# **ORIGINAL ARTICLE - PUBLIC HEALTH**

# POST COVID SEQUELAE AMONG PEOPLE INFECTED WITH COVID-19 IN TAMIL NADU – A CROSS SECTIONAL STUDY

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#### Abstract

BACKGROUND : Tamil Nadu witnessed three pandemic peaks since the first COVID-19 case on March 7, 2020. Long-term effects, termed long COVID, persist with various symptoms and organ involvement. Despite the Indian government's guidelines, there's limited data on long COVID among survivors in India. This study was done to find the burden of post covid symptoms among individuals who tested positive for Covid-19 between March 2020 and February 2022 in Tamil Nadu, other than Chennai.

METHODS : A cross-sectional study in Tamil Nadu, excluding Chennai, was conducted among 1673 COVID-19 cases in June 2023 who were selected by stratified random sampling, stratified by age groups. Trained health staff gathered data using a semi-structured questionnaire, defining persistent post-COVID-19 symptoms as lasting more than 12 weeks. Data was entered in Excel and analysed using JASP software.

RESULTS : Among 1673 patients approached, 380 participants could not be contacted even after multiple attempts. Among the rest 1293 patients, seventy three patients(5.6%) were reported to have died. The overall prevalence of persistent post Covid symptoms was 21.3% (95% CI -19.04% - 23.72%). The most common symptom reported was loss of appetite and persistent fatigue. there is no significant association between gender, age group, pandemic wave, number of episodes of covid infection, covid vaccination and persistent post covid symptoms. However, hospitalisation, oxygen requirement, ventilatory support requirement, lung involvement and presence of any comorbidities was significantly associated with persistent post covid syndrome.

CONCLUSION : Targeted interventions for individuals with a history of severe COVID-19, pre-existing comorbidities, and specific post-COVID complications, healthcare systems can better support the holistic recovery and well-being of those affected by the long-term effects of the virus.

**KEY WORDS** : Long Covid, Post Covid, Persistent Post Covid Symptoms

#### **INTRODUCTION**

Tamil Nadu had the 1st case of Covid -19 on March 7th, 2020, ever since then there had been an increase in the number of cases with the state having witnessed 3 peaks of the pandemic in the year 2020 ,2021and 2022. There are evidences which states that Covid -19 does not end with acute infection, but continue to have long term effects affecting multiple organs. In a meta-analysis done by Leon's et al, reported more than 50 different long-term effects of Covid -19 with the time duration ranging from 14 to 110 days post viral infection. The meta-analysis reported that 80% of the infected people continued to have at least one effect even after 2 weeks of the infection. The 5 most common symptoms reported was fatigue, headache, attention deficit, hair loss and dyspnoea. But no studies from India was included in the meta-analysis.1 WHO had reported that the time duration how long the post covid 19 condition also called as long Covid or Long Haulers persist as non-predictable.<sup>1</sup> In a recent prospective study conducted in China reported that 55% of Covid -19 survivors had long Covid effects at the end of 2 years, though there was a persistent decrease in the symptoms over a period of time.<sup>2</sup> Long term effects of Covid

-19 are also referred as post COVID condition, long COVID, post COVID syndrome etc. While there is still a debate on defining post COVID-19 condition, WHO defines it as , 'an illness that occurs in people who have a history of probable or confirmed SARS-CoV-2 infection; usually three months from the onset of COVID-19, with symptoms and effects that last for at least two months. The symptoms and effects of post COVID-19 condition cannot be explained by an alternative diagnosis.<sup>6</sup> The Ministry of Health & Family Welfare, Government of India (MOH&FW, GOI) defines post COVID syndrome as a condition characterised by signs and symptoms that develop during or after an infection consistent with COVID-19 which continue for more than 12 weeks and are not explained by alternative diagnosis.<sup>3</sup>

While the Government of India, had framed guidelines for management of post Covid sequelae, there are very scarce data available from Indian context to understand the burden



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of long Covid among Survivors of Covid -19.3 A standing parliamentary committee headed by Lok Sabha member PP Chaudhury, has suggested the Union Government to take up studies on long term impact of Covid -19 in India.4 This gives the sense of a dire need for estimating the burden of Long covid effects among survivors of Covid -19 post 2 years of infection. However, the long-term effect of the Covid-19 infection among the survivors has been studied in Tamil Nadu piecemeal. In a study done by ICMR among hospitalised patients with COVID-19 found that Dyspnoea, fatigue and mental health issues as the common post common conditions reported at the end of 1 year follow up and this also reported 4.3% death within 60 days post discharge. The study also compared the three waves of the pandemic and found that the post- discharge death before the first followup was highest among the patients admitted during the third wave of COVID-19.5 This study was done only among hospitalised patients and did not have any information about non-hospitalised patients. In another study conducted to find the burden of post COVID\_19 condition during the 12-14 post recovery period of COVID-19 in Chennai, Tamil Nadu, reported 24% to have post covid symptoms. However, this study was done only within 12-14 week recovery period and included only patients from Chennai.<sup>6</sup> To overcome these gaps, a cross-sectional study was conducted among patients who tested positive for Covid -19 between March 2020 - February 2022 to find the burden of post Covid-19 condition in Tamil Nadu other than Chennai.

#### **METHODS**

A cross sectional study covering population infected at different time interval after Covid infection from March 2020- 31st March, 2022 in Tamil Nadu other than Chennai was done. The study was conducted in the month of July 2023. Assuming 50% variability, and 95% confidence level and 5% absolute precision, the required sample size is 384. To get the result stratified across different time interval post Covid infection starting from 1 year to 3 years post covid irrespective of the severity of infection, the sample size was corrected. To account for non-response rate of 30%, the corrected sample size is 1492, which was rounded off to 1500. However, 1673 patients was included in the survey. In Tamil Nadu, RT-PCR was the only method of testing for diagnosing Covid -19. The line list of RT-PCR positive cases with their contact numbers is updated in the Directorate of Public Health & Preventive Medicine. The line list of all Covid -19 infection who tested positive from March 2020 -31st March 2022 was obtained to form the sampling frame,

from which the required sample size was randomly selected by stratified random sampling method. The list was stratified into 5 different age groups, <30years, 31-45 years, 46-60 years, 61-75 years, >75 years. The necessary sample from each age group was obtained based on population proportion to size . All the selected individuals were contacted by the trained health staff of the respective district through phone using the contact details available. For those participants, who could not be contacted through phone, the field health workers attempted to visit them in person in the given address. Participants were explained about the purpose of study using a standard transcript which was read by the health staff and verbal consent obtained for participating in the study. Those who give consent were interviewed using a semi- structured questionnaire. Data collection was done by trained health staff who were trained adequately on the study protocol, obtaining consent, interviewing using the semi-structured questionnaire. Details regarding demographic profile, history related to Covid -19 infection and vaccination, co-morbidities and post Covid symptoms were obtained. The operational definition for persistent Post COVID-19 symptoms is the presence of clinical symptoms that developed during or after an infection consistent with COVID-19, persistent for more than 12 weeks. The list of post covid-19 symptoms were taken from the meta-analysis done by Leon et al which reported on the various long term effects.7The patients were grouped based on the date of their latest infection with respect to the three waves of the pandemic, considering first wave from the beginning of the pandemic until 1 February 2021, second wave from 2 February 2021 until 15 December 2021, and the third wave from 16 December 2021 to 31 March 2022.

COVID 19: Current Status - Comparison of positive cases in 3 Waves (5/6) (10.06.2020 to 10.04.2022, N= 3452899 2 weeks interval)



### Figure 1. Covid Pandemic Waves in Tamil Nadu Source: Office of Directorate of Public Health and Preventive Medicine

Symptoms are presented as frequency and proportions, while continuous data are presented as mean (SD) or median (IQR), as appropriate. The frequency of post COVID symptoms was also segregated by the three waves of the pandemic, corresponding to alpha, delta and omicron wave. Odds ratio (OR) with 95% confidence interval (95% CI) for the association between hospitalization, severity of infection , pandemic wave, vaccination and persistent symptoms. Data

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analysis was carried out using JASP software.

#### **RESULTS**

Among 1673 patients approached, 380 participants could not be contacted even after multiple attempts. Among the rest 1293 patients, seventy three patients(5.6%) were reported to have died. The demographic profile of the deceased patients is given in table 4. The mean age of the study participants was 41.1 years (SD -17.2 years) with age ranging from 1 year to 90 years. Table 1 gives details about the demographic profile and Covid-19 infection of 1220 patients who responded to the survey. Larger proportion of the study participants reported infection in the 2nd wave and around 41% had hospitalization history. Around seven percentage of study participants reported to have repeated covid infection.

# Table 1. Demographic and Covid -19 infection related details of the study participants(n- 1220)

Variable		Frequency	Proportion
	1-10	30	2.5%
	11-20	103	8.4%
	21-30	235	19.3%
	31-40	268	22.0%
Age Group	41-50	211	17.3%
	51-60	203	16.6%
	61-70	115	9.4%
	71-80	41	3.4%
	81-90	14	1.1%
Candan	Male	690	56.6%
Gender	Female	530	43.4%
	Illiterate	130	10.7%
	1 <sup>st</sup> -5 <sup>th</sup> standard	131	10.7%
Education Status	6 <sup>th</sup> -10 <sup>th</sup> standard	267	21.9%
Education Status	Higher Secondary	215	17.6%
	Graduate	414	33.9%
	Post graduate	63	5.2%
Latest infection Pandemic	1st wave	301	24.6%
	2nd wave	724	59.3%
wave	3rd wave	195	15.9%
No of episodes of Covid 19	1	1134	93%
infection	>1	86	7%
Hospitalization for Covid -19		507	41.6%
Oxygen requirement		106	8.6%
Ventilatory support		18	1.4%
Lung involvement as radiolog	gical finding	213	17.5%
Covid -19 Vaccination with a	t least 1 dose	1056	86.6%
Single dose vaccination		72	5.9%
Two dose vaccination		786	64.4%
Booster dose vaccination		197	16.1%

Table 2 gives the comorbidity profile among study participants. The most common comorbidity prevalent among participants was diabetes and hypertension. With regards to arrythmia, cancer, cardiac failure and avascular necrosis of femur, more than 50% were reported after Covid-19 infection.

Table 2. Comorbidities amon	g the study	participants	s(n- 1220)
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Comorbidities			Before Covid 19		Incidence After Covid 19		
	Frequency n=1220	Percent (%)	Frequency (n=1220)	Percent (%)	Frequency	N	Percent (%)
Diabetes Mellitus	189	15.5	158	13	31	1062	2.9
Hypertension	166	13.6	140	11.5	26	1080	2.4
COPD / Bronchial asthma	24	2	17	1.4	7	1203	0.6
Chronic Kidney Disease	14	1.1	11	0.9	3	1209	0.2
Dyslipidaemia	30	2.5	20	1.6	10	1200	0.8
Thyroid disorders	31	2.5	24	2	7	1196	0.6
Myocardial Infarction	28	2.3	17	1.4	11	1203	0.9
Cardiac Failure	6	0.5	2	0.2	4	1218	0.3
Arrythmia	10	0.8	5	0.4	5	1215	0.4
Stroke	14	1.1	8	0.7	6	1212	0.5
Avascular necrosis	8	0.7	1	0.1	7	1219	0.6
Cancer	23	1.9	10	0.8	13	1210	1.1





The overall prevalence of persistent post Covid symptoms was 21.3%(95% CI -19.04% - 23.72%). The most common symptom reported was loss of appetite and persistent fatigue.



Figure 2: Post Covid Symptomology (N-1220)

Table 3 shows that there is no significant association between gender, age group, pandemic wave, number of episodes of covid infection, covid vaccination and persistent post covid symptoms. However, hospitalisation, oxygen requirement, ventilatory support requirement, lung involvement and presence of any comorbidities was significantly associated with persistent post covid syndrome.

Table 3. Prevalence of Post Covid -19 by demographic
profile and Covid 19 infection

Variable		Post-Covid-19 symptoms	OR (95% CI)	p-value	
Sender	Male(n-600)	140(20.3%)	1 140(0 8731-1 5143)	0.320	
Jender	Female(n-530)	120(22.6%)	1.145(0.0751-1.5145)	0.520	
a group	<18 vers	14(15.1%)	Not applicable	0.08	
ree Fronb	18-45 years	121(18.8%)	riot applicable	0.00	
	46-60 years	76(24.2%)			
	>60 years	40(28.8%)			
Pandemic wave	1st wave	67 (22 25%)	Not applicable	0.750	
and chile wave	2nd mave	140 (20 58%)	1 tot applicable	0.750	
	3rd wave	44 (22 56%)			
No of enisodes of	One enisode	238(20.9%)	1 294(0 781-2 144)	0.317	
Covid infection	More than 1 enisode	22(25.5%)	1.254(0.701-2.144)	0.517	
Inspitalisation	Vec	136(26.8%)	1 741(1 321- 2 204)	<0.001	
rospitalisation	No	124(17.4%)	1.741(1.521-2.254)		
Ixvgon	Vec	36 (33 0%)	2 043(1 332- 3 134)	<0.001	
equirement	No	224 (20 10%)	2.045(1.552- 5.154)	~0.001	
Ventilatory	Vec	8(44.4%)	3 015(1 178-7 720)	0.021	
upport	No	252(20.0%)	5.015(1.178-7.720)	0.021	
	No	20/22 00/)	2 22 4(1 607 2 070)	-0.001	
Jung	ies	72(55.8%)	2.224(1.00/-3.0/9)	<0.001	
nvolvement	NO	188(18.0%)		0.000	
ovid	Yes	224(21.2%)	0.957(0.642-1.425)	0.829	
accination	No	36(21.9%)			
Presence of	Diabetes Mellitus	52(27.5%)	1.519(1.047-2.203)	0.024	
omorbidities	No diabetes	208(20.2%)			
oefore covid 19	Hypertension	60(36.1%)	2.372(1.638-3.434)	< 0.001	
	No Hypertension	200(19%)			
	COPD / asthma	12(50%)	3.348(1.528-7.335)	< 0.001	
	No COPD/Asthma	248(20.7%)			
	CKD	9(64.3%)	10.33(3.647 - 29.274)	< 0.001	
	No CKD	251(20.8%)			
	Dyslipidaemia	19(63.3%)	8.034(3.563-18.117)	< 0.001	
	No dyslipidaemia	241(20.3%)			
	Thyroid disorders	15(48.4%)	3.673(1.748-7.717)	< 0.001	
	Normal thyroid	245(20.6%)			
	Myocardial Infarction	18(64.3%)	12.078(4.741 - 30.771)	< 0.001	
	No MI	242(20.3%)			
	Cardiac Failure	6(100%)	15.647(3.301-74.167)	< 0.001	
	No Cardiac Failure	254(20.9%)			
	Arrythmia	7(70%)	4.549(1.514-13.662)	0.006	
	No Arrythmia	253(20.9%)			
	Stroke	10(71.4%)	6.815(1.978-23.475)	< 0.001	
	No Stroke	250(20.7%)			
	Avascular necrosis	8(100%)	13.792(2.846-66.82)	< 0.001	
	No AVN	252(20.8%)			
	Cancer	6(85.7%)	7.798(1.936-31.410)	0.003	
	No Cancer	254(20.9%)			

Table 4. Age profile of deceased patients among the selected

			Age specific mortality
Age group	survived	death	rate (%)
01-10 years	30	0	0
11-20 years	103	1	0.9%
21-30	235	2	0.8%
31-40	268	2	0.7%
41-50	211	10	4.5%
51-60	203	18	8.1%
61-70	115	27	19.0%
71-80	41	11	21.1%
81-90	14	2	12.5

#### participants

#### DISCUSSION

The findings of this study provide valuable insights into the prevalence and factors associated with persistent post-COVID symptoms, underscoring the need for comprehensive understanding and management of long-term COVID-19 effects. The documented prevalence rate of 21.3% highlights the significant impact of persistent post-COVID symptoms on a substantial portion of the affected population. These symptoms are present even after 1 year past the infection. In a study conducted by Kumar et al among those who required hospitalisation following Covid 19 infection in India,31% reported to have symptoms in the 30-60 day follow up period.<sup>5</sup> In another study done in Tamil Nadu, 24% reported persistent symptoms during the 12–14 weeks post recovery period of COVID-19.<sup>6</sup> In another cross sectional study conducted among health care workers with Covid-19 history, the prevalence of COVID sequelae was found to be 30.34% after 12–52 weeks of their discharge.<sup>8</sup> While these studies have looked at a shorter follow up time, in the current study the minimum duration since the last infection was 1 year and the maximum was 3 years. Hence, the prevalence of persistent Covid symptoms could be low compared to the other studies. However, one fifth of the patients still continuing to report at least one of the symptoms even after a long recovery period, indicates the long term effect of Covid -19.

Among the selected study participants, 5.6% was reported to have died. The age specific mortality rate was following the rates in general population.<sup>9</sup> In fact, there was no death reported among the vulnerable children age group between 1-10 years of age.

The most common symptom reported in this study was loss of appetite and persistent fatigue, followed by joint pain/swelling and anxiety. Fatigue was the most common symptom reported in other studies as well.<sup>57,10</sup> While the other studies have reported dyspnoea as one of the most commonly reported symptom, it was not the most common symptom in our study. The symptom wise prevalence ranged from 0.3% -4.3%, unlike other studies, where the individual symptoms prevalence was high. Kumar et al reported dyspnoea among 11.9% of patients at end of 100 day follow up.<sup>5</sup> Similarly in the meta-analysis by Leon et al, 58% was the prevalence of fatigue.<sup>7</sup> Fatigue is the most common symptom reported in 17.5–72% of post-COVID cases, followed by residual dyspnoea with an incidence ranging from 10–40%.

The most common comorbidity among the study participants was diabetes and hypertension. However, the concerning incidence rates of arrhythmia, cancer, cardiac failure, and avascular necrosis of the femur reported after COVID-19 infection underscore the wide-ranging and potentially severe complications associated with the virus. A review by Oronsky et al explores underlying mechanisms and possible manifestations of persistent post-COVID syndrome.11 Among patients with Avascular Necrosis of Femur (AVN) 87.5% reported only after Covid -19 infection. AVN as a possible sequelae of Covid -19 is being reported as many case series and reports are published.<sup>12,13,14,15</sup> Patients with Covid 19 are facing the dual burden of the effect of steroid used as a therapy for Covid-19 and the hypercoagulable state induced by the infection itself, leading to increased risk of AVN.<sup>12</sup> Persistent hypercoagulable state following Covid infection and other factors like production of neutrophil extracellular traps, increased platelet activity,

impaired fibrinolysis and overall decreased anticoagulant function of the endothelium, explains the increased rate of MI and Stroke post covid.<sup>11,16</sup> These findings call for heightened vigilance and tailored follow-up care to monitor and address the increased risk of developing these specific health complications post-COVID-19, further emphasizing the necessity for integrated, multidisciplinary healthcare approaches to manage the diverse long-term sequelae of the disease.

On an attempt to find the factors determining the presence of persistent post covid symptoms, there was no significant difference based on gender. Gender was not a significant factor in other studies as well.<sup>5,6</sup> However, some studies state that female gender had an increased odds of reporting post covid symptoms.8,17,18 While there was an increasing prevalence of long Covid with increasing age, it was not statistically significant. Advancing age was a significant factor associated with Long Covid in other studies.<sup>5,6,18</sup> There was also no significant difference in the prevalence based on the pandemic wave, whereas in the study by Kumar et al, specific symptoms like dyspnoea, fatigue, and mental health issues were common among those infected in the 2nd wave.<sup>5</sup> There was no difference in the prevalence based on the Covid Vaccination status or the number of episodes of covid infection. Covid vaccination was not increasing the risk of post covid as indicated in other studies.8,19

This study showed that patients who had severe Covid as presented as requiring hospitalisation, oxygen or ventilatory support and lung involvement had higher odds of the having COVID sequelae. Similarly, presence of any comorbidity increased the risk of post covid symptoms, emphasizing the critical role of the severity of the initial COVID-19 infection and pre-existing health conditions in influencing long-term health outcomes. This finding demonstrates a high degree of consistency on comparison with studies done in different research context.<sup>68,10,18,20,21,22</sup> This finding also highlights the need for targeted management strategies for individuals with these underlying health conditions to mitigate the potential exacerbation of post-COVID.

This study is done among all patients irrespective of their hospitalisation status and the follow up was after a long recovery period extending from 1- 3years post Covid infection. This study had also incorporated the new criterion of persistence of symptoms for at least 3 months as per MOHFW definition of long Covid. However, this study has certain limitations. This was a questionnaire based study and no investigations were carried out to rule out any specific diagnosis. This could impact the reliability of the Persistent post covid symptom estimate leading to both under and over estimate.

#### CONCLUSION

In light of these findings, healthcare professionals and policymakers should prioritize the development of comprehensive post-COVID care protocols that account for the multifaceted nature of persistent post-COVID symptoms and their associated risk factors. By incorporating targeted interventions for individuals with a history of severe COVID-19, pre-existing comorbidities, and specific post-COVID complications, healthcare systems can better support the holistic recovery and well-being of those affected by the long-term effects of the virus. Further research is crucial to unravel the underlying mechanisms driving the persistence of post-COVID symptoms and to inform evidence-based interventions that improve the quality of life for individuals navigating the aftermath of COVID-19.

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