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Original article

Title: Predictors of adverse clinical outcomes of recovered COVID-19 patients from a tertiary care hospital, Gujarat, India.

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Abstract:

Background:

SARS-CoV 2 virus infection present as varying degree of severity with many post viral complications.Although initial research was focused on the epidemiology, risk factors, clinical syndrome and treatment options; sufficient data is needed on sequelae of the patients who got discharged. The present study aimed to identify long term outcomes of COVID 19 recovered patients to safeguard their life in future.

Methods: The present longitudinal study included all 443 COVID 19 recovered patients who were admitted during the second wave at our tertiary care hospital from 1stApril to 25th May, 2021 and interviewed telephonically with series of questionnaire. Baseline demographic profile, comorbidities, clinical characteristics and investigatory findings were obtained from the hospital records and analysed for the long term symptoms and outcomes.

ISSN 2515-8260 Volume 09, Issue 06, 2022

Results: Over a mean follow up period of 152 days, around 6% of the patients who recovered after acute COVID 19 infection died after the discharge. More than two third of patients were male. Diabetes and hypertension were most common comorbidities among the study population. Most common persistent symptoms was fatigue among the recovered population at follow up. Multivariate logistic regression analysis against the odds of post discharge mortality revealed patients receiving advanced respiratory support (AOR 5.2, 95% CI 1.8-15.1) and ICU stay during the hospitalisation (AOR 6.67, 95% CI 1.18-37.7) were predictors of post discharge mortality.

Conclusion: Fatigue was the most common symptoms observed after 5 months of discharge from acute COVID 19 infection. Overall post discharge mortality was 6% and admission in ICU and use of advanced respiratory support were associated mortality among recovered patients.

Keywords: COVID-19 infection, follow –up, post discharge death, risk factors

Introduction:

The unexpected pandemic, caused by novel coronavirus 2019, has created havoc among the people worldwide affecting 597 millions of lives worldwide until 18th August, 2022. [1] It is serious illness which has a high attack rate and case fatality rate across the globe. The epidemiological and clinical characteristics, pathogenesis, and complications of patients with COVID -19 at acute phase have been described in various studies, but post discharge long term sequelae needs exploration.[2,3] There are evidences that some symptoms like malaise, shortness of breath, bodyache, cough, and chest pain may continue even after convalescence phase has subsided.[4,5] The presence of symptoms after recovery from a viral disease is broadly recognised as a post-viral syndrome.[5]

Reports have suggested that disease severity during acute phase is independently associated with extent of lung diffusion impairment at follow-up, with 56% of patients requiring high-flow nasal cannula, non-invasive ventilation, and invasive mechanical ventilation during hospital stay.[6]

The rate at which SARS Cov 2 virus is evolving and mutating and cases are rising in several parts of the world with some evidences of prolonged effect post recovery, the disease burden will only rise. Therefore, our primary aim was to recognise long term prognosis of the recovered patients during the second wave of COVID-19 and to identify predictors during acute phase at the time of hospitalisation that may contribute to poor outcome post discharge.

Materials and Methods

Study design and Area

The presented longitudinal observational study was approved by the Institutional Ethical Committee of our tertiary care hospital attached to a medical college, Gujarat, India. All procedures followed were in accordance with Good clinical practice and applicable regulatory requirement. Telephonically recorded consent was taken during interview of the patients.

ISSN 2515-8260 Volume 09, Issue 06, 2022

Data collection

As seen in figure 1, a total of 494 patients infected with severe acute respiratory syndrome coronavirus 2(SARS CoV-2) who were discharged from our tertiary care hospital during the second wave of the COVID 19 from 1st April to 25th May, were contacted telephonically between October to November 2021 to complete a single follow-up questionnaire between 4 to 6 months after onset of acute illness during April-May 2021.[7] Final analysis included 443 patients who were traced and gave consent. Demographic profile, risk factors and clinical parameters were obtained from medical record files or electronic medical records system (EMS) of our hospital. Each patient was then questioned about the admission details for cross-checking with the hospital data for their identity. Comorbidities included hypertension, diabetes, renal impairment, history of Ischaemic heart disease (IHD), thyroid disorders. Diabetes was defined as having a glycosylated haemoglobin (HBA1C) level of 6.5% or higher in the preceding three months or patients already on diabetic medication or random blood glucose level more than 200mg/dl on admission without any history of steroids intake. Kidney function was ascertained from the serum creatinine measurement at the time of discharge, where available, and was converted into the eGFR (e glomerular filtration rate) using the chronic kidney disease epidemiology collaboration (CKD-EPI) equation; with reduced kidney function grouped into eGFR <60 ml min^{-1} per 1.73 m^2.[8] Thyroid disorders were considered for the patients who were already taking anti-thyroid medications. The laboratory test results before the discharge date were only considered for the analysis. Mega drive for nationwide rollout of COVISHIELD vaccine was launched on 16th January, 2021 in India so patients were also asked for any number of COVISHIELD vaccine doses taken before contracting SARS CoV 2 infection.[9] Later, the extracted data was reviewed by the team of authors for accuracy and completeness.

Statistical Analysis

We utilized IBM SPSS version 20.0 statistical package software for the analysis. We conducted descriptive statistics to determine frequency and percentage of various characteristics of the study population. Univariate logistic regression method were used to adjust for the effects of patient's age, risk factors, usage of advanced respiratory support and admission at Intensive care unit or high dependency unit at the time of admission and poor post discharge outcome. Then the factors which were found to be significant in univariate analysis ($p < 0.05$) were only considered for multiple logistic regression analysis. We optimised our results as adjusted odds ratios (AORs) with 95% confidence intervals (CIs) and P-values < 0.05 as significant.

Results:-

In total, 433 patients participated in the study, out of which 153 (34.54%) were females as seen in Table 1. Risk factors like diabetes and hypertension were present in almost one third of study population followed by renal impairment (15.12%). Mean duration of follow up was 149.96 $\pm$ 14 days. Post COVID persistent symptoms were present in around 10% of patients on follow up even at 5 months from 418 patients who survived. The most common symptom was fatigue (32 out of 418) followed by dry cough (26 out of 418) and few patients reported other symptoms as seen in figure 2. Seventy four patients had already taken one dose of COVISHIELD vaccine

before contracting COVID 19 infection during the second wave while only eight patients were vaccinated with two completed doses of COVISHIELD. It is important to mention that as none of the patients who died after the discharge had taken any dose of COVISHIELD vaccine, we could not assess them for further analysis to observe vaccination effect on long term outcomes of the patients.

We observed that 5.64% death rate in our study population; out of which more than two third of patients died within a week and the remaining 24% of the patients succumbed to death within one month and only one patient died after 96 days of the discharge as depicted in Figure 3. Seven patients out of these 25 patients who died after the discharge were reported to have deaths at home while remaining patients got re-admitted and had hospital deaths. The overall readmission rate in our study was around 8% after the discharge.

As presented in table 2, we performed univariate and multivariate logistic regression analysis between the patients who succumbed to death after discharge and who survived. Univariate logistic regression analysis revealed that patients who had ICU admission during hospitalisation and patients receiving advanced respiratory support in terms of Bi-PAP and mechanical ventilation were associated with mortality after discharge. Multivariate also revealed that both risk factors ICU admission (AOR 5.2, 95% CI 1.8-15.1) and use of higher respiratory support (AOR 6.67, 95% CI 1.18-37.78) are the most important risk factors that led to increase in post discharge mortality in our study.

Discussion:-

In this group of individuals with COVID-19 who were followed up for as long as 6 months after illness, only 10% reported persistent symptoms while it was noted to be as high as 30% at 9 months of follow up study.[10] This lower prevalence of consistent symptoms in this study could be due to high proportion of patients (88%) given only ward care during hospitalisation for mild to moderate disease.

Fatigue being the most common symptom at follow up mentioned here is consistent with other existing research.[11-13] However, the proportion of patients having fatigue at 5 months follow up was only 7.2% which is significantly low as compared to other studies where fatigue was common in 53% to 71% of the patients. [11-13] This discrepancy could be explained by varying degree of duration of follow up.

Interestingly, after discharge from the hospital from COVID-19 acute illness, 8% of patients were readmitted in the current study at mean follow up of 149 days but readmission rate was noticed to be much higher, 29% in the study from the United Kingdom at follow up of 140 day; this higher readmission is mostly on the account of multi-centric data of the later study.[14]

Moreover, around 6% of mortality among the recovered patients from COVID 19 noted in our study; likewise a study from the United States reported 9% deaths within 60 days follow up.[15] Nevertheless a large cohort from the UK demonstrated death rate of 12%.[14] The illustrated divergence of deaths in recovered individuals explained by different age groups, ethnicity heterogeneity, varying prevalence of risk factors and discrepancy in duration of follow up of the available studies.

ISSN 2515-8260 Volume 09, Issue 06, 2022

It is observed in findings from the UK study that patients discharged from the ICU after COVID 19 infection had higher rates of deaths and readmission. [14] Furthermore, we also surmised that ICU admission and higher respiratory support during the hospital stay have emerged as major predictor of the post recovery mortality.

Conclusion:-

Our follow up study reported important long term post-viral symptom fatigue in recovered patients at 5 months. This warrants proper long-term follow up planning and at least counselling of such patients. We also report two important determinants of post discharge demise; ICU admission and requirement of major respiratory support during the hospital stay. Recognising these factors and managing patients with more clinical vigilance can help in reducing the post discharge mortality.

Study limitations:-

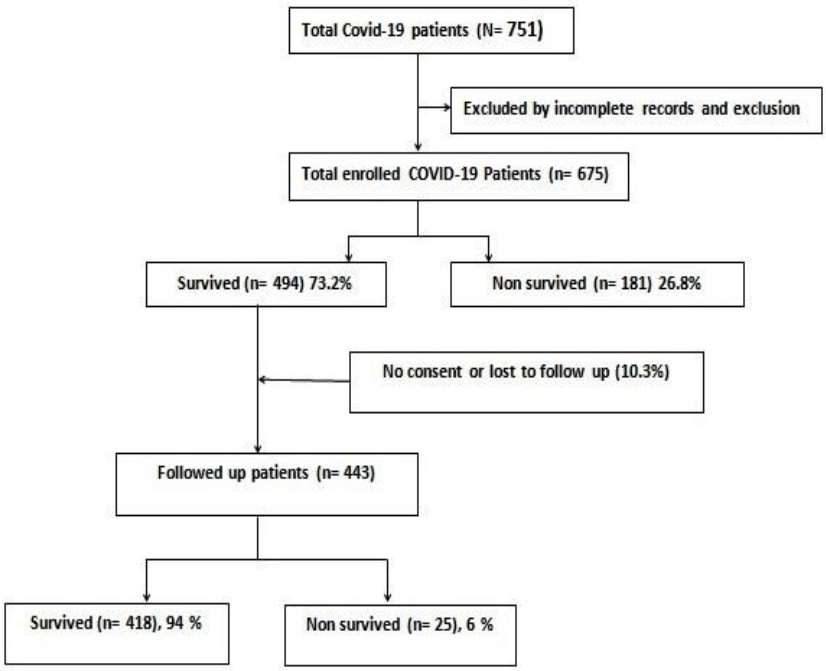
We acknowledge that this was a single centre study and findings were not compared with the control groups. Furthermore, there is always a possibility of some recall bias in follow-up studies. As in our study vaccine history did not aid into any relevant inference; further research is suggested in this direction.

References

1. Https://www.worldometers.info/coronavirus/.
2. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA* 2020;**324:** 782–93.
3. Cevik M, Kuppalli K, Kindrachuk J, Peiris M. Virology, transmission, and pathogenesis of SARS-cov-2. *BMJ* 2020; **371:** m3862.
4. Banda JM, Singh GV, Alser OH, Prieto-Alhambra D. Long-term patient-reported symptoms of COVID-19: an analysis of social media data. Medrxiv; 2020. DOI: 10.1101/2020.07.29.20164418.
5. Kashif, A., Chaudhry, M., Fayyaz, T. *Et al.* Follow-up of COVID-19 recovered patients with mild disease. *Sci Rep* **11,** 13414 (2021). Https://doi.org/10.1038/s41598-021-92717-8
6. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021; published online Jan 8. Https://doi.org/10.1016/S0140-6736(20)32656-8)
7. Prasad Bogam, Aparna Joshi, SanketNagarkar, Divyashri Jain, Nikhil Gupte, LS Shashidhara*et al*. Burden of COVID-19 and case fatality rate in Pune, India: an analysis of the first and second wave of the pandemic, IJID Regions 2022;2:74-81.
8. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI *et al.* CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009 May 5;150(9):604-12

9. https://www.who.int/india/news/feature-stories/detail/india-rolls-out-the-world-s-largest-covid-19-vaccination-drive
10. Logue JK, Franko NM, McCulloch DJ, et al. Sequelae in Adults at 6 Months After COVID-19 Infection. *JAMA Netw Open*. 2021;4(2):e210830. doi:10.1001/jamanetworkopen.2021.0830
11. TenfordeMW, Billig Rose E, Lindsell CJ, et al; CDC COVID-19 Response Team. Characteristics of adult outpatients and inpatients with COVID-19—11 academic medical centers, United States, March-May 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(26):841-846
12. Carfì A, Bernabei R, Landi F; GemelliAgainst COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. *JAMA*. 2020;324(6):603-605.
13. Garrigues E, Janvier P, Kherabi Y, et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J Infect*. 2020;81(6):e4-e6.
14. Donnelly JP, Wang XQ, Iwashyna TJ, Prescott HC. Readmission and death after initial hospital discharge among patients with COVID-19 in a large multihospital system. *JAMA* 2021;325:304-6.
15. Ayoubkhani D, Khunti K, Nafilyan V, Maddox T, Humberstone B, Diamond I et al. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study BMJ 2021; 372 :n693.

Figure 1: Flowchart of patients' selection



ISSN 2515-8260 Volume 09, Issue 06, 2022

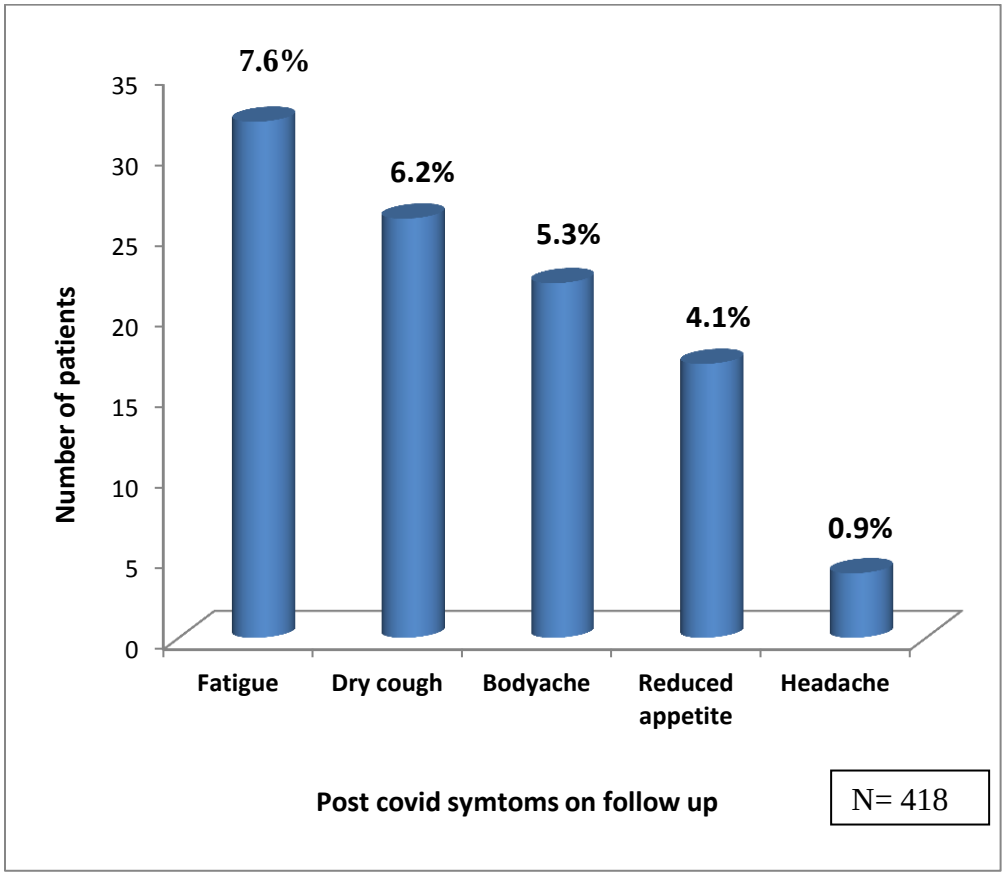
Table 1: Demographic and clinical characteristics of the study population

	Total recovered individuals (n=443)	Percentage
Age (mean ± SD in years)	54.97 ± 15.35	
Sex		
Men	290	65.46
Co-morbidities		
Hypertension	125	28.22
Diabetes	125	28.22
Hypothyroidism	9	2.03
Ischemic Heart Disease	6	1.35
Renal impairment	67	15.12
Highest level of care accessed during acute illness		
Ward	390	88.04
HDU*	38	8.58
ICU†	15	3.39
Persistent symptoms (n=418)	43	10.3
Number of patients who got one dose of COVID vaccine	74	16.70
Number of patients who got two doses of vaccine	8	1.81
Duration of the hospital stay (mean ± SD in days)	8.6 ± 4.5	
Readmission after the discharge	36	8.1
Post discharge death	25	5.64

*****High Dependency Unit, †Intensive Care unit

ISSN 2515-8260 Volume 09, Issue 06, 2022

Figure 2: Number of patients reported post COVID-19 symptoms on follow up



ISSN 2515-8260 Volume 09, Issue 06, 2022

Figure 3: Distribution of deaths of the patients Vs duration of days after discharge from acute illness.

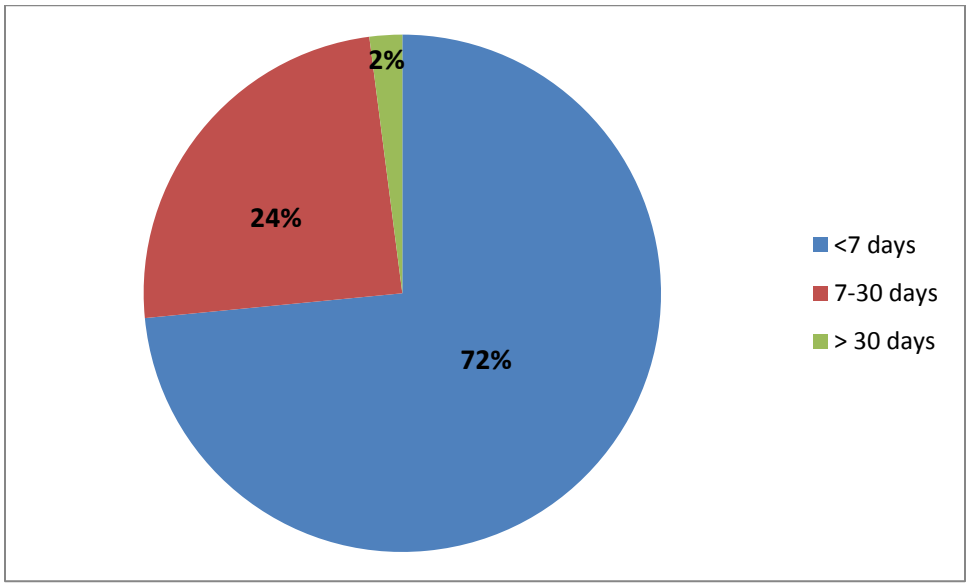


Table 2: Factors associated with increased Odds of Mortality among post discharged COVID 19 patients

Variable	Univariate Analysis			Multivariate analysis		
	OR	95% CI	P-Value*	OR	95% CI	P-Value*
Age						
< 50 (Ref)†						
≥ 50	1.97	0.71-5.48	0.19			
Hypertension						
No (Ref)						
Yes	1.67	0.67-4.15	0.27			
Diabetes						
No (Ref)						
Yes	2.01	0.82-4.9	0.13			
CKD						
No (Ref)						
Yes	2.27	0.85-6.1	0.10			

Cardiovascular disease						
No (Ref)						
Yes	3.89	0.43-34.88	0.23			
ICU admission during hospitalization						
No (Ref)						
Yes	7.83	3.13-19.55	<0.0001	5.2	1.8-15.1	0.002
Patient receiving advanced respiratory support (Bi-PAP or Mechanical ventilation)						
No (Ref)						
Yes	30.67	6.36-147.9	<0.0001	6.67	1.18-37.78	0.03
High CRP / Ferritin level						
No (Ref)						
Yes	1.16	0.44-3.07	0.77			

* <0.05 significant, †reference