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REVIEW ARTICLE

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Long Covid-19: The Postsymptom Onset and its Association with the Antibody Body Titre

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ABSTRACT

The term "long COVID-19" refers to the long-term medical issues that may develop following infection with the new coronavirus (COVID-19). Fatigue, breathlessness, chest pain, trouble concentrating, and headaches are a few symptoms that can occur. Following their initial infection, people with long COVID-19 may continue to have these symptoms for weeks, months, or even longer. Managing the postsymptom onset of Long COVID-19 is a crucial factor to take into account. In this review, we looked into the relationship between long COVID-19 and its postsymptom onset with antibody body titre. It demonstrates that the postsymptom onset of extended COVID-19 was substantially correlated with the antibody body titre. The term "long COVID-19" refers to the long-term medical issues that may develop following infection with the new coronavirus (COVID-19). Fatigue, breathlessness, chest pain, trouble concentrating, and headaches are a few symptoms that can occur. Following their initial infection, people with long COVID-19 may continue to have these symptoms for weeks, months, or even longer. Managing the postsymptom onset of Long COVID-19 is a crucial factor to take into account. In this review, we looked into the relationship between long COVID-19 and its postsymptom onset with antibody body titre. It demonstrates that the postsymptom onset of extended COVID-19 was substantially correlated with the antibody body titre.

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Introduction

The worldwide healthcare calamities and strained healthcare assets due to the pandemic coronavirus disease 2019 (COVID-19) were caused by the pathogen named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Nalbandian et al., 2021). Until April 25, 2021, data of 3,092,410 deaths and 146,054,107 infections was demonstrated by the World Health Organization (WHO) globally [1]. According to reports, the death rate linked to COVID-19 is almost 3.5 times greater than that of seasonal influenza [2] [Figure 1].

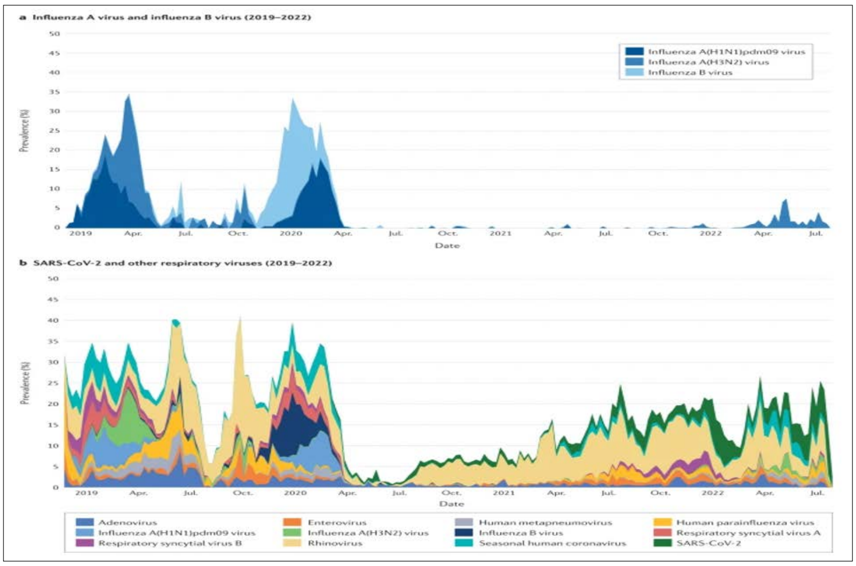

Figure 1: a. The incidence of the influenza A and B viruses (2019–2022).

b. SARS-CoV-2 and other respiratory viruses prevalence as indicated by the statistic: b.

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Respiratory samples from epidemiological weeks 47 in 2018 to 30 in 2022 are included; 154,740 samples in all were tested: 957 in 2018, 25,019 in 2019, 64,869 in 2020, 48,458 in 2021, and 15,437 in 2022. A custom-arrayed reverse transcription-PCR platform (Thermo Fisher) 3 was used to evaluate respiratory specimens. Picture from Seattle Flu alliance's [3].

The propensity of SARS-CoV-2 to develop to elevated amounts in the upper respiratory tract [4] and, as a result, to easily transmit to other individuals, was a crucial element contributing to the COVID-19 pandemic. After infection SARS-CoV and MERS-CoV are more prevalent in the upper respiratory tract, which is associated with the capacity to prevent transmission using effective public health infection-prevention strategies [5].

Long Covid-19

It is known that some persons with COVID endure several post-acute health issues well following their disease beginning, even though SARS-CoV-2 is forecast as an acute illness. The term "long COVID" has been used to describe this condition of long-term persisting symptoms[6]. The World Health Organization defined COVID-19 sequelae as follows: "A condition that occurs in individuals with a history of probable or confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, usually 3 months from the onset of COVID-19 with symptoms, and that lasts for ≥2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction, and others; moreover, it generally affects everyday functioning" [7]. It is also known as COVID-19 long-haulers, long-haul COVID-19 or post-COVID-19 syndrome.

In 2019, during the COVID-19 outbreak, various epidemiological investigations have discovered that a significant proportion of patients have long COVID [8-10]. Relying on a conservative estimate of 10% of infected people and more than 651 million COVID-19 cases documented globally, it is estimated that at least 65 million people worldwide have long COVID; however, due to the unreported cases, this count is likely to be much higher [11]. Long COVID can persist for weeks, months, or beyond than acute COVID, which generally lasts 3 weeks [12-15]. In an Italian study, 87% of patients had symptoms that remained 60 days following the initiation of COVID-19 [8]. A similar large cohort research from China revealed that 76% of individuals with COVID-19 still have some symptoms six months after their symptoms first appeared [16].

Different nations utilize distinct long COVID diagnosis criteria. The US guidelines define post-COVID illness as persistent symptoms that last for more than 4 weeks well after initial infection [17,18]. However, The UK standards' summary states that long COVID is classified as acute COVID-19, ongoing symptomatic COVID-19, and post-COVID-19 syndrome, depending on how long symptoms have persisted after the onset of COVID-19: up to 4 weeks, up to 12 weeks, and more than 12 weeks, respectively [19,20]. Additionally, Japan does not currently have a specific standard for long COVID but patients with Long COVID may access services from facilities employing certificates proving single vaccination and healing if the antibody titer following a single vaccination in those patients is similar to or higher than that in fully vaccinated noninfected persons. It is yet unknown, though, how postvaccination antibody titers and symptom alterations following a single vaccination in individuals with Long COVID relate to one another [21].

IgG and IgM Antibodies

The COVID-19 infection's clinical course could be asymptomatic, or it could entail mild to severe symptoms. In extreme cases, multiorgan dysfunction outside the lung might be observed, along with abnormalities in many tissues and organs that necessitate artificial breathing [22]. There is little and inconsistent information available regarding how antibodies affect infection severity and how long antibody responses last after the disease. In one investigation, for instance, COVID-19-specific antibodies were shown to be constant for about 82 days, whereas in other studies, a decline was observed in antibodies titre 2-3 months after infection [23]. Moreover, people with COVID-19 symptoms that are modest have been observed to have decreased antibody responses [24,25]. Patients with severe COVID-19 have highly expressed antibodies specific to the virus in their sera [26].

It has been reported that there exists not only a significant but also mutually distinctive functions between antibodies including immunoglobulin M (IgM) and immunoglobulin G (IgG), and nucleocapsid (N) and spike (S) proteins of SARS-CoV-2 in the host immune system [27]. While recovering from the infection, the sustainable production of IgG keeps eradicating the virus in severe acute respiratory syndrome (SARS) by an ancestral coronavirus of SARS-CoV-2 which is the causative agent [28]. It has also been noted that a high antibody titer and disease severity are positively correlated [29]. Likewise, starting two weeks after the onset of symptoms and continuing up to two months, IgG antibody titers were observed high in Long COVID patients [28]. Delays in antibody production responses were linked to Middle East Respiratory Syndrome (MERS) severity in one study, although the study's patient population as a whole was rather small [30].

Postsymptom Onset & Association with Antibody Titre

The potential associations with antibody titre usually include age, symptom severity, gender, medications, BMI, and concomitant chronic disease. Individuals with poor antibody responses typically had, loss of smell and anxiety issues, whereas those with robust antibody responses frequently had chest pain [31]. There exists a positive correlation between persistent fever, advanced age, and antibody titers [32]. However, myalgia shows contrasting behaviour in different studies with antibody titre [31,32].

A recent meta-analysis found that males are more likely to have a higher mortality rate than females from COVID-19 [33]. Besides males had considerably greater antibody titers against COVID-19 in the first two months than females [34]. Yet, in one cohort, both men and women had the same antibody response. The antibodies' binding potency was the same in both critical disease-affected men and women. Only in the hospitalised group male anti-receptor binding domain (anti-RBD) have antibody binding strength that differs from female anti-RBD antibody binding strength. This suggests that the variation in illness severity between males and females is not primarily due to the main antibody response. It's likely that differences between the innate immune systems of the sexes in their response, such as the complement system, could be crucial [35-37].

Post-COVID-19 syndrome was substantially correlated with the existence of IgG antibodies [38]. The age group ≤36 shows less prevalence of fever symptoms relative to the age group of 47 to

57. Males appear to be more susceptible to a fatal illness, serious illness, and poor outcomes [35]. Therefore, men experienced statistically more fever, shortness of breath, and chest pain than women. The antibody response (AbR) in two weeks and chest discomfort were found to be positively correlated. Unexpectedly, there was a significant negative correlation between AbR at 15, 30, and 60 days with myalgia symptoms; over two months time period, there was a negative correlation between AbR and anxiety and loss of smell [31,39]. In addition, whereas drugs, BMI, concurrent chronic disease, medications, and disease severity did not alter the antibody response, gender and age did [31].

Significant evidence points to abnormalities in the brain in COVID-19 [40-45]. While comparing the affected and unaffected groups, there were several significant longitudinal effects. The thickness of grey matter and parahippocampal gyrus and orbitofrontal cortex tissue contrast have substantially reduced. Also, the tissue damage in areas physiologically connecting to the primary olfactory cortex has identified alteration in their markers and the SARS-CoV-2 cases, a clear overall brain size reduction. Also, those who had SARS-CoV-2 infection demonstrated a larger average cognitive impairment between the two time points [46].

In patients even with prior SARS-CoV2 infection, non-vaccination increases the risk of reinfection[47]. Thus, vaccination is essential for Long COVID patients to avoid reinfection. Prevaccination antibody titers are often equivalent to or lower than those following a single vaccination in healthy individuals [48]. Postvaccination symptoms (olfactory anomalies, joint pain, fatigue, and taste) in 17%, 21%, and 62% of patients were relieved, made worse, or remained the same, respectively. The peak antibody titer ratio was substantially more significant in the worsened group than in the non-worsened group, indicating an overactive immunological response to the vaccine that was linked to the severity of sequelae. Also, compared to the later group, the worsened group displayed a considerably larger change ratio in the antibody titer [49].

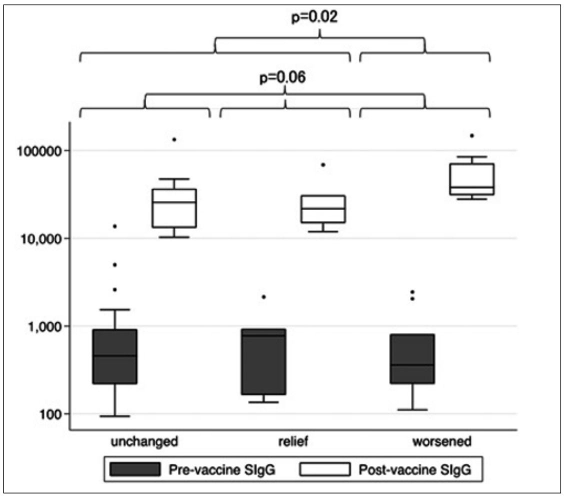

Figure 1: This graph compares the antibody titers before and after immunisation across three groups (unchanged, relieved, and worsened).

There are no discernible differences between the pre-and post-vaccination antibody titers ratios (Kruskal-Wallis test, $p = 0.06$). In a comparison to the non-worsened group, the worsened group exhibits a significantly higher antibody titer ratio [46].

Summary

The levels of antibodies in those who experienced symptoms for three or more weeks were studied in the study. The findings demonstrated that those with more severe symptoms had considerably greater antibody titres in patients with extended COVID-19. According to these findings, a person's antibody titres will likely be higher the longer they experience symptoms, indicating that they have been exposed to more of the virus. Males are more susceptible to postsymptoms as compared to females. The study also discovered that, over time, the antibody titres fell, suggesting that the body's immunological response may be weakening. This study offers additional proof that the body's immune response to the virus is dynamic and adapts over time. The results imply that the antibody body titre may be a useful tool for clinicians in the management of protracted COVID-19 since it may be employed to anticipate the postsymptom onset but more extensive research is required to develop a clear understanding of the association between postsymptom onset and antibody titre.

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