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The Incidence of Probable Reinfection with Sars Cov 2 and the Frequency of Post Covid Syndrome Among Convalescents from Covid 19 at the Frantz Fanon Hospital Bejaia University Hospital Algeria

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Abstract

Summary

The rate of reinfection with SARS-CoV-2 is low while post-COVID syndrome is increasingly present. The aim of this study is to estimate the incidence of probable SARS-CoV-2 reinfection and post-COVID complications in patients previously infected with the virus.

Methods

We included patients in the convalescence phase of a SARS-CoV-2 infection confirmed by RT-PCR into our study. Follow-up started from the 90th day after clinical recovery from the first episode of COVID-19 and extended over a period of 12 months, from September 20, 2020 to September 30, 2021. A total of 96 convalescents were included in the study. During this follow-up period, we also assessed the frequency as well as the most common symptoms of post-COVID syndrome in previously infected convalescents.

Results

Of the 96 convalescents included in our study, only four were identified as having been infected twice, thus representing 4.17% of the positive cases diagnosed during the follow-up period. The clinical presentation of these 04 cases was benign. This low incidence of reinfection with SARS-CoV-2 among convalescents indicates a relative reduction in reinfection among previously infected people and that the risk of hospitalizations and death has also been reduced, moreover, the frequency of post COVID syndrome was 57.3%. Among the different symptoms observed, fatigue turned out to be the most common symptom (47.9%). These results highlight the importance of long-term monitoring of COVID-19 convalescents, highlighting aspects of reinfection as well as persistent manifestations of post-COVID syndrome.

Conclusion

This study found that the risk of reinfection with SARS-CoV-2 remained considerably lower while post-COVID syndrome is increasingly common, clinical and virological analysis indicates a decrease in the rate of reinfection in recovered patients as well as the persistence of post-COVID symptoms in most convalescents. These data show that convalescent patients maintain functional antibody responses for at least 12 months after infection, suggesting a strong and durable response after symptomatic illness that may provide prolonged protection that may reduce the risk of reinfection.

Keywords: SARS-CoV-2, COVID-19, Reinfection and Post Covid Syndrome

1. Introduction

As large numbers of people continue to be infected with SARS-CoV-2, the effectiveness and duration of natural immunity in terms of protection against SARS-CoV-2 reinfection and severe disease is of crucial importance for the future. National surveys have documented that prior SARS-CoV-2 infection is associated with a significantly reduced risk of reinfection with efficacy lasting at least one year and relatively moderate waning immunity. Importantly, natural immunity showed roughly similar levels of effectiveness in protecting against reinfection by different SARS-CoV-2 variants. Similarly, the risk of hospitalizations and death was also reduced in SARS-CoV-2 reinfections compared to primary infections [1]. Our primary objective in this study is to determine the incidence of probable reinfection with SARS-CoV-2 in convalescents from COVID-19 and post-COVID complications.

2. Patients and Methods

This is a prospective descriptive and longitudinal study, carried out in the infectious diseases department of the Frantz Fanon hospital of Bejaia University Hospital, Algeria over a period from June 20, 2020 to September 30, 2021. The patients in the study are patients aged 16 or over, with confirmed COVID-19 and who have no prior history of exposure to SARS-CoV-2, hospitalized at the Bejaia University Hospital from June 20 to September 30, 2020, i.e. during the first wave from COVID-19 in Bejaia and who recovered, each patient hospitalized during this period was followed for 12 months. This study offered a unique opportunity to assess the risk of reinfection following a previous COVID-19 with longitudinal monitoring of convalescent individuals during a period that encompasses the three waves of COVID-19 experienced in Bejaia (Algeria). Convalescents (n=96) from a first SARS-CoV-2 infection were confirmed based on a first positive PCR test result for SARS-CoV-2. The primary outcome was the incidence of probable SARS-CoV-2 reinfection, defined as a new positive polymerase chain reaction (PCR) occurring 90 days or more after complete resolution of the first infection. The follow-up period began just at the end of the 90-day pre-follow-up period and continued until September 30, 2021. Thus, the start of the follow-up period varied depending on when each case tested positive for the first time. For example, cases who first tested positive on June 20, 2020 had a follow-up start date of no earlier than September 20, 2020, while some cases who first tested positive in September 2020 saw their follow-up period begins in December 2020. During this follow-up period, the incidence rate of reinfection was calculated as follows; this is the number of reinfected cases out of the total number of convalescents from a first SARS-CoV-2 infection during 12 months. Thus, during the study period, we also examined the most common symptoms as well as the frequency of post-COVID syndrome among our convalescents. The table below represents the characteristics of our study population.

Features	Results
Median Age (IQR)	51 Years (q1= 45 Years ; q3= 60,75 Years)
Sex	
Man	61 (63,5 %)
Women	35 (36,5 %)
Comorbidities	
Without Comorbidity	30 (31,25 %)
With Comorbidity	66 (68,75 %)
Obesity (BMI ≥ 30 kg/m²)	44 (45,8 %)
High Blood Pressure	35 (36,5 %)
Diabetes	24 (25 %)
Heart Disease	09 (9,4 %)
Chronic kidney Failure (CKD)	04 (4,2 %)
Chronic Respiratory Pathology	02 (2,1 %)
Immunosuppression	02 (2,1 %)
BMI	
< 25 kg/m²	19 (19,8 %)
25-29.9 kg/m²	32 (42,1 %)
≥ 30 kg/m²	44 (45,8 %)
Clinical signs	
Fatigue	92 (95,8 %)
Fever	69 (71,9 %)
Cough	63 (65,6 %)
Dyspnea	39 (40,6 %)
Desaturation	24 (25 %)
Chest pain	33 (34,4 %)
Anosmia	60 (62,5 %)
Ageusia	59 (61,4 %)
Sore throat	37 (38,5 %)
Dizziness	38 (39,6 %)

Clinical severity	
Mild COVID	07 (7,3 %)
Moderate COVID	71 (74 %)
Severe COVID	18 (18,7 %)
Chest scan	
With SARS-CoV-2 Pneumonia	88 (91,7 %)
Without SARS-CoV-2 Pneumonia	08 (8,3 %)

Table 1: Epidemiological Clinical and Radiological Data from Participants in This Study

Patient Consent

All patients were recruited with their informed consent. Only patients who have given their written consent will be candidates for follow-up.

Conflicts of Interest

No conflict of interest is declared.

3. Results

3.1. Incidence of Probable Reinfection with SARS-CoV-2 Among Convalescents From COVID-19

We assessed the relative incidence of SARS-CoV-2 reinfection in our convalescents during follow-up. After an average of 8 months and 4 days of follow-up (min 90. Max 365), we recorded 04 reinfections with positive RT PCR achieving an incidence rate of 4.17% (table 2). In our study, the 04 cases of probable reinfection with SARS-CoV-2 were all symptomatic and mild cases. They occurred 6 to 12 months after the resolution of the first infection so they met the definition of a reinfection.

It should be noted that no systematic RT-PCR testing was performed during follow-up. PCR was performed only in individuals with symptoms suggestive of COVID-19. Thus, it was not possible to carry out genome sequencing to demonstrate the presence of different strains between episodes of infection and reinfection, because this practice was not common and not available in our laboratory. Indeed, the sequencing of SARS-CoV-2 strains was exclusively carried out by the virological unit of the Pasteur Institute in Algiers, mainly for epidemiological purposes, and was not systematically applied to all patients.

Participants (n)	Infetcted at start (n)	Reinfected (n)	Incidence of reinfection	Average Time between pPrimary Infection and Reinfection
96	96	04	**4,17 %**	8 months et 4 days

Table 2: Incidence Rate of SARS COV-2 Reinfection Among Covid-19 Convalescents

3.2. Post-Covid Complications

During this follow-up, we also looked for post- COVID complications in our convalescents. 57.3% of patients, or 55 cases, experienced post-COVID syndrome (95% CI: 46.21; 65.92) (figure 1)

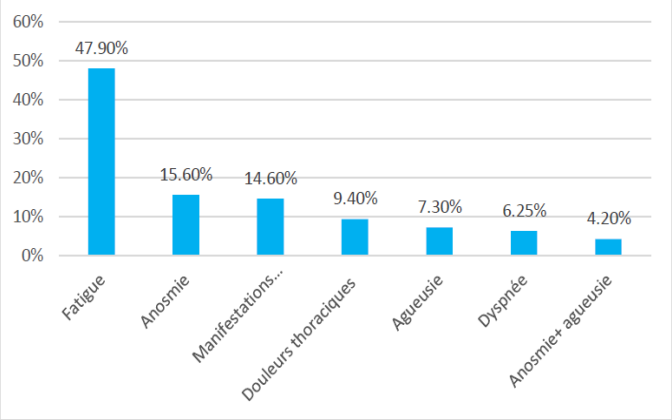

Figure 1: Frequency of Post-COVID Syndrome Among Our Convalescents

The most frequently observed post-COVID symptoms were fatigue in 46 convalescents (47.9%), anosmia in 15 convalescents (15.6%), neuropsychiatric manifestations (headache, insomnia, memory and concentration problems) in 14 convalescents (14.6%), as well as chest pain in 9 convalescents (9.4%) (figure 2). Other symptoms have been reported at different percentages.

The figure below represents the most common post-COVID symptoms among convalescents

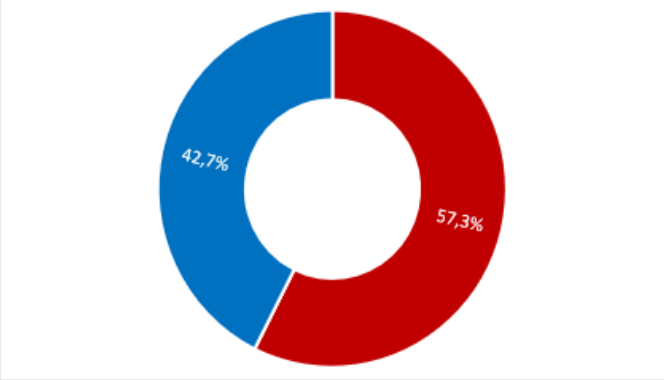

Figure 2: Post-COVID Symptoms in Order of Frequency

4. Discussion

4.1. Convalescent Patients with Re-Exposure to Sars-Cov-2, A Report Of 04 Cases

Our hospital faced three waves of COVID-19, from June to September 2020 for the first wave, from September to December 2020 for the second wave, and from May to September 2021 for the third wave. During the period from September 2020 to September 2021, only four cases (04) of reinfection were reported among our participants. A key element to highlight in our study is the drop in the number of cases of reinfection (04 reinfections with an incidence rate of 4.17%) despite the fact that the wilaya has experienced multiple waves with mutant strains since 2020.

This result is consistent with several studies; an Italian study where there was no case of reinfection during 8 months of follow-up in 32 convalescents [2]. In a meta-analysis of 19 studies [3], the incidence of reinfection in recovered COVID-19 patients ranged from 0 to 20%. The pooled reinfection rate was 0.65% (95% CI: 0.39 to 0.98%). In a high-risk population (unvaccinated frontline health workers), there were 8/247 reinfections (incidence of 3.23%) [4], a rate that was lower compared to our study but shows that the reinfection rate remains low among those previously infected. In a Spanish study, the dataset provides an indication of the frequency of reinfection in 173 primary infections with three probable reinfections (interval > 90 days according to CDC guidelines) and one suspected reinfection (<90 days between primary infection and reinfection). Therefore, there was a minimum overall reinfection rate of 4/173 (2.31%) [5]. This rate contrasts with what was found in another cohort of healthcare workers followed for a seroprevalence study. of 7 months in which no reinfection was detected [6-7]. In a study done in Abu Dhabi, which followed 113 patients with COVID-19, this study shows a sustained and prolonged positive immune response in patients recovered from COVID-19. None of the recovered patients were reinfected during the 6-month follow-up period [8].

Studies (Ref.)	Participants infected at baseline (n)	Reinfections (n)	Tracking time	Incidence of reinfection
Italy [2]	32	00	8 months	00 %
Spain [6]	578	00	7 months	00 %
Abu Dhabi [8]	113	00	6 months	00 %
Spain [9]	173	04	12,5 months	2,3 %
Barcelona [4]	247	08	20,5 months	3,23 %
Algeria	**96**	**04**	**12 months**	**4,17 %**

Table 3: Number and Incidence Rate of Sars-Cov-2 Reinfection in International Studies

A study by Abu-Raddad LJ et al. in Qatar assessed the cumulative risk as well as the incidence rate of SARS-CoV-2 reinfection in a national cohort of 43,044 antibody-positive individuals. This study with a follow-up period of up to 35 weeks, demonstrated and confirmed by viral genome sequencing that reinfection with SARS-CoV-2 occurs, but "only rarely" with a cumulative risk of approximately 2 per 1000 people and an incidence rate of reinfection < 1 per 10,000 person-weeks compared to the complementary cohort of 149,923 sero-negative people with a much higher cumulative risk of reinfection (~31 per 1000 people after 46 weeks of follow-up) and an estimated incidence rate of infection (~14 per 10,000 person-weeks). The estimated effectiveness of natural infection against reinfection was 95%. Additionally, this study showed no evidence of waning protective immunity against reinfection in this cohort for

more than 7 months [10]. Additional studies in the general population on this question have been derived from national health data from Qatar, large cohort studies in the United States, and population-based surveys in Italy and the United Kingdom are listed in the Table 4 which is limited to population-based studies providing group comparisons for infection risk in individuals with and without a history of PCR-confirmed SARS-CoV-2 infections [11-18]. In summary, all of these epidemiological studies have consistently documented that prior SARS-CoV-2 infection confers substantially broad protection against reinfections.

Studies (Ref.)	Infected at start (n)	Reinfections (n)	Incidence of reinfection
Austria [12]	14840	40	0,27 %
Denmark [11]	11068	72	0,65 %
Qatar [13]	44 821	263	0,59 %
Qatar [16]	158 608	214	0,13 %
United States [15]	50 327	40	0,08 %
United States [18]	41 647	593	1,42 %
United States [14]	8845	62	0,70 %

Table 4: Incidence of Sars-Cov-2 Reinfection in Population-Based Studies

This low number of reinfection cases indicates a relative reduction in the incidence of SARS-CoV-2 reinfection in the previously infected group. Emerging data suggest that immunity acquired after primary SARS-CoV-2 infection provides protection against re-exposure [19-20], and that reinfection was rare 1 year after primary infection, likely due to of the protective effect of natural infection [21]. The presence of detectable antibodies translates into residual immunity, as several studies have shown protection against reinfection in people recovering from COVID-19 up to a year after primary infection [11-12] [22-23]. Overall, our results indicate that the risk of reinfection within 1 year of infection remains low. This study confirms previous findings of a low risk of reinfection with SARS-CoV-2, suggesting that the protection conferred by natural immunity may last at least 12 months. These results are consistent with the available literature, where all published cohort studies reported reinfection rates below 1% Furthermore, in our study, the 04 cases of probable reinfection with SARS-CoV-2 were all symptomatic and mild cases. In a cohort in Barcelona, 7 cases of 8 reinfections were symptomatic, 85.7% had similar clinical symptoms in both episodes and 14.3% had a milder form of the disease in the second episode. In no case was the second infection more severe than the first, which is consistent with our study, unlike another study where 27.8% of reinfected patients had more severe symptoms in the second episode [29]. Available data showed that reinfections had a lower risk of symptomatic infection and severe disease than primary infections and were more likely to be mild, which is consistent with previous findings [29] and with the results of our study [3-26].

4.2. Post-Coved Complications

This study revealed that a large proportion of recovered patients, i.e. 57.3%, present with post-COVID syndrome 3 to 12 months after recovery from the acute phase of COVID-19. However, the available studies on post-COVID syndrome are very heterogeneous. The frequency of post-COVID syndrome that we found was lower than that reported in other studies [30-33] but it confirms that this syndrome is common in patients recovered from COVID-19. Thus, in other studies evaluating general post-COVID manifestations, results have clearly demonstrated that the prevalence of post-COVID manifestations is 35% to 90.5% among 4664 participants [31-37]. Fatigue was almost present in all studies focusing on multi-system disease in cured patients, which is consistent with the results found in our study. According to a systematic review including 63 studies on post-COVID syndrome, fatigue, dyspnea, sleep disturbances and difficulty concentrating were the most commonly reported symptoms, but there was substantial heterogeneity between studies for all reported symptom prevalences [38]. Other manifestations such as anosmia, neuropsychiatric manifestations and chest pain were among the most frequent post-COVID symptoms, which is consistent with other studies les manifestations neuropsychiatriques et les douleurs thoraciques étaient parmi les symptômes post-COVID les plus fréquents ce qui concorde avec d'autres études [27-41].

Studies (Ref.)	Country	Number of patients (n)	Post COVID frequency (%)	Most frequence post-COVID events
Halpin et al., 2020	United Kingdom	100	72 %	Fatigue, dyspnea, Neuro- manifestations psychiatric
Goertz, et al., 2020	Netherlands Belgium	457	87 %	Fatigue, dyspnea, headaches
Angelo et al.,2020	Italy	143	87,4 %	Fatigue, dyspnea, joint pain, chest pain, anosmia
Kamal, et al., 2020	Egypt	287	89,2 %	Fatigue, anxiety, joint pain, headaches
Algeria	**Algeria**	**96**	**57,3 %**	Fatigue, anosmia, neuro manifestations psychiatric, chest pain

Table 5: The Frequency and Most Widespread Clinical Manifestations of Post-Covid Syndrome in Different International Studies

4.3. Limitations of The Study

The sample size is still modest and the study results need to be corroborated by larger studies. Assessment of reinfection was based on participant reports during visits, as no RT-PCR monitoring was planned in the study. Therefore, it cannot be excluded that SARS-CoV-2 positive participants had unnoticed asymptomatic reinfection during follow-up. Another limitation is that we did not sequence the viral genome from the first infection and even for reinfections; therefore, we could not confirm reinfection with another SARS-CoV-2 variant.

5. Conclusion

In our study, 04 cases of probable reinfection with SARS-CoV-2 were noted, which gives an incidence rate of 4.17%, this low number of cases of reinfection indicates a relative reduction in the incidence of reinfection with SARS-CoV-2 in the previously infected group and that humoral immunity plays an important role in protection against reinfection, therefore, studies monitoring immune responses after natural infection and characterizing responses of long-term antibodies are of great importance in determining the incidence of reinfection. The 04 cases of probable SARS-CoV-2 reinfection found in our study were all symptomatic and mild cases. Available data showed that reinfections had a lower risk of symptomatic infection and severe disease than primary SARS-CoV-2 infection. The results of our study are consistent with recent studies reporting antibody persistence suggesting that immunity induced against SARS-CoV-2 by natural infection could be very effective against reinfection and could persist for at least 12 months.

These results provide insight into the interaction between the virus and the host immune system, as well as the persistence and duration of antibodies against SARS-CoV-2. Finally, globally, the number of patients recovering from SARS-CoV-2 infection with post-COVID syndrome continues to grow at an unprecedented rate. Therefore, we also undertook this study to estimate the frequency of the most common persistent symptoms, signs and post-COVID manifestations in our convalescents during the 12 months of follow-up after the acute phase of COVID-19. According to the results, we observed that a large proportion of convalescents presented persistent and variable symptoms for several months after the acute infection where the frequency of post-COVID syndrome was 57.3%. Fatigue, anosmia and neuropsychiatric manifestations were the most frequent symptoms among our convalescents.

In conclusion, the results of the study indicate that the chances of reinfection seem very low or zero for at least the first six months following infection, however post-COVID syndrome is increasingly present among those convalescents from a previous infection.

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