

ORIGINAL RESEARCH

Risk factors, co-morbidities and outcome of COVID-19 positive patients at tertiary care Centre in Indian population

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ABSTRACT

Background: In India, on 30th January 2020, the first case of COVID-19 was reported. Several co-morbidities and demographic factors are associated with mortality in COVID-19 patients. The present study was undertaken to evaluate risk factors, comorbidities, and mortality of COVID-19 positive patients at tertiary care centre in Indian population. **Methods:** A total 640 COVID-19 positive patients of age 13 years and above were enrolled in the study and evaluated for risk factors, comorbidities, biochemical markers, and outcomes. These variables were compared among survived and dead of COVID-19 positive patients. **Results:** Out of 640 participants, 475 (74.2%) were alive and 165 (25.8%) died. History of contact with COVID-19 positive patients (71.6%) was found to be significant risk factor. Cough (69.7%), breathlessness (63.6%), fever (60.6%) were the commonest clinical features. There was significant difference between survived and dead with respect to breathlessness, ($p=0.0001$). Comorbidities leading to increased risk of mortality were hypertension (26.4%), Diabetes (25.3%) and COPD (20.6%). Inflammatory markers were positively correlated with severity of COVID-19, deranged Neutrophil: Leukocyte ratio and CRP being the most sensitive followed by D-DIMER, serum LDH and IL-6. Higher CT severity scores were related to worse outcomes in COVID-19 patients. COVID-19 positive patients with HIV had 100% mortality due to immune-compromised state. Increased mortality was seen in patients who needed O₂ therapy and NIV. **Conclusion:** CARP protocol and nasogastric feeding was found to be more effective to improve outcome in COVID-19 positive patients on NIV, NRBM and O₂ masks. Chest physiotherapy, strict glycaemic control, adequate hydration, and positive energy have key role in managing COVID-19 positive patients.

Key words: COVID-19, risk factors, comorbidities, mortality, CRP, D-DIMER, NIV

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It primarily presents with respiratory symptoms caused by inflammatory lesions of the lungs and can result in damage to the digestive, nervous and cardiovascular systems. Because the disease progresses rapidly, it can lead to multiple organ failure and even death.¹The

WHO declared the new CORONA virus a public health emergency of worldwide concern on January 30, 2020. On February 11, 2020, the WHO designated it as COVID-19.^{2,3} COVID-19 is a new disease that has spread over the globe as a pandemic. In India, the first case of COVID-19 was detected on January 30, 2020, in Kerala. Following its initial detection, COVID-19 had become prevalent throughout India,

thereafter country has faced two waves with disastrous second wave.⁴ However, a total of about 34 million cases and 4.68 lakh deaths have been reported so far from India.⁵ Few studies have reported death rate as 5.7% among COVID-19 patients with at least one co-existing medical condition, as compared to 0.7% in patients without any comorbidity.⁶ Several comorbidities and demographic factors are associated with mortality in Covid-19 patients. Though, advanced age, male gender and comorbidities such as diabetes mellitus, obesity, systemic hypertension, renal illness, coronary artery disease and cancer were all described as risk factors for COVID-19 mortality in several studies.^{7,8} Apart from symptoms such as fever, cough, dyspnoea, sore throat, loose motions, laboratory parameters such as increased levels of total leukocyte count, deranged N:L ratio, raised CRP, IL-6, D-DIMER, which provide early clues to the severity of disease, and an increased efficacy of specific antiviral and targeted immunomodulatory therapy still unknown, risk classification and prediction of death provide a reasonable strategy to allocating health resources.¹⁹ With this background we have done the study of risk factors, co-morbidities, and mortality of COVID-19 positive patients at tertiary care centre in Indian population.

MATERIALS AND METHODS

After obtaining institutional scientific and ethical committee approval and written informed consent from all the patients, this cross-sectional study was conducted in 640 patients admitted in COVID ward- COVID 19 positive patients at tertiary care hospital from December 2020 to November 2021. RT-PCR

and/or RAT COVID-19 positive patients as well as ANC and PNC COVID 19 positive patients of age 13 years and above with chronic illness, coming to outpatient department and casualty, patients who were willing to give their consent for the study were included in the study. Patients aged below 13 years and patients with RTPCR negative report for COVID-19 and patients unwilling for giving their consent were excluded from the study.

All the relevant information were recorded in case record form and diagnosis was based on RTPCR report for COVID-19. Then the selected patients were evaluated for risk factors and comorbidities. All routine investigation were done and COVID profile was sent. Information regarding social demographic factors such as age, gender and clinical features, contact history, various risk factors, comorbidities and biochemical markers was collected. Outcome measure such as mortality, mean hospital and ICU stay was collected and comparison of these above variables was done among survived and dead COVID-19 positive patients.

STATISTICAL ANALYSIS: The data was collected and entered in Microsoft Excel 2019 Spreadsheet and analyzed using IBM SPSS 21.0 version. The categorical variables were presented as frequency and percentages and continuous variables was presented as mean and standard deviation. The comparison of distribution of categorical variables was done using chi square test and comparison of distribution of continuous variables was done by unpaired T test. P-value less than 0.05 was considered statistically significant.

RESULTS

Table 1: Demographic data of patients

Demographic data	Frequency	Percentage	
Age in years	13-30	22	3.4
	31-40	92	14.4
	41-50	143	22.3
	51-60	213	33.3
	>60	170	26.6
Gender	Male	407	63.6
	Female	233	36.4

It was seen from Table 1 that out of 640 patients, 407 were males and 233 were females. Majority of

patients were from the age group of 51-60 years (33.3%), followed by >60 years (26.6%).

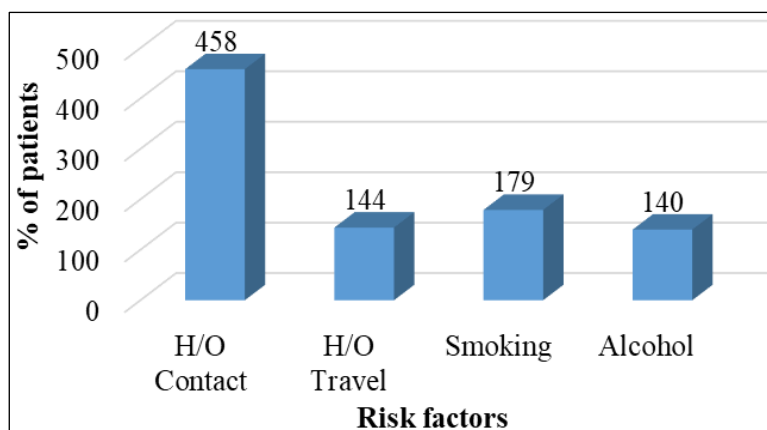


Fig 1: Distribution of study participants according to risk factors

As seen from Figure 1 that the history of contact with COVID-19 positive patients (71.6%) was found to be a significant risk factor.

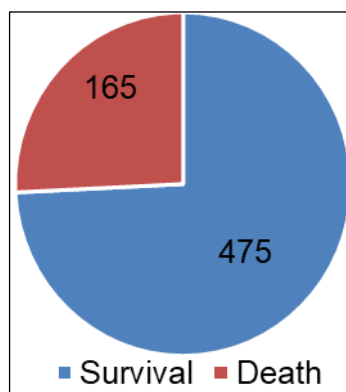


Fig 2: Distribution of study participants according to Outcome

As observed from Figure 2 that out of 640 study participants, 475 (74.2%) were Alive and 165 (25.8%) died.

Table 2: Association of study participants between mortality and clinical features

Clinical features	Total	Survived	Dead	P value
Fever	388 (60.6%)	287 (60.4%)	101 (61.2%)	0.858
Cough	446 (69.7%)	332 (69.9%)	114 (69.1%)	0.847
Breathlessness	407 (63.6%)	269 (56.7%)	138 (83.6%)	0.0001
Loose stools	190 (29.7%)	138 (29.1%)	52 (31.5%)	0.551
Chest pain	83 (13.0%)	64 (13.5%)	19 (11.5%)	0.519
Headache	203 (31.7%)	143 (30.1%)	60 (36.4%)	0.137
Sore throat	198 (30.9%)	144 (30.3%)	54 (32.7%)	0.564

It was seen from Table 2 that cough (446; 69.7%), breathlessness (407; 63.6%) and fever (388; 60.6%) were the commonest clinical features in COVID-19 positive patients. Other features like headache, sore throat, loose stools and chest pain were also seen. There was significant difference between survived and dead with respect to breathlessness.

Table 3: Association of study participants between mortality and co-morbidities

Co-morbidities	Total	Survived	Dead	P value
Hypertension	169 (26.4%)	113 (23.8%)	56 (33.9%)	0.011
Diabetes	162 (25.3%)	111 (23.4%)	51 (30.9%)	0.05
COPD	132 (20.6%)	82 (17.3%)	50 (30.3%)	0.0001
CKD	38 (6.0%)	10 (2.1%)	28 (17%)	0.0001
Cardiac illness	28 (4.4%)	15 (3.2%)	13 (7.9%)	0.011
Malignancy	19 (3.0%)	10 (2.1%)	09 (5.5%)	0.02

Hypothyroidism	39 (6.1%)	27 (5.7%)	12 (7.3%)	0.462
HIV	09 (1.4%)	00 (0.0%)	09 (5.5%)	0.0001
HBsAg	05 (0.8%)	05 (1.1%)	00 (0.0%)	0.186
HCV	03 (0.5%)	02 (0.4%)	01 (0.6%)	0.764
ANC	15 (2.3%)	06(1.3%)	09 (5.5%)	0.002
PNC	12 (1.9%)	07(1.5%)	05 (3%)	0.204
Anaemia	47 (7.3%)	27(5.7%)	20 (12.1%)	0.006

As observed from Table 3 that the comorbidities leading to increased risk of mortality in COVID-19 positive patients were hypertension (26.4%), diabetes (25.3%), COPD (20.6%), CKD (6%). There was significant difference between survived and dead with

respect to hypertension, diabetes, COPD, CKD, Cardiac Illness, Malignancy, HIV, ANC and anaemia. All HIV positive patients who got infected with COVID 19 virus succumbed due to immune-compromised state.

Table 4: Association of study participants between mortality and hospitalization and treatment

Hospitalization and treatment		Total	Survived	Dead	P-value
Hospitalization	ICU	227 (35.5%)	68(14.3%)	159(96.4%)	0.0001
	Ward	413 (64.5%)	407(85.7%)	6(3.6%)	
O2 Supplementation		337 (52.6%)	332 (69.9%)	5 (3%)	0.0001
Broad Spectrum Antibiotics		384 (60%)	224(47.2%)	160(97%)	0.0001
Anti-Viral		365 (57%)	202(42.5%)	163(98.8%)	0.0001
Steroids		275 (43%)	148(31.6%)	127(77%)	0.0001
Anticoagulants		256 (40%)	96(20%)	160(97%)	0.0001
Supportive treatment		128 (20%)	28(5.9%)	100(60.6%)	0.0001

It was seen from Table 4 that among study participants, broad spectrum antibiotics were used in 384(60%), anti-viral in 365(57%), O2 Supplementation used in 303(47.3%), Steroids use among 275(43%), anticoagulants for 256(40%) and

supportive treatment like nebulization for 128(20%). There was significant difference between survived and dead in regards to hospitalization, broad spectrum antibiotics, anti-viral, steroid use, anticoagulants and O2 supplementation.

Table 5: Association of study participants between mortality and biochemical markers

Biochemical markers		Total	Survived	Dead	P-value
TLC	Normal	75 (11.7%)	58(12.2%)	17(10.3%)	0.512
	Abnormal	565 (88.3%)	417(87.8%)	148(89.7%)	
NLR	Normal	170 (26.6%)	131(27.6%)	39(23.6%)	0.323
	Abnormal	470 (73.4%)	344(72.4%)	126(76.4%)	
D-Dimer	Normal	434 (67.8%)	351(73.8%)	83(50.3%)	0.0001
	Abnormal	206 (32.2%)	124(26.1%)	82(49.7%)	
LDH	Normal	471 (73.6%)	356(74.9%)	115(69.7%)	0.188
	Abnormal	169 (26.4%)	119(25.1%)	50(30.3%)	
IL6	Normal	501 (78.3%)	380(80%)	121(73.3%)	0.05
	Abnormal	139 (21.7%)	95(20%)	44(26.7%)	
CRP	Normal	378 (59.1%)	303(63.7%)	75(45.5%)	0.0003
	Abnormal	262 (40.9%)	172(36.2%)	90(54.5%)	

It was observed from Table 5 that abnormal TLC count (88.3%) raised Neutrophil to Leukocyte ratio (73.4%) and CRP (40.9%) were the most sensitive biochemical markers for indicating severity and increased risk of mortality in COVID19 positive

patients followed by D- Dimer (32.2%), LDH (26.4%) and IL6 (21.7%). There was significant difference between survived and dead in regards to Bio chemical markers CRP, D-Dimer, IL6.

Table 6: Distribution of study participants between mortality and CT severity score

CT Severity Score	Total	Survived	Dead	P-value
0	329 (51.4%)	328(69.1%)	1(0.6%)	0.0001
1-5	90 (14.1%)	76(16%)	14(8.5%)	
6-10	130 (20.3%)	59(12.4%)	71(43%)	
11-15	45 (7.0%)	11(2.3%)	34(20.6%)	

16-20	30 (4.7%)	1(0.2%)	29(17.6%)
21-25	16 (2.5%)	00 (0.0%)	16(9.7%)
Total	640 (100%)	475(100%)	165(100%)

It was seen from Table 6 that majority of patients were admitted in general ward (64.5%), and (35.5%) were admitted in ICU. Normal CT findings were seen in 329(51.4%) patients. Among Survived CT Score 0 was 328(69.1%), 1-5 score was 76(16%), 6-10 score was 59(12.4%), 11-15 score was 11(2.3%), 16-20 score was 1(0.2%). Among Dead, CT Score of 6-10 scores was 71(43%), 11-15 score was 34(20.6%), 16-20 score was 29(17.6%), 21-25 score was 16(9.7%) and 1-5 score was 14(8.5%) and Score of 0 was among 1(0.6%). There was significant difference between survived and dead with respect to CT severity score. No O₂ requirement was seen in 337(52.6%) patients. bag and mask were used for 121(18.9%), NIV for 94(14.7%), nasal prongs for 55(8.6%) and ventilator support for 33 (5.2%). Patients on mechanical ventilator had poor outcome in terms of survival.

DISCUSSION

In the present study, the mortality among COVID-19 patients was 25.8%. Among study participants majority of patients were from the age group of 51-60 years (33.3%), followed by >60 years (26.6%) and 41-50 years (22.3%). Majority of patients were males (63.6%) and 36.4% were females. These finding is consistent with the findings of previous studies.¹⁰⁻¹²

As age increase there was significant increase in mortality as is evidenced by previous studies.^{13, 14}In the present study, statistically higher risk of mortality in middle and elderly age group as compared to other age groups.

Cough (69.7%), breathlessness (63.6%), fever (60.6%) were the commonest clinical features in COVID-19 positive patients. History of contact with positive patients present in 71.6%, smoking present among 28%, history of travel in 22.5% and alcohol intake in 21.9%. However, there was significant difference between survived and dead with respect to breathlessness. These findings are comparable with the study done by Marimuthu Y *et al.*¹⁰, Ramkumar R *et al.*¹⁵ and Jain S *et al.*¹⁶ Also, smoking and alcohol use were strongly linked with COVID-19 mortality, which is consistent with the findings of other investigations.^{17,18} The most common co-morbidities in current study were hypertension (26.4%) and diabetes (25.3%). Similar findings are reported in Marimuthu Y *et al.*¹⁰ and Ramkumar R *et al.*¹⁵ Risk factors for COVID-19 mortality with statistically significant value include hypertension, diabetes mellitus, COPD, CKD, Cardiac illness, HIV positivity and ANC patients and anaemia which is comparable with the study done by Praveen JV *et al.*¹¹ and Kayina CA *et al.*¹⁹ Similarly, as patients with co-morbidities were most likely to have death than patients without

death. The findings were comparable with previous studies.^{20,21}

Among study participants, broad spectrum antibiotics were used in 384(60%), Anti-viral in 365(57%), O₂ supplementation used in 303(47.3%), Steroids use among 275(43%), Anticoagulants for 256(40%) and Supportive Treatment like Nebulization for 128(20%). There was significant difference between survived and dead with respect to hospitalization, broad spectrum antibiotics, anti-viral, steroid use, anticoagulants and O₂ supplementation. Similar findings were found in study done by Roy DB *et al.*²² In regard to biochemical markers, abnormal TLC count (88.3%), raised Neutrophil to Leukocyte ratio (73.4%) and CRP (40.9%) were the most sensitive biochemical markers for indicating severity and increased risk of mortality in COVID19 positive patients followed by D- Dimer (32.2%), LDH (26.4%) and IL6 (21.7%). Inflammatory markers were positively correlated with severity of COVID-19, deranged Neutrophil: Leukocyte ratio and CRP being the most sensitive followed by D-DIMER, serum LDH and IL-6. There was significant difference between survived and dead with respect to biochemical markers CRP, D-Dimer, IL6. These results are comparable with the study conducted by Malik P *et al.*²³

Normal CT findings were seen in 329(51.4%) patients. Mild among 90(14.1%), Moderate among 175(27.3%) and Severe among 46(7.2%). According to CT Severity Score, 0 Score was seen in 329(51.4%), 6-10 score among 130(20.3%), 1-5 score among 90(14.1%), 11-15 score among 45(7%), 16-20 score among 30(4.7%) and 21-25 score among 16(2.5%). There was significant difference between survived and dead with respect to CT Severity Score. Majority of patients were admitted in general ward (64.5%) and (35.5%) were admitted in ICU. The average age of COVID-19 positive patients requiring ICU admission during hospitalization was 60 years or older. Furthermore, individuals above the age of 60 had the greatest fatality rate. In addition to the results mentioned above, the presence of co-morbidities at the time of admission aided in the course of the disease. In resource-constrained environments, this specific subset of patients should be prioritized for immediate medical intervention. According to mode of delivery of O₂, No O₂ Requirement was 337(52.6%), bag and mask were used among 121(18.9%), NIV among 94(14.7%), Nasal prongs among 55(8.6%) ventilator support among 33 (5.2%). Patients on mechanical ventilator had poor outcome in terms of survival.

Mortality as an outcome, was directly associated with age of the patients and fever, cough, breathlessness as clinical symptoms. Patients with mild symptoms and

without O₂ requirement were discharged early or were advised home isolation. Higher CT severity scores were related to worse outcomes in COVID-19 positive patients. COVID 19 positive patients with HIV had 100% mortality due to immune-compromised state. Increased mortality was seen in patients who needed O₂ therapy and in patients who needed NIV. Patients on mechanical ventilation were found to have least cure rate. These findings are correlated with the study done by Marimuthu Y *et al.*¹⁰ and Galbadageet *al.*²⁴ People with uncontrolled medical problems such as diabetes, hypertension, chronic lung disease, liver disease, or renal illness, as well as those on immune-suppressants, are at a higher risk of COVID-19 infection.²⁵ The intensity of symptoms, clinical outcome, and duration of stay in hospitalized patients are all affected by underlying medical disorders.

LIMITATIONS

The limitation of study was all COVID-19 patients (study participants) were selected from one tertiary care center.

CONCLUSION

CARP protocol and nasogastric feeding was found to be more effective to improve outcome in COVID-19 positive patients on NIV, NRBM and O₂ masks. Chest physiotherapy, strict glycemic control, adequate hydration, and positive energy have key role in managing COVID-19 positive patients. There is a need for further vigilance and surveillance to monitor advancements in the COVID-19 disease.

REFERENCES

1. Wang H, Xing Y, Yao X, Li Y, Huang J, Tang J, *et al.* Retrospective study of clinical features of covid-19 in inpatients and their association with disease severity. *Med Sci Monit.* 2020;26:e927674.
2. COVID-19 Coronavirus Pandemic Worldometer. Available from: <https://www.worldometers.info/coronavirus>. Last Accessed on 25th December 2021.
3. COVID-19 public health emergency of international concern (PHEIC) global research and innovation forum [Internet] [cited 2020 Aug 17], Available from: [https://www.who.int/publications/m/item/COVID-19-public-health-emergency-of-internationalconcern-\(pheic\)-global-research-and-innovation-forum](https://www.who.int/publications/m/item/COVID-19-public-health-emergency-of-internationalconcern-(pheic)-global-research-and-innovation-forum).
4. Zothantluanga JH, Lalthanzara H, Shakya A, Chetia D. The Outbreak of COVID-19 in Mizoram, India. *Assam; Rizug;* 2020. Available from: https://www.researchgate.net/publication/347947640_The_outbreak_of_COVID-19_in_Mizoram_India. [Last Accessed on 25th December 2022].
5. Available from: <https://www.worldometers.info/coronavirus/#countries> [Last accessed on 2021 October 31].
6. Gupta R, Singh B, Gautam A, Singh G, Khan M & Kumar V. SARS-CoV-2 infection related mortality and comorbidities in a dedicated COVID-19 facility: A record-based analysis from Uttar Pradesh. *Asian Journal of Medical Sciences* 2022;13(3):3–10.
7. Shaikh FS, Aldhafferi N, Buker A, Alqahtani A, Dey S, Abdulhamid S *et al.* Comorbidities and Risk Factors for Severe Outcomes in COVID-19 Patients in Saudi Arabia: A Retrospective Cohort Study. *J MultidiscipHealthc.* 2021;14:2169-83.
8. Dessie ZG., Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. *BMC Infect Dis* 2021;21:855.
9. Gopalan N, Senthil S, Prabakar NL, Senguttuvan T, Bhaskar A, Jagannathan M, *et al.* Predictors of mortality among hospitalized COVID-19 patients and risk score formulation for prioritizing tertiary care-An experience from South India. *PLoS ONE* 2022;17(2):e0263471.
10. Marimuthu Y, Kunnivil R, Anil NS, Nagaraja SB, Satyanarayana N, Kumar J, Ramya B. Clinical profile and risk factors for mortality among COVID-19 inpatients at a tertiary care centre in Bengaluru, India. *Monaldi Arch Chest Dis.* 2021;91(3):25-28.
11. Praveen JV, Kumar KM. Initial oxygen saturation at presentation as a predictor of mortality in COVID19 positive cases in a tertiary care center in South India. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS).* 2021;20(7):23-27.
12. Soni SL, Kajal K, Yaddanapudi LN, Malhotra P, Puri GD, Bhalla A, *et al.* Demographic & clinical profile of patients with COVID-19 at a tertiary care hospital in north India. *Indian J Med Res.* 2021;153(1&2):115-25.
13. Cui J, Li F & Shi ZL. Origin and evolution of pathogenic coronaviruses. *Nat. Rev. Microbiol.* 2019;17:181-92.
14. Wu JT, Leung K. & Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 2020;395:689-97.
15. Ramkumar R, Rani D, Bhattacharjee S, Aggarwal R, Soni KD, Aravindan A, Gupta A, Ayub A, Prakash K, Ganesh V, Trikha A. Epidemiology and clinical characteristics of COVID- 19 patients requiring critical care in a Tertiary care teaching hospital. *J Anaesthesiol Clin Pharmacol.* 2021;37(3):366-70.
16. Jain S, Mohanty V, Gangil N, Arora S, Bajaj A. Awareness regarding COVID-19 preparedness among dentists: A cross-sectional survey. *J Indian Assoc Public Health Dent* 2022;20:153-58.

17. Hui DS. *et al.* The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health-the latest 2019 novel coronavirus outbreak in Wuhan, China. *Intl. J. Infect. Dis.* 2020;91:264-66.
18. Deng SQ. & Peng HJ. Characteristics of and public health responses to the coronavirus disease 2019 outbreak in China. *J. Clin. Med.* 2020;9:575.
19. Kayina CA, Haritha D, Soni L, Behera S, Nair PR, Gouri M, *et al.* Epidemiological & clinical characteristics & early outcome of COVID-19 patients in a tertiary care teaching hospital in India: A preliminary analysis. *Indian J Med Res.* 2020;152(1&2):100-104.
20. Han, Q., Lin, Q., Jin, S. & You, L. Coronavirus 2019-nCoV: a brief perspective from the front line. *J. Infect.* 2020;80:373-77.
21. Zhu, N. *et al.* A Novel Coronavirus from patients with pneumonia in China, 2019. *N. Engl. J. Med.* 2020;382:727-33.
22. Roy *et al.* Outcome of Different Therapeutic Interventions in mild COVID-19 Patients in a Single OPD Clinic of West Bengal: A Retrospective study.
23. Malik P, Patel U, Mehta D, Patel N, Kelkar R, Akrmah M, Gabrilove JL, Sacks H. Biomarkers and outcomes of COVID-19 hospitalizations: systematic review and meta-analysis. *BMJ Evid Based Med.* 2021;26(3):107-08.
24. Galbadage T, Peterson BM, Awada J, Buck AS, Ramirez DA, Wilson J and Gunasekera RS. Systematic Review and Meta-Analysis of Sex-Specific COVID-19 Clinical Outcomes. *Front. Med.* 2020;7:348-50.
25. Chen Y, Guo Y, Pan Y, *et al.* Structure analysis of the receptor binding of 2019-nCoV. *BiochemBiophys Res Commun* 2020;525:135-40.