International Journal of Community Medicine and Public Health
Purushothaman S et al. Int J Community Med Public Health. 2023 Feb;10(2):723-728
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20230228

Original Research Article

Multi-center study to analyse outcome of integrated treatment approach in COVID-19 patients

Suraj Purushothaman[1], Prashant Kumar Dhotre[1]*, Kamlesh Prakash Vanarase[2], Gajanan Kisan Jadhao[2], Abhay Gyanchand Maurya[2], Sanjay Mohnalal Gupta[2], Vijaykumar Gawali[3]

[1]Department of Critical Care, [2]Medical Officer, [3]Department of Medical Research and Education, Bhaktivedanta Hospital and Research Institute, Mira Road, Maharashtra, India

Received: 23 November 2022
Revised: 14 January 2023
Accepted: 16 January 2023

***Correspondence:**
Dr. Prashant Kumar Dhotre,
E-mail: pdhotre@gmail.com, drvijay

ABSTRACT

Background: This study presents the outcome of integrated treatment approach based on government mandated standard allopathic treatment along with alternatives in COVID-19 patients. The aim of our study was to investigate the outcome of treatment strategy, co-morbid status, recovery and mortality rate of COVID-19 patients at Bhaktivedanta Hospital and Research Institute.
Methods: Post ethics committee approval for multiple centers, data for 1049 COVID-19 patients (RTPCR confirmed cases) of all age groups and genders which were admitted in a dedicated covid hospital from March 2020 to November 2020 was analysed retrospectively.
Results: This study highlights the management of COVID-19 patients with an integrated approach. In our cohort with 36.7%, 44.70 %, 18.58% of mild, moderate and severe cases respectively, mortality rate was only 3.43% of total positive patients admitted at our hospital.
Conclusions: We emphasize that even in healthcare facilities with limited resource and poor infrastructure and lack of ICU facilities, clinical observation-based management can help to reduce mortality considerably. Unique features of our study include use of progesterone as an immune modulator, use of dual antiviral agents and use of age-related lower limit of oxygen saturation.

Keywords: COVID-19, Limited resource setting, Minimal use of oxygen, Mortality, Patient outcome, Progesterone as immunomodulator, Treatment strategy

INTRODUCTION

COVID-19 pandemic is a public health emergency which poses lot of pressure on health care systems. Most of the patients with COVID-19 infection has mild symptoms (80%) and moderate symptoms (14%) and significant proportion of patients with co-morbidities and other complications require timely hospitalization to reduce risk of mortality.[1] Integrated approach can help manage the symptoms/treatment in the vulnerable population with complex symptoms.[2]

There are various current treatments which exists and include anti-inflammatory drugs like statins, antiviral drugs like remdesivir, anticoagulants and antibody therapy which produce different levels of therapeutic effects on patients.[2] It has also been noticed that patients with COVID-19 and having some underlying cardiovascular diseases have shown and increased rate of mortality upto 10.5%.[3] The drugs commonly used in covid era like remdesivir and tocilizumab were commonly used allopathic drugs but these drugs posed some problems. Hence, it is worthwhile to have an

alternate approach as well. Here we are presenting the outcome of integrated treatment approach based on government mandated standard allopathic treatment along with alternatives in COVID-19 patients. The aim of our study was to investigate outcome of treatment strategy, co-morbid status, recovery and mortality rate of COVID-19 patients at Bhaktivedanta Hospital and Research Institute.

METHODS

The study was initiated after obtaining approval from the Institutional Ethics Committee and approval from the Ministry of Health (EC/NEW/INST/2019/245). In this multicentre retrospective study, data of 1049 consecutive discharged and death patients with COVID-19 positive by rRT-PCR (nucleic acid amplification) test was included and analysed. The patients were admitted in a dedicated COVID-19 hospital including all genders and age groups from March 2020 to November 2020 were included in the study. Patients who did not have COVID-19 test done were excluded from the study. All patients received appropriate supportive care and regular clinical and laboratory monitoring. Patients information inclusive of demographics (age, sex, nationality), clinical features including severity based on saturation on air at the time of admission and CT severity score; co-morbid conditions, number of patients requiring BiPAP, date of admission and discharge, patient mortality rate, nCoronavirus, rRT-PCR and other laboratory results were extracted from medical records.

Apart from the exercise schedule, emphasis was also put on therapeutic positioning. Patients were clinically observed to explore most appropriate position in order to ensure optimal saturation. Various position viz sitting, standing, left lateral, right lateral, semi-prone, prone, head low, supine were assessed. Best and worst positions was documented. Best position was used whenever patient showed worsening of saturation. Age specific lower limit of acceptable oxygen saturation was followed as per respiratory care guide for clinical practice. Following are the treatments given to patients who maintained SpO_2 levels above 94 and were categorized as mild cases (Table 1a). First, a 1600 mg dose of favipiravir tablet was given twice daily on day 1, then 800 mg twice daily for the following seven days while uric acid levels were continuously monitored. For seven days, a 200 mg Doxy tablet was administered stat and then twice daily. Ivermectin tablets were given out in a single dose of 12 mg. An intramuscular injection of vitamin D was given at a dose of 1/3 6 lac units. Additionally, 75 mg of aspirin was administered each day. For patients categorized as moderate to severe (Table 1b); remdesivir was administered intravenously on day 1 in doses of 200 mg and 100 mg for the following five days. Only when absolutely necessary was a 40 mg dose of methyl prednisolone intravenous injection given. According to the need for mechanical ventilation and the demand for oxygen, the steroid dose was altered. Depending on the coagulation parameters, a second subcutaneous injection of alexam/clexane at a dose of 0.6 mg was given. An intramuscular injection of vitamin D was given at a dose of 1/3 6 lac units. Aditionally, 75 mg of aspirin was administered each day. Descriptive statistics were reported as mean (SD) or median for continuous variables and as counts and percentages for categorical variables. No imputation was made for missing data. Analyses were performed with the use of SPSS version 20.

Table 1a: Treatment given to patients who maintained SpO_2 levels above 94 and were categorized as mild cases.

Treatment	Dose	Frequency	Comments
Tab. Favipiravir	1600 mg	Twice a day on day 1	-
	800 mg	Twice a day for next 7 days	With regular monitoring of uric acid levels
Tab. Doxy	200 mg	Stat and then twice a day for 7 days	-
Tab. Ivermectin	12 mg	stat.	-
Inj. Vitamin D	1/3 6. lac units	Intra Muscular stat.	-
Aspirin	75 mg	Once a day	-

Table 1b: Treatment given to patients categorized as moderate to severe.

Treatment	Dose	Frequency	Comments
Inj. Remdesivir	200 mg_intravenous	Day 1	-
	100 mg_intravenous	Next 5 days	-
Ing Methyl Pred	40mg i.v.	SOS	Dose of steroid adjusted as per oxygen demand and need for mechanical ventilation
Ing Alexam /Clexane	0.6 mg	Subcutaneous once a day	Depending on the coagulation parameters.
T. Aspirin FV	75 mg	Once a day	-
Inj. Vit D	1/3 6 lac units	Intramuscular stat.	-

RESULTS

Data of total of 1049 patients of laboratory confirmed COVID-19 test by RT-PCR at Bhakti Vedanta Hospital and Research Institute was analysed. The mean age of patients was 49.19 (SD 14.1) years and 752 (74.07%) of them were males. A summary of demographic characteristics of the study participants is represented in Table 2. The three most prominent management strategies in combination with ayurvedic treatment included the use of steroids (42.70%; n=448), remedisivir (36.3%; n=384), and tocilizumab (6.76%; n=71). Clinical severity of patients was assessed on the basis of CT severity and SPO_2 recorded at the time of admission. Patients were categorized as mild, moderate, severe as per CT severity and SPO2 recorded at the time of admission, clinical guidance for management of adult COVID-19.[2] 385 (36.7%) were mild cases, 469 (44.70%) cases were moderate remaining 195 (18.58%) were severe cases (Figure 1). Of all patients 36 (3.43%) patients expired and remaining 1013 patients have subsequently recovered and were discharged. Median duration of stay in the hospital was 9 (37) days. Patients had one or more co-morbidities.

Table 2: Demographic characteristics of the study participants (N=1049).

Variables	No. of patients	No. of patients requiring Bipap /NIV support	Patient with discharged as per variable	Total death as per variable
Age (years)-Mean (SD)	49.19 (14.1)			
Gender (male)	752 (71.68%)			
Diabetes	317(30.2%)	27 (8.51%)	296	21
Ischemic heart disease	70 (6.67%)	9(12.8%)	65	5
Chronic kidney disease	31(2.95%)	2(6.6%)	28	3
Asthma	27(2.57%)	1(3.84%)	27	0
COPD	6(0.57%)	3(50%)	6	0
ILD	3(0.28%)	0	3	0
Bronchitis	1(0.09%)	0	1	0
Co-morbid condition	382	42	353	29 (7.59%)
No comorbidity	667	26 (3.89%)	656	11(1.64 %)
Mild cases as per CT severity score and SpO_2 level at admission	385 (36.7%)	-		
Moderate cases as per CT severity score and SpO_2 level at admission	469 (44.70%)	-		
Severe cases as per CT severity score and SpO_2 level at admission	195(18.58%)			
Overall mortality	36(3.43%)			

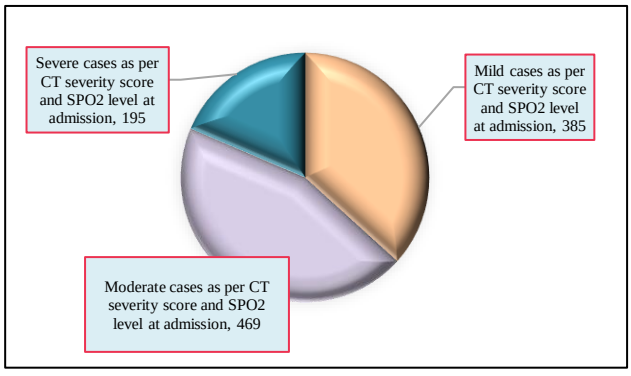

Figure 1: Clinical severity of patients on the basis of CT severity score and SpO_2 level at the time of admission

Diabetes mellitus was the leading co-morbid condition with frequency of 30.2% followed by ischemic heart disease (6.6%), CKD (2.95%), asthma (2.19%), COPD (0.47%), ILD (0.28%) and bronchitis (0.1%) (Figure 2). Overall mortality of patients was 3.43%. Patients with different co-morbid conditions requiring Bipap support and their outcome is shown in Table 2.

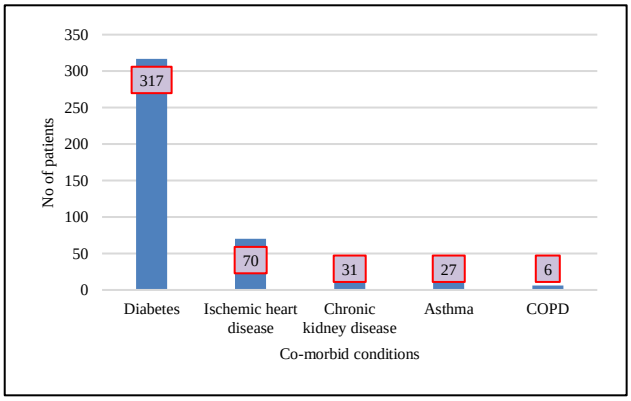

Figure 2: Co-morbid conditions (number of patients).

DISCUSSION

We report outcome of the 1049 patients admitted to Bhaktivedanta hospital and research institute. Mean age of the patient was found to be 49.19 years. As per studies reported earlier risk of severe COVID-19 illness and mortality is higher among men, elderly, and in individuals with comorbidities, especially diabetes.[3] Our data shows that more males (71.68%) are infected as compared to females which is consistent with the result of other studies reported earlier with ranges between 60-93%.[4-9]

The presence of comorbidities such as diabetes mellitus (DM), hypertension (HTN), chronic obstructive pulmonary disease (COPD) or old age leads to poorer clinical outcomes in COVID-19 patients.[10-14] Our finding are similar to these studies Table 3.

Table 3: Outcome of patients.

Variables	All patients n=1049	Patient with co-morbidity n=382	Patient with no co-morbidity n=667
Died	36 (3.43%)	29 (3.89%)	11(1.64%)
Discharged	1013	353	656

Table 4: Summary of outcomes mortality of various COVID-19 studies reported.

Indian studies	No of patient admitted in hospital	Mortality
Malhotra et al[15]	10,314	1415 (13.72%)
Bhandari et al[16]	987	80 (8.1%)
Mohandas et al[17]	3345	142(4.2%)
Bhargava et al[18]	565	30.4%
Current study	1049	36 (3.43%)
Western studies	**No of patient admitted in hospital**	**Mortality**
Gray et al[19]	86,356	31.2%
Vlachos et al[20]	429	26%
Docherty et a[21]	..	10-15%
Docherty et al[22]	..	26%
Grasselli et al[23]	..	26%
Olivas-Martínez et al[24]	..	30.1%
Rieg[25]	..	25%
COVID-19 mortality[26]	..	25.1%
Suleyman et al[27]	463	40.4 %

However as compared to some other studies death in co morbid conditions is less in our study which reflects an improved outcome with the integrated approach adopted by our hospital.[28-30] In our study, the most common comorbidities were diabetes followed by cardiovascular problems. Similar results were reported by Liu et al in a systematic review and metanalysis comprising of 24 peer reviewed articles.[31]

Better clinical outcomes were observed as apart from required treatment, regular monitoring of CBC, D-dimer levels, creatinine and liver enzymes (SGOT/ SGPT) were conducted. Additionally, Ayurcov as adjuvant with standard of care was associated with significantly earlier resolution of COVID-19 related symptoms than standard of care alone.[32] Also all patients were clinically monitored for heart rate, SpO_2, respiratory rate. Patients also were monitored twice a day by the min walk test to assess for progressing hypoxia. All patients after 7-10 days of illness and on 5 litres O_2 or less were trained by a cardiorespiratory physiotherapist in breathing exercises which were mandatory to be performed 4 times per day. The exercises incorporated were diaphragmatic breathing, thoracic expansion exercises and segmental expansion exercises. Breath holding and use of incentive spirometer were avoided. Along with the breathing exercises, all patients were asked to undertake walking as a form of aerobic activity starting with as less as 2-5 minutes/session. The entire exercise schedule including breathing and walking were repeated at least 3-5 times/day. This study highlights the management of COVID-19 patients with an integrated approach. In our cohort with 36.7%, 44.70%, 18.58% of mild, moderate and severe cases respectively, mortality rate was only 3.43% of total positive patients admitted at our hospital. In a study reported by Macedo et al the mortality rate was reported to be 17.1%.[31] We also found that mortality was low in Indian subcontinent as compared western countries (Table 4).

The limitation of the study is that, firstly, it was only conducted at one centre. Secondly, since the study was retrospective in nature, the analysis was based on existing patient data.

CONCLUSION

We emphasize that even in healthcare facilities with limited resource and poor infrastructure and lack of ICU facilities, clinical observation-based management can help to reduce mortality considerably. Unique features of our study include the use of progesterone as an immuno-modulator, use of dual antiviral agents and use of age-related lower limit of oxygen saturation.

ACKNOWLEDGEMENTS

Authors would like to thank Ms. Vrutti Hitendrakumar Mistry for data collection process and processing paper publication.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Ministry of Health (EC/NEW/INST/2019/245)

REFERENCES

1. Wang C, Wang Z, Wang G, Lau JY, Zhang K, Li W. COVID-19 in early 2021: current status and looking forward. Signal Transduction and Targeted Therapy. 2021;6(1):1-4.
2. Icmr.gov.in. 2021. Available from: https://www.icmr.gov.in/pdf/covid/techdoc/COVID_Management_Algorithm_17052021.pdf. Accessed on17 July 2021.
3. Chidambaram V, Tun NL, Haque WZ, Majella MG, Sivakumar RK, Kumar A, et al. Factors associated with disease severity and mortality among patients with COVID-19: a systematic review and meta-analysis. PloS One. 2020;15(11):e0241541..
4. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13.
5. Soneja M, Kumar R, Bhattacharya B, Meena V, Aggarwal A, Tripathi M, et al. Characteristics and outcomes of 231 COVID-19 cases admitted at a tertiary facility in India: an observational cohort study. J Fam Med Prim Care. 2020;9(12):6267.
6. Baidya D, Kayina C, Haritha D, Soni L, Behera S, Nair P, et al. Epidemiological and clinical characteristics and early outcome of COVID-19 patients in a tertiary care teaching hospital in India: a preliminary analysis. Indian J Med Res. 2020;152(1):100.
7. Bhandari S, Singh A, Sharma R, Rankawat G, Banerjee S, Gupta V, et al. Characteristics, treatment outcomes and role of hydroxychloroquine among 522 COVID-19 hospitalized patients in Jaipur City: an epidemio-clinical study. J Assoc Phys India. 2020;68(6):13-9.
8. Mohan A, Tiwari P, Bhatnagar S, Patel A, Maurya A, Dar L, et al. Clinico-demographic profile and hospital outcomes of COVID-19 patients admitted at a tertiary care centre in north India. Indian J Med Res. 2020;152(1 and 2):61-9.
9. Bairwa M, Kumar R, Ajmal M, Bahurupi Y, Kant R. Predictors of critical illness and mortality based on symptoms and initial physical examination for patients with SARS-CoV-2: a retrospective cohort study. J Infect Public Health. 2021;14(8):1028-34.
10. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J. 2020;55(5):2000547.
11. Wang B, Li R, Lu Z, Huang Y. Does comorbidity increase the risk of patients with COVID-19: evidence from meta-analysis. Aging. 2020;12(7):6049.
12. Singh AK, Gupta R, Misra A. Comorbidities in COVID-19: outcomes in hypertensive cohort and controversies with renin angiotensin system blockers. Diabetes Metab Syndr Clin Res Rev. 2020;14:283-7.
13. Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab. 2020;31:1068-77.
14. Osibogun A, Balogun M, Abayomi A, Idris J, Kuyinu Y, Odukoya O, et al. Outcomes of COVID-19 patients with comorbidities in southwest Nigeria. PloS One. 2021;16(3):e0248281.
15. Malhotra V, Basu S, Sharma N, Kumar S, Garg S, Dushyant K, et al. Outcomes among 10,314 hospitalized COVID-19 patients at a tertiary care government hospital in Delhi, India. J Med Virol. 2021;93(7):4553-8.
16. Bhandari S, Tak A, Singhal S, Shukla J, Shaktawat AS, Gupta J, et al. Patient flow dynamics in hospital systems during times of COVID-19: Cox proportional hazard regression analysis. Front Public Health. 2020;8:585850.
17. Mohandas P, Periasamy S, Marappan M, Sampath A, Sundaram VK, Cherian VK. Clinical review of COVID-19 patients presenting to a quaternary care private hospital in South India: a retrospective study. Clin Epidemiol Glob Health. 2021;11:100751.
18. Bhargava A, Szpunar SM, Sharma M, Fukushima EA, Hoshi S, Levine M, et al. Clinical features and risk factors for in-hospital mortality from COVID-19 infection at a tertiary care medical center, at the onset of the US COVID-19 pandemic. J Intensi Care Med. 2021;36(6):711-8.
19. Gray WK, Navaratnam AV, Day J, Babu P, Mackinnon S, Adelaja I, et al. Variability in COVID-19 in-hospital mortality rates between national health service trusts and regions in England: a national observational study for the getting it right first time programme. E Clin Med. 2021;35(100859):100859.
20. Vlachos S, Wong A, Metaxa V, Canestrini S, Lopez Soto C, Periselneris J, et al. Hospital mortality and resource implications of hospitalisation with COVID-19 in London, UK: a prospective cohort study. Crit Care Res Pract. 2021;2021:8832660.
21. Docherty AB, Mulholland RH, Lone NI, Cheyne CP, De Angelis D, Diaz-Ordaz K, et al. Changes in in-hospital mortality in the first wave of COVID-19: a multicentre prospective observational cohort study using the WHO clinical characterisation protocol UK. Lancet Respir Med. 2021;9(7):773-85.
22. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: prospective observational cohort study. BMJ. 2020;369:m1985.
23. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and Outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA. 2020;323(16):1574-81.
24. Olivas-Martínez A, Cárdenas-Fragoso JL, Jiménez JV, Lozano-Cruz OA, Ortiz-Brizuela E, Tovar-

Méndez VH, et al. In-hospital mortality from severe COVID-19 in a tertiary care center in Mexico city; causes of death, risk factors and the impact of hospital saturation. PLoS One. 2021;16(2):e0245772.
25. Rieg S, von Cube M, Kalbhenn J, Utzolino S, Pernice K, Bechet L, et al. COVID-19 in-hospital mortality and mode of death in a dynamic and non-restricted tertiary care model in Germany. PLoS One. 2020;15(11):e0242127.
26. COVID-19 mortality rate rose by 40% in 2nd wave, more deaths among people under 45 years, finds study. Firstpost.com. 2021. Available from: https://www.firstpost.com/india/covid-19-mortality-rate-rose-by-40-in-2nd-wave-more-deaths-among-people-under-45-years-finds-study-9763471.html. Accessed on 19 July 2021.
27. Suleyman G, Fadel RA, Malette KM, Hammond C, Abdulla H, Entz A, et al. Clinical characteristics and morbidity associated with Coronavirus disease 2019 in a series of patients in metropolitan Detroit. JAMA Netw Open. 2020;3(6):e2012270.
28. Lindner S, Kubitschke L, Lionis C, Anastasaki M, Kirchmayer U, Giacomini S, et al. Can integrated care help in meeting the challenges posed on our health care systems by COVID-19? Some preliminary lessons learned from the European VIGOUR Project. Int J Integr Care. 2020;20(4).
29. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19). JAMA. 2020;323(18).
30. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. JAMA. 2020;323(13).
31. Liu H, Chen S, Liu M, Nie H, Lu H. Comorbid chronic diseases are strongly correlated with disease severity among COVID-19 patients: a systematic review and meta-analysis. Aging Dis. 2020;11(3):668-78.
32. Sankhe AP, Memane NS, Gawali VP, Memane SN, Ramakrishnan G, Kundu T, et al. A randomized, controlled, blinded, parallel group, clinical trial to study the role of Ayurcov (AyurCoro3), one day regimen as an adjuvant therapy for COVID-19 disease management, at dedicated Covid Hospital (DCH) in India. Complement Therap Med. 2022;67:102824.

Cite this article as: Purushothaman S, Dhotre PK, Vanarase KP, Jadhao GK, Maurya AG, Gupta SM, et al. Multi-center study to analyse outcome of integrated treatment approach in COVID-19 patients. Int J Community Med Public Health 2023;10:723-8.