after complete recovery from the first phase of infection with a negative RT-PCR. **Results:** Of the 12 participants, 75% (n=9) were male and mean age of the participants were 40.1±9.7 years. Mean duration between the first and second phase of infection was 184±68.9 days. Patients presenting with mild infection in the first phase largely developed moderate to severe infection in the second phase. None of them were vaccinated. **Conclusion:** The pandemic of COVID-19 is on the rise and repeated infection from SARS-CoV-2 is occurring.

Keywords: SARS-CoV-2; COVID-19; Vaccination; Reinfection

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INTRODUCTION

COVID-19 pandemic is an ongoing public health issue around the globe. Despite the vaccination rollout started on 19th December 2020 and vaccinating around 7.79 billion of individuals around the globe is expected over time[1], the number of COVID-19 cases are still on rise as the highest weekly incidence has been reported from 12th April 2021 to 18th April 2021.[2] We report a case series of confirmed SARS-CoV-2 repeated infections from Pakistan. Immunity against SARS-CoV-2 in the already infected individuals is largely unknown[3] which is leading to the question that if immunity cannot be sustained with infection to SARS-CoV-2 then vaccination could be the only way appearing as an strategy against this ongoing pandemic. We call it CoVexit; where V stands for vaccination.

MATERIAL AND METHODS

In this case series we identified a total of 12 patients in Khyber Pakhtunkhwa, Pakistan diagnosed with real-time reverse transcriptase–polymerase chain reaction (RT-PCR) tests for COVID-19 nucleic acid for both the first and second infection of SARS-CoV-2[4] from 25 April 2020 to 16 March 2021. Written informed consent was taken from each study participants after explaining purpose of the study. Patients Information was collected about the demographic characteristics, history of exposure, investigations conducted alongside with the SARS-CoV-2, and signs and symptoms of the patients during the first and second infection of SARS-CoV-2. Ethical approval of the study was granted by the ethical review board of Khyber Medical University Peshawar.

RESULTS

Of the 12 selected patients, 75% were male with a mean age of 40.1±9.7 years and mean duration of 184±68.9 days between the first and second episodes of infection (min 57 days, max 285 days). Half of the patients presented with mild nature of disease in the first phase of infection and 25% (n=3) were asymptomatic in the first phase of infection. Patients who experienced mild nature of disease in the first phase, developed moderate and moderate to severe nature of disease in the second episode of SARS-CoV-2 infection (Table-1). None of the patients were vaccinated.

Case-1

A 45 years old male diagnosed with SARS-CoV-2 on 19th June 2020 RT-PCR assay test. The infection was mild in nature and managed at home. The patient had no comorbid condition and developed symptoms of cough, fever, shortness of breath, sore throat and headache. After complete recovery from the first infection, the person again developed symptoms of SARS-CoV-2 after a period of 154 days and tested positive on RT-PCR assay on 20th November 2020. This time the patient experienced moderate to severe nature of the disease with symptoms of cough, fever, shortness of breath, pneumonia, acquired respiratory distress syndrome, diarrhoea, chills and rigors. Patient was managed at home.

Case-2

A 53 years old female working in a Government setup diagnosed with SARS-CoV-2 on 15th May 2020 on RT-PCR Assay test. Disease severity was mild in nature and managed at home. The patient was having hypertension as underlying condition and developed symptoms of fatigue, myalgia and sore throat. After complete recovery from the first infection, she again developed symptoms related to SARS-CoV-2 after a period of 194 days and tested positive for SARS-CoV-2 on RT-PCR Assay on 25th November 2020. This time the patient experienced moderate nature of infection with symptoms of fatigue, nausea, headache, arthralgia, myalgia and rhinorrhoea. On physical examination, she had high systolic (180 mmHg) and diastolic (110 mmHg) blood pressure with RBS 200 mg/dL.

Case-3

A 49 years old male diagnosed with SARS-CoV-2 on 25th April 2020 on RT-PCR Assay test. The patient had no comorbid condition and remained asymptomatic. After complete recovery from the first infection, he got exposed to a positive case of SARS-CoV-2 after a period of 214 days and tested positive for SARS-CoV-2 on RT-PCR Assay on 25 November 2020. This time the patient experienced moderate nature of infection with symptoms of fever, fatigue, nausea, headache, chills & rigors, rhinorrhoea, and sore throat. Patient was managed at home.

Case-4

A 30 years old male working in Government setup diagnosed with SARS-CoV-2 on 5th June 2020 on RT-PCR assay test. The infection was moderate in nature and managed at home. The patient developed symptoms of cough, fever, shortness of breath, chills with rigors and sore throat. After complete recovery from the first infection, after a period of 164 days he tested positive for SARS-CoV-2 on RT-PCR Assay on 16 November 2020. This time also the patient experienced moderate nature of infection and developed symptoms of cough, fever, shortness of breath, sore throat, chills with rigors, myalgia, headache and nausea. Patient was managed at home.

Case-5

A 39 years old made working in a private setup diagnosed with SARS-CoV-2 on 4th June 2020 on RT-PCR assay test. The infection was mild in nature and managed at home. The patient developed symptoms of cough, fever, malaise, fatigue and sore throat. After complete recovery from the first infection, the individual again developed symptoms related to SARS-CoV-2 after a period of 189 days and tested positive for SARS-CoV-2 on RT-PCR for SARS-CoV-2 on 10th December 2020. This time the patient experienced moderate nature of infection and developed symptoms of cough, fever, fatigue, nausea, headache, arthralgia, myalgia, and chills with rigors, rhinorrhoea and sore throat. Patient was managed at home.

Case-6

A 31 years old male working in private setup diagnosed with SARS-CoV-2 on 20th July 2020 on RT-PCR Assay test. The patient remained asymptomatic. After complete recovery from the first infection the individual became symptomatic and after a period of 123 days again tested positive for SARS-CoV-2 on RT-PCR Assay on 20th November 2020. This time the patient experienced moderate nature of the disease and developed symptoms of cough, fever, shortness of breath fatigue and malaise. Patient was managed at home.

Case-7

A 29 years old female health care worker in a public sector hospital diagnosed with SARS-Cov-2 on RT-PCR Assay on 9th November 2020. The patient experienced moderate nature of disease and developed symptoms of cough, fever, shortness of breath, fatigue and malaise and managed at home. After complete recovery from the first infection and a period of 57 days, she again developed symptoms and tested positive for SARS-CoV-2 on RT-PCR Assay on 5th January 2021. Also, this time, the patient experienced moderate nature of disease with symptoms of shortness of breath, cough, fever, fatigue, malaise, rhinorrhoea and sore throat. Patient was managed at home.

Cas-8

A 41 years old male health-care worker in a public sector hospital diagnosed with SARS-CoV-2 on RT-PCR Assay on 6th June 2020. The patient experienced moderate nature of disease and developed symptoms of fever, headache, sore throat and fatigue. Bilateral infiltrates were noted on chest X-rays. After complete recovery from the first infection and a period of 4 months and 13 days, he again developed symptoms and tested positive for SARS-CoV-2 on RT-PCR Assay test on 1st November 2020. This time the patient experienced mild nature of the disease with headache, fever and shortness of breath. Patient was managed at home.

Case-9

A 50 years old male health care worker working in public sector diagnosed with SARS-CoV-2 on 3rd of June 2020 on RT-PCR-Assay test. The patient experienced moderate nature of disease and developed symptoms of sore throat, body aches and high fever. Laboratory investigations showed that the patient's CRP was raised to 32 mg/dL and D-dimer 750 ng/mL. Patient was managed at home. After complete recovery from the first infection, the patient again became symptomatic and tested positive for SARS-CoV-2 on November 2nd 2020 on RT-PCR Assay test. The patient experienced mild nature of disease and developed

symptoms of temperature and body aches. Patient was managed at home.

Case-10

A 31 years old male healthcare worker diagnosed for SARS-CoV-2 on 18th May 2020 on RT-PCR Assay. The patient experienced moderate nature of disease and developed symptoms of fever, cough and diarrhea. Patient was managed at home. After complete recovery from first infection and after a period of 9 months, he again developed symptoms of SARS-CoV-2 and tested positive for SARS-CoV-2 on RT-PCR Assay on 17th February 2021. The patient experienced moderate to severe nature of infection and developed symptoms of cough, fever, shortness of breath, diarrhoea and pneumonia. In the second infection the oxygen saturation was 84 in comparison to 99 in the earlier phase of infection. Patient was managed at home.

Case 11: A 53 years old female working in a government setup diagnosed for SARS-CoV-2 on 3rd June 2020 on RT-PCR Assay. The patient remained asymptomatic throughout course of the disease. After complete recovery from the first infection and a period of 9 months and three days the lady again tested positive for SARS-COV-2 on RT-PCR Assay. This time the patient experienced moderate nature of disease and developed symptoms of fatigue, malaise, headache, arthralgia and myalgia. Patient was managed at home.

Case-12

A 30 years old male diagnosed for SARS-CoV-2 on 4th June 2020 on RT-PCR Assay. The patient experienced moderate nature of disease and developed symptoms of high-grade fever, malaise, fatigue, diarrhoea, headache, chills and rigors. Patient was managed at home. After complete recovery from first infection and a period of over 9 months, the patient tested positive for SARS-CoV-2 on 16th March 2021 on RT-PCR Assay. This time the patient experienced mild nature of disease and developed symptoms of fever, diarrhoea, myalgia and sore throat. Patient was managed at home.

DISCUSSION

We report repeated infections of SARS-CoV-2 from a developing country. Participants were largely male and middle age grouped. Patients who were asymptomatic or developed mild nature of disease, developed moderate to severe infection in the second phase of infection at large. The duration between the two phases of infections were six months on average (ranging from minimum of 2 months to a maximum of 9 months).

The COVID-19 pandemic has affected almost all countries around the globe and new cases are being reported from all regions around the globe including majority of the countries.[2] A large number of patients with SARS-CoV-2 have recovered and been discharged. While a number of recovered patients test positive again or even have a recurrence of clinical symptoms. Protective immunity following SARS-CoV-2 infection is not yet fully understood and evidence of reinfection poses challenges for public health and vaccination efforts to protect against the COVID-19 pandemic.[5] On the other hand, COVID-19 vaccination has been started in earlier December 2020[6] but the number of new COVID-19 infections are on rise especially in Asia. It has been assumed that a positive retest for SARS-CoV-2 may be explained by reactivation or relapse of the infection while others emphasize the reinfection hypothesis. According to the evidence confirming reinfection, it may occur with low incidence. However, the reinfection rate may be underestimated as a result of asymptomatic infections in one or both episodes.[7]

Despite evidence of an effective acquired immune response after COVID-19, some studies have shown that patients with mild symptoms have developed a weaker and less lasting immune response to the virus, with a decrease in the level of antibodies after 2–3 months of infection. As the patient maintained intense exposure to SARS-CoV-2 in those 3 months between clinical episodes, had different symptoms and antibody detection only recently, this suggests reinfection by different strains of SARS-CoV-2. Therefore, the hypothesis of herd immunity and duration of protection afforded by vaccines, is questioned.[8]

Alongside with this, it has been reported that there exist more than 30 potential vaccines under trial but it can't be guaranteed that it will end the pandemic because the scientists further need to understand that how the SARS-CoV-2 affects the body and accordingly the level of protection against the reinfection.[9]

Achieving the herd immunity[10] is the way out which is a two-way phenomenon including vaccination of the people or infection of the vulnerable groups with a risk of 2% mortality from SARS-CoV-2 around the globe[2]. On the other hand, it has been reported that the natural immunity against SARS-CoV-2 is not constant and is varying from person to person and still needs to be studied[11] which is indicating that reinfection might be a common phenomenon with decreased severity of the disease once vaccinated. We need to support the COVID-19 vaccination rollout around the globe in order to make "CoVexit" possible.

Limitation of this case series is lack of data about anti Covid antibodies which is neither offered by the health system nor is requested by the patients.

Table 1: Clinico-demographic details of patients with repeated COVID-19 infection (n=12)

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12
Age (yrs)	45	53	49	30	39	31	29	41	50	31	53	30
Gender	Male	Female	Male	Male	Male	Male	Female	Male	Male	Male	Female	Male
Chronic Medical Illness	Nil	Hypertension	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Diagnosis date of first infection	19 June 2020	15 May 2020	25 April 2020	5 June 2020	4 June 2020	20 July 2020	9 November	6 June 2020	3 June 2020	18 may 2020	3 June 2020	4 June 2020
Severity of disease in 1st infection	Mild	Mild	Mild	Moderate	Mild	Mild	Moderate	Moderate	Moderate	Moderate	Mild	Moderate
Signs and symptoms	Cough, fever, SOB, sore throat and headache	Fatigue, myalgia and sore throat	Asymptomatic	Cough, fever, SOB, chills & rigors and sore throat	cough, fever, malaise, fatigue and sore throat	Asympto matic	cough, fever, shortness of breath, fatigue and malaise	fever, headache, sore throat and fatigue	sore throat, body aches and high fever	fever, cough and diarrhoea	A-symptomatic	fever, malaise, diarrhoea, headache, chills
Diagnosis date of 2nd infection	20 November 2020	25 November 2020	25 November 2020	16 November 2020	10 December 2020	20 November 2020	5 January 2021	1 November 2020	2 November 2020	17 February 2021	3 march 2021	16 March 2021
Severity in 2nd infection	Moderate to severe	Moderate	Moderate	Moderate	moderate	Moderate	Moderate	Mild	Mild	Moderate to severe	Moderate	Mild
Signs and symptoms	Cough, fever, SOB, ARDS, pneumonia, diarrhoea, chills & rigors	Fatigue, myalgia, nausea, headache, arthralgia and rhinorrhoea	Fever, fatigue, nausea, headache, chills & rigors, rhinorrhoea and sore throat	cough, fever, shortness of breath, sore throat, chills & rigors, myalgia, headache and nausea	cough, fever, headache, arthralgia, myalgia, chills, rhinorrhoea and sore throat	cough, fever, shortness of breath fatigue and malaise	shortness of breath, cough, fever, fatigue, malaise, rhinorrhoea and sore throat	headache, fever and shortness of breath	Fever and body aches	cough, fever, shortness of breath, diarrhoea and pneumonia	fatigue, malaise, headache, arthralgia and myalgia	fever, diarrhoea, myalgia and sore throat
Period for occurrence of 2nd infection	154 Days	194 Days	214 Days	164 Days	189 Days	123 Days	57 Days	133 Days	152 Days	275 Days	273 Days	285 Days

AUTHORS' CONTRIBUTION

ZU-H, SF, YM-Y conceived the study. MN, AK-I, AI, NU & AS collected the data. ZU-H, SF, YM-Y monitored the data. ZU-H, SF, YM-Y, MN, AK-I, AI, NU & AS confirmed the cases. ZU-H, SF, YM-Y wrote the manuscript. All authors reviewed and critically appraised the manuscript.

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