

A glimpse into Long COVID characteristics and the mental health impact within a highly vaccinated population: a Malta observational study

Sarah Cuschieri¹, Stephan Grech² and Victor Grech³

¹Department of Anatomy, Faculty of Medicine & Surgery, University of Malta, Msida, Malta

²Department of Trauma & Orthopaedics, Mater Dei Hospital, Msida, Malta

³Department of Paediatrics, Mater Dei Hospital, Msida, Malta

Abstract

Background. Post-acute COVID-19 consequences are gaining global recognition. This study explores Long COVID characteristics and associated mental health impact/s among the highly vaccinated adult population of Malta.

Methods. A social media survey gathered demographics, vaccination, and COVID-19 data. Generalised Anxiety Disorder and Patient Health Questionnaire-9 assessment tools were used for anxiety and depression. Quantitative analyses were performed.

Results. 41% reported Long COVID, mostly female, 30-39 years, absence of chronic disease/s and vaccinated. Shortness of breath commonest persistent symptom among males, and fatigue for females. Significantly higher depression scores were present in Long COVID cohort compared to no persistent symptoms ($p=0.001$) and never acquiring COVID-19 ($p<0.01$). A significant higher anxiety scores was present for Long COVID cohort than never acquiring COVID-19 ($p<0.01$).

Conclusions. Long COVID occurs even in healthy individuals and vaccinated, while exacerbating mental health burdens. Urgent action is required to manage Long COVID and preventing the sequela.

Key words

- coronavirus
- vaccines
- population health
- mental health
- post-acute COVID-19 syndrome
- Malta

BACKGROUND

The coronavirus disease 2019 (COVID-19) has spread across the globe resulting in a spectrum of clinical outcomes from asymptomatic to fatal disease [1]. It became evident quite early on that some infected individuals were experiencing persistent symptoms beyond the acute phase due to prolonged viral involvement affecting multiple organs [2]. These individuals were labelled as experiencing Long COVID. Indeed, a plethora of different persistent symptoms were reported among Long COVID individuals [3]. Another pandemic induced problem is the increased mental health burden, especially in terms of stress, anxiety and depression that arose from implemented restrictions, isolation, job loss and fear of acquiring the viral infection [4, 5]. Furthermore, the occurrence of Long COVID also impacts on the mental health of the sufferer [6]. As COVID-19 vaccines became available, it was anticipated that the protection provided by the vaccine lowered the viral infectivity rate as well as the development of

Long COVID when compared to unvaccinated [7]. A recent study reported that COVID-19 vaccine inoculation with at least one dose reduces the mental distress among the population [8]. As most countries are moving into the post-acute pandemic phase and vaccination rates have stabilised, it is essential that Long COVID and its associated burden including mental burden, are prioritised in the recovery agenda which brings forward the need for extensive research in this area.

The European Islands of Malta, like the rest of the world, experienced surges in COVID-19 infectivity rates with an estimated loss of 5,478 years of full health over the first year of the pandemic [9]. Indeed, similarities in COVID-19 epidemiological trends and mitigation measures were identified between Malta and other European countries and microstates [10, 11]. Additionally, it was noted that Long COVID led to the highest morbidity over one year in Malta [9]. Malta's COVID-19 vaccination rollout along with the low vaccine hesitancy among the population led to a successful

rapid vaccination coverage of almost the whole eligible population by summer of 2021 [12]. The end of summer 2021 saw a surge in Delta variant cases and prompted the initiation of a booster dose [13]. The local high vaccination uptake and the fact that Long COVID was a predominant contributor to morbidity prior to vaccination makes Malta an ideal geographical location to evaluate the characteristics of Long COVID. Furthermore, Malta has been recognized by the director of the World Health Organization for the Region of Europe as being an exemplary country for the COVID-19 commitment over the two years of the pandemic [14]. Considering recent findings [7, 8], that a high vaccination rate could decrease the occurrence of Long COVID among populations with a reduction in mental health burden, Malta is the ideal research setting to validate this finding and understand the impact of Long COVID and the mental health burden. This study evaluates the presence and characteristics of Long COVID among the adult population of Malta and their perspectives on the COVID-19 vaccine while assessing anxiety and depression levels among these individuals.

MATERIALS AND METHODS

This study was a cross-sectional study conducted using an anonymous online survey. Google Forms® platform was used to host the survey that was designed by the authors to target adults residing in Malta. The survey was disseminated through social media via a snowball technique between the 25th of January and the 6th of February 2022. Social media is mostly used to share public opinion and its users represent a substantial proportion of the global population, making social media an ideal platform for dissemination of this survey [15]. Indeed, in 2021 it was reported that 420,000 social media users were registered in Malta [16]. Dissemination through snowball technique, also known as responder-driven sampling, was considered adequate due to the sensitivity of some of the questionnaire questions [17]. Additionally this sampling technique was reported to enable asymptotically unbiased estimates [18].

The survey gathered information on the demographic profile of the participants, their medical history, COVID-19 vaccination status, their perspectives on the COVID-19 vaccine, whether they acquired COVID-19 and had persistent symptoms post-acute infection that lasted beyond two months [19]. Additionally, the survey incorporated the GAD-7 (Generalised Anxiety Disorder) assessment tool to evaluate the level of anxiety the participants experienced by providing 7 different concerns with the following question stem “Since the end of Summer (2021), how often have you been bothered by any of the following concerns?” [20]. The PHQ-9 (Patient Health Questionnaire-9) assessment tool was used to evaluate the level of depression by providing 9 different concerns with the following question stem “Since the end of Summer (2021), how often have you been bothered by any of the following concerns?” [21]. The end of summer 2021 saw the shift from a low case number to a surge in COVID-19 cases and mortality in Malta, as well as a high population vaccination coverage with the initiation of the booster dose. This makes

this period the ideal starting point to evaluate the anxiety and depression levels among the population.

Ethical approval was granted by the University of Malta Research Ethical Committee (MED-2022-00017).

Data analyses

The GAD-7 score was calculated as per published guidelines [22]. The sum of the GAD-7 questionnaire score for each participant was categorised into ≤ 4 as having no symptoms; 5-9 as mild symptoms; 10-14 as moderate symptoms and >15 severe symptoms. The PHQ-9 score followed published guidelines where the total score and depression severity were divided and defined as follows: 0- 4 score as “minimal depression”; 5-9 score as “mild depression”; 10-14 score as “moderate depression”; 15-19 score as “moderate severe depression” and 20-27 score as “severe depression” [23]. The GAD-7 and PHQ-9 scores were compared between those that reported to have persistent symptoms (Long COVID-19) and those that had COVID-19 with no persistent symptoms as well as with those that never acquired COVID-19, through Chi Square analysis. Descriptive analyses and chi squared testing for categorical comparisons were performed using Microsoft Excel®.

RESULTS

A total of 611 adults participated in the survey, with 20.20% ($n=122$) reporting having acquired COVID-19, with a female predominance (71.3%). Out of those having COVID-19, 41% (CI 95%: 32.7-49.9; $n=50$) reported having symptoms beyond 2 months following their initial diagnosis, with a female majority (82%; CI 95%: 69.0-90.5; $n=41$). None of the participants suffering from Long COVID-19 were admitted to hospital for their acute infection. Persistent symptoms were mostly reported among the younger age groups, especially those between 30-39 years of age, those that did not suffer from any chronic diseases and were vaccinated. A summary of the Long COVID-19's cohort characteristics is shown in *Table 1*. The commonest persistent symptom reported by males was shortness of breath (33.33% CI 95%: 12.0-54.9; $n=3$) while fatigue was predominately reported by females (17.1% CI 95%: 8.2-31.6; $n=7$). Different long-standing symptoms were reported, as can be seen in *Table 2*.

On exploring for anxiety and depression levels using the GAD-7 and PHQ-9 scores (*Figure 1*), it was noted that those reporting having Long COVID-19 had a significantly higher anxiety score than those never acquiring COVID-19 ($p<0.01$). Additionally, the Long COVID-19 cohort had significantly higher moderate and severe depression scores when compared to both those acquiring COVID-19 with no persistent symptoms ($p=0.001$) and those never acquiring COVID-19 ($p<0.01$).

Although the majority opted to be fully vaccinated including taking the booster dose, their perception on the COVID-19 vaccination varied, as shown in *Table 3*. Indeed, a proportion perceived the vaccine to be restricting their freedom (48%) and that the vaccine is responsible for more side-effects than those reported (36%).

Table 1
Long COVID-19 cohort characteristics

| | | Acquired COVID-19 infection | | Chi p-value |
|--|-------------------------|-----------------------------|-------------------------------|-------------|
| | | Long COVID (n=50) | No persistent symptoms (n=72) | |
| Gender | male | 18.0% | 36.1% | 0.03 |
| | female | 82.0% | 63.9% | |
| Age group | 18 - 19 | 0.0% | 1.4% | 0.04 |
| | 20 - 29 | 10.0% | 25.0% | |
| | 30 - 39 | 62.0% | 33.3% | |
| | 40 - 49 | 16.0% | 23.6% | |
| | 50 - 59 | 10.0% | 6.9% | |
| | 60 - 69 | 2.0% | 8.3% | |
| | 70 - 79 | 0.0% | 1.4% | |
| Chronic diseases | yes | 16.0% | 25.0% | 0.23 |
| | no/do not know | 84.0% | 75.0% | |
| Vaccination status | vaccinated/boostered | 96.0% | 80.6% | 0.01 |
| | no booster and anti-vax | 4.0% | 19.4% | |
| COVID-19 positive following vaccination | yes | 47.9% | 56.9% | 0.36 |
| | no | 52.1% | 43.1% | |

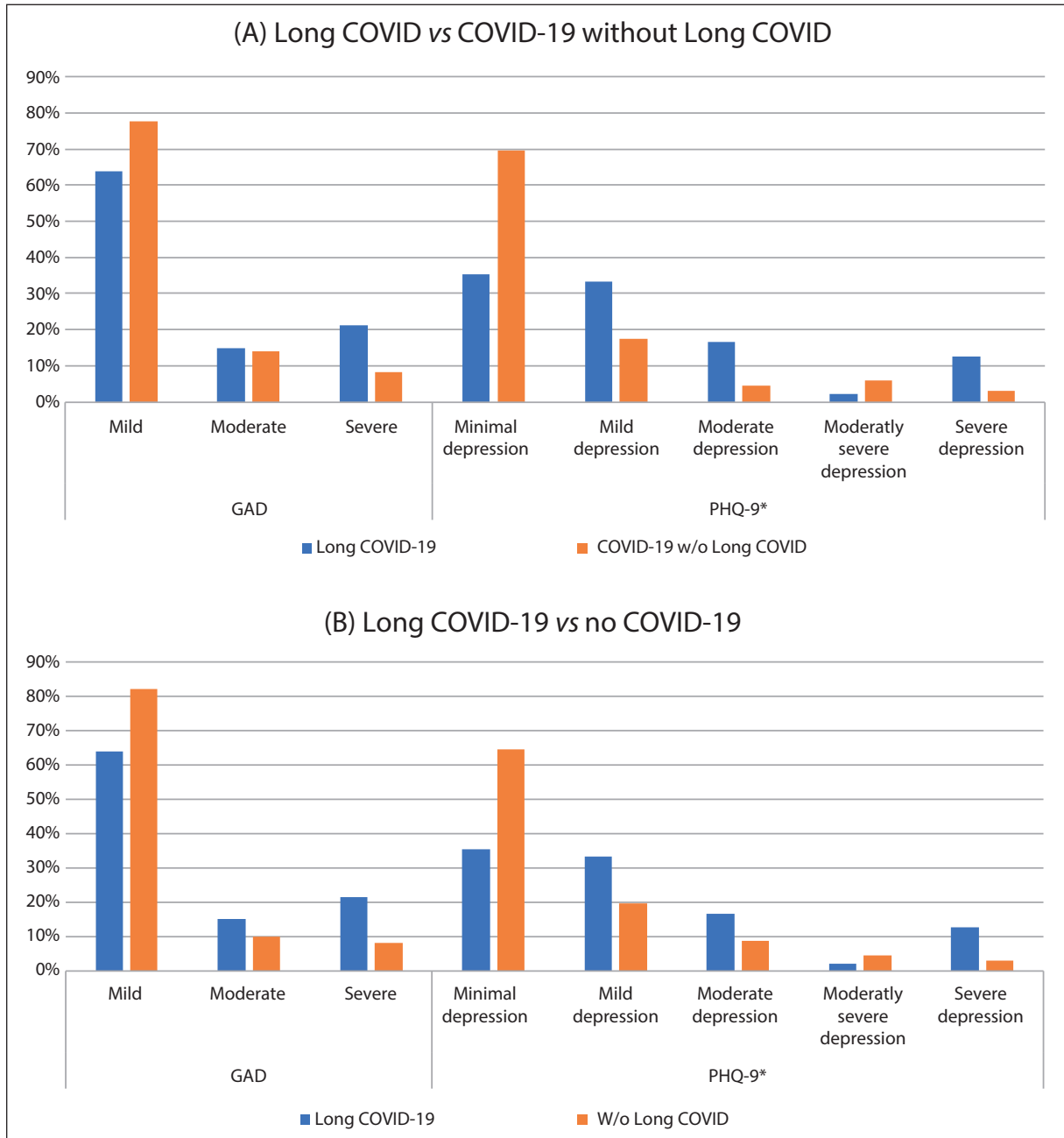
Table 2
Persistent most common symptoms reported by the Long COVID-19 cohort

| | Male (n=9) | Female (n=41) |
|--|------------|---------------|
| Shortness of breath and back pain | 33.3% | 4.9% |
| Aches and pains in joints | 11.1% | 2.4% |
| Aches and pains in your joints, fatigue/tired, dizziness | 11.1% | 2.4% |
| Aches and pains in your joints, shortness of breath, fatigue/tired, aches in heels | 0.0% | 4.9% |
| Headaches | 11.1% | 0.0% |
| Headaches, cough, dizziness | 11.1% | 17.1% |
| Headaches, aches and pains in the joints, shortness of breath, Dizziness and back pain | 0.0% | 4.9% |
| Loss of smell and taste | 0.0% | 4.9% |
| Loss of taste and headaches | 11.1% | 0.0% |
| Shortness of breath and fatigue | 11.1% | 7.3% |
| Shortness of breath and cough | 0.0% | 4.9% |
| Back pain | 0.0% | 4.9% |
| Fatigue | 0.0% | 7.3% |

DISCUSSION

A proper comprehension of the underlying pathophysiology leading to Long COVID among selected infected COVID-19 positive individuals is still in the early stages although various theories have been put forward including autoimmunity, aberrant immune response/s and virus persistence in immune-privileged sites [24]. Several continuing symptoms have been reported with

fatigue and dyspnea being common ones [3, 25, 26], as noted in this study. Despite this, the current study observed a gender specific trend. The higher female susceptibility for Long COVID is consistent with other reports [27]. However in this study, unlike previously reported [28], the Long COVID cohort were mostly previously healthy and did not require hospitalization for their acute infection. It is currently debatable whether vaccination protects against the occurrence of Long COVID [29]. It has been reported that vaccination halves the chance of getting Long COVID, with the over-60s being at greater risk of experiencing this if a breakthrough infection occurs [30, 31]. While this is a relatively small study, the observations cannot be dismissed, where despite high vaccination rates, including uptake of the booster dose across all age groups, a high proportion of Long COVID was reported even among the younger adults (<60 years). Further research is recommended as these observations may have non-trivial public health consequences necessitating urgent action. This is particularly the case since long-term trajectory of this disability is unknown, [32] affecting the young generation with related economic, social and health sequela [33, 34]. It is therefore not surprising that experiencing Long COVID led to different perspectives on the COVID-19 vaccine, although inoculation was perceived as providing protection against the virus, coinciding with another study [35]. Additionally, Long COVID individuals expressed a positive perspective on the importance of mass vaccination especially among the vulnerable population even though vaccines were perceived to be responsible for more side effects than those reported. This demonstrates the individuals' acceptance of vaccines for the common good despite potential misgivings and fear of side effects.

**Figure 1**

(A) Comparison analyses of the anxiety score (GAD) and depression score (PHQ-9) between the cohorts suffering from Long COVID, acquiring COVID-19 but have no persistent symptoms and (B) Comparative analyses between those suffering from Long COVID and those never acquiring COVID-19.

w/o: without.

*Chi square test between Long COVID cohort and COVID-19 w/o persistent symptoms.

**Chi square test between Long COVID cohort and those never acquiring COVID-19.

Negative perceptions were also evident including a significant impact on the mental health of the affected cohort. The population's mental health burden has been a public health concern since before the onset of the pandemic. The COVID-19 pandemic has driven this burden further exacerbated with the implemented restrictions in addition to COVID-19 morbidity and mortality [36, 37]. The continuous media coverage along with the unpredictable outcome of the disease also

contributed to the negative impact on the population's mental health burden [38, 39]. Therefore, acquiring the infection while continuing to suffer from persistent symptoms is expected to take a toll on mental health. This was reflected in this current study. However, as the vaccination rate increased, it was expected to lead to a reduction in the occurrences of Long COVID and the associated mental health impact [6, 8]. Yet, as observed in this study, where most of the population was fully

Table 3
Perspectives of the Long COVID-19 cohort on vaccination

| Perspectives on COVID-19 vaccination | | Long COVID-19 cohort |
|---|-----------|----------------------|
| The COVID-19 vaccine provides protection from getting the infection | Agree | 38% |
| | Disagree | 30% |
| | Undecided | 32% |
| The COVID-19 vaccine causes more side effects than those reported | Agree | 36% |
| | Disagree | 34% |
| | Undecided | 28% |
| Mass vaccination is essential for the population to be protected against COVID-19 | Agree | 68% |
| | Disagree | 6% |
| | Undecided | 26% |
| It is essential to continue wearing masks, maintaining physical distance and hand washing following vaccination | Agree | 76% |
| | Disagree | 8% |
| | Undecided | 12% |
| The COVID-19 vaccine provides long term protection against COVID-19 infection | Agree | 12% |
| | Disagree | 48% |
| | Undecided | 40% |
| Those suffering from health issues should take the vaccine | Agree | 60% |
| | Disagree | 10% |
| | Undecided | 28% |
| The COVID-19 vaccine reduced deaths and hospitalisation | Agree | 54% |
| | Disagree | 16% |
| | Undecided | 28% |
| Taking the COVID-19 vaccine is useless | Agree | 6% |
| | Disagree | 58% |
| | Undecided | 34% |
| The COVID-19 vaccine is the solution to returning to normality | Agree | 44% |
| | Disagree | 16% |
| | Undecided | 38% |
| The COVID-19 vaccine is controlling our lives and freedom | Agree | 48% |
| | Disagree | 32% |
| | Undecided | 16% |

vaccinated and some even had the booster, the occurrence of Long COVID along with the anxiety and depression aftermath were still evident. A potential reason to the Long COVID occurrence could be the reduced efficacy of the vaccination against the Delta and the Omicron variants [40]. This brings forward the need to investigate further these occurrences and their consequences with the possibility of labelling Long COVID a new chronic disease. The burden of mental health does not appear to be subsiding therefore it is imperative that psychological help is readily available to support affected individuals. Tackling mental health burden should be high up on agenda as its occurrence has multifactorial impacts on the quality of life, the work force as well as healthcare systems.

This study should be considered in the context of its

strengths and limitations. This is the first study in Malta to explore Long COVID characteristics and its impact on mental health, providing timely information that public health officials and policy makers can utilize as part of the post-pandemic recovery plans. This observational study managed to capture a good proportion of adults across different socio-economic strata, even if its distribution was through social media. However, due to the study's mode of distribution it was deemed difficult to achieve a sample size based on the population, as was the calculation of a response rate. Every effort was made to recruit as many adult participants as possible. Yet, a small sample size was still achieved with potential low statistical power. The vast majority of the Maltese population are known to access social media platforms (420,000 users out of 443,000 population) and thus, with the usual provisos of selection bias inherent in any form of survey, participation was dependent on responder-driven dissemination with reasonable (albeit impossible to exactly define) coverage. [16]. It needs to be noted that both shortness of breath and fatigue symptoms, that for this study were considered as Long COVID symptoms, although these could have been the result of anxiety and depression, respectively. Therefore, we cannot exclude the possibility of over-estimation of Long COVID. This was a cross-sectional study, hence even though participants were instructed to provide an indication of their anxiety and depression levels since the end of summer, the scores provided are only indicative of their mental health status at the point in time of participation. Furthermore, more females participated than males in the survey, a phenomenon already reported where females tend to respond to surveys more than males [41], however this might have led to responders' bias. Considering that this study ran less than 2 months from the Omicron variant dominance in Malta, all participants reporting Long COVID had their acute infection during periods where the vaccines had substantial effectiveness against COVID. Therefore, it is safe to say that the Long COVID participants had breakthrough infections whilst being ostensibly vaccine protected. However, the sample size was small and does not necessarily reflect the complete experiences, attitudes, and perspectives of all the general adult population and COVID-19 positive individuals in Malta. This small size affected the ability to undergo regression analyses and fully test the current hypothesis, therefore a larger study is recommended. There is also the possibility of self-reporting and recall bias, as with any survey. Additionally, the occurrence of Long COVID among the participants might have changed following the completion of this survey.

CONCLUSIONS

Long-term sequela of COVID-19 are becoming a common occurrence among positive individuals, and it appears that being previously healthy, and young does not preclude suffering from Long COVID. Long COVID is exacerbating mental health burdens with potential long-term consequences at an individual and a national level. Therefore, Long COVID and mental health should be high up on the public health and policy mak-

ers agendas to ensure timely management and prevention of the associated debilitating consequences.

Authors' contributions

SC designed the concept of the study. All Authors were involved in the developing of the survey. SC was responsible for the data analysis and for writing the draft article. All Authors reviewed and approved the final version of the manuscript.

Availability of data and materials

Data is available upon request.

Ethics approval and consent to participate

Ethical approval was granted by the University of Malta Research Ethical Committee (MED-2022-

00017). Participants provided their informed consent on accepting to participate in the survey.

Consent for publication

Participants provided consent for publication on accepting to participate in the survey.

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Conflict of interest statement

Authors declare they have no competing interests to declare.

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