Success rate of Remdesivir, Convalescent Plasma, and Tocilizumab in moderate to severe Covid-19 pneumonia: our experience in a tertiary care center

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ABSTRACT

Introduction: After the first case of Covid-19 was identified in Wuhan City, China, the numbers increased rapidly all over the world putting a huge burden on the entire healthcare system. Managing these cases posed a great challenge to the treating clinicians in the absence of targeted therapy. At this juncture, few modalities got approved as EUA (Emergency use under authorization) drugs namely Remdesivir, Convalescent Plasma (CP), and Tocilizumab (TCZ) to treat this deadly disease. Aim: To analyze the success rates of EUA therapies for Covid-19 pneumonia in our hospital. Materials and Methods: This was a prospective observational study conducted from April 2020 to October 2020 in the department of Medicine at Tata Main Hospital, Jamshedpur, Jharkhand. All adults with moderate to severe Covid-19 as per the WHO criteria were enrolled in the study with their informed consent. Patients with estimated glomerular filtration rate <30 mL/min, deranged liver function tests, electrocardiographic abnormalities, and deranged hematological parameters were excluded from the study. Thorough clinical evaluation was done in all cases. Routine investigations together with CRP, LDH, serum Ferritin, D Dimer and IL6, Chest X-Ray, and HRCT thorax were done in all cases. ECG was done in all cases and 2D-ECHO in selected ones. Depending on their clinical and radiological criteria, patients were treated with various modalities approved under EUA with close monitoring of clinical, biochemical, and radiological parameters. Presenting symptoms, clinical findings, co-morbidities, laboratory parameters, and radiological assessment were analyzed, and statistical analysis was done. The survival rate and in-hospital mortality was analyzed. Observations and Results: We had a total of 448 patients who were included in our study, out of which 326 were males and 122 were females with a male to female ratio of 2.7:1. Their age varied between 16 and 91 years with an average of 51.4 years with a standard deviation (SD) of +/-6.4 years. About 255 patients (57%) received only Remdesivir (176 males, 79 females), 139 (105 males, 35 females) patients (31%) received Remdesivir along with two units of CP, and 38 (32 males, 6 females) patients received a combination of Remdesivir, CP, and TCZ. All patients in our study tolerated the drugs well. About 5% of patients who received CP had minor transfusion reactions. One patient had TRALI and three patients had TACO, which was managed aggressively. Asymptomatic transaminitis was seen in 36% patients. The survival rate in patients treated with Remdesivir was 78%, those with Remdesivir and CP was 44%, and those with all three was 13%. The mean length of stay was 14.23 days with a SD of 9.06 days in patients treated with TCZ in comparison to other two modalities, which was 13.88 days with a standard variation of +/-8.71 days in Remdesivir and 13.88 days with a SD of 8.73 days in patients treated with CP that was stastically significant. Conclusions: Though the success rate of various drugs under EUA varies in different studies from all over the world, the data to support their use are encouraging. We also observed satisfying results in our study specially with the use of Remdesivir. Therefore, EUA agents should be used early to fight against COVID-19 along with the other measures as per the protocol laid by ICMR and MoHFW.

Keywords: Convalescent plasma, in-hospital mortality, novel corona virus SARS-CoV-2, pneumonia, Remdesivir, success rate, Tocilizumab

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Introduction

Zhu et al[1] reported the first case of COVID-19 caused by the novel corona virus SARS-CoV-2 in Wuhan City, Hubei Province in China. Then on, there was a rapid rise in the cases leading to a global pandemic declared by WHO in March 2020. Managing this deadly disease poses a great challenge to clinicians all over the world especially in the absence of a definite and targeted treatment. At this juncture, approval of drugs like Remdesivir, Convalescent Plasma (CP) and Tocilizumab (TCZ) under EUA (Emergency use under Authorization) brought a ray of hope in fighting the pandemic. Remdesivir, a broad-spectrum antiviral medication was approved by US. Food and Drug Administration as EUA[2] to treat COVID19 in around 50 countries. Cantini et al[3] in their systematic review recommended antiviral therapy for Covid-19. The NIH study[4] showed that Remdesivir shortened the time to recovery even in advanced Covid-19. In the United States, Remdesivir was indicated for use in adults and adolescents (aged 12 years and older with body weight of at least 40 kg) for the treatment of COVID19 requiring hospitalization. The European Union also recommended Remdesivir in adults with pneumonia requiring supplemental oxygen. Preliminary data from an international multi-center, placebo controlled double-blind randomized trial carried out by the US National Institutes of Health[5] showed that Remdesivir decreased the recovery time from 15 to 11 days in COVID19 patients. A study by Wang et al[6] also showed similar results with Remdesivir. The National Institute of Allergy and Infectious Diseases (NIAID) declared that Remdesivir was better than a placebo in reducing recovery time in COVID19 pneumonias. However, the study concluded that there is high mortality. A Chinese study published in The Lancet did not show significant benefits of Remdesivir, concluding that further research is required to understand the effectiveness of the drug. Final data from the Adaptive Covid-19 Treatment Trial[7] suggested that Remdesivir was effective in reducing the recovery time from 15 to 10 days. CP was approved under EUA by FDA as a potential promising agent to fight against COVID-19 in August 2020. Multiple studies have reported the use of CP to treat COVID-19 patients. PLACID (PLAsma Convalescent InDia) Trial conducted by the Indian Council of Medical Research (ICMR) showed signs of clinical improvement and faster viral clearance, but no survival benefit.[8] Li et al[9] did not show a clear benefit with CP in treatment of Covid-19 in their series. Cytokine storm played an important role in the progression to respiratory and multiorgan failure in patients with Covid-19. TCZ, an interleukin-6 receptor antagonist, was approved under EUA for the treatment with the hope that its use may reduce the severity of the cytokine release storm. Zhang C and his team had shown that TCZ may be the key to reduce mortality.[10] Channappanaver R and Periman S described the immunopathology and role of cytokine storm in their study.[11] Beneficial effect of Remdesivir in the treatment of Covid-19 was published in New England Journal of Medicine.[12] A study by Beigel JH et al.[13] also documented benefits of treatment with Remdesivir. With this background, we undertook a study in our hospital, which is a 985- bedded tertiary care setup with 450 dedicated beds for Covid-19, with the aim to find the success rate of Remdesivir alone and in combination with CP and TCZ in moderate to severe cases of Covid-19 pneumonia.

Materials and Methods

This was a prospective observational study conducted from April 2020 to October 2020 in the Department of Medicine at Tata Main Hospital, Jamshedpur, India after ethical clearance. All patients above 16 years of age, both male and female with positive RT-PCR for SARS-CoV-2, with features of lower respiratory tract infection (moderate to severe Covid-19 and as per the WHO criteria) were taken into the study design with their informed consent. Patients with Covid-19 are considered to have severe illness if they have SpO2 <94% on room air at sea level, a respiratory rate of >30 breaths/min, PaO2/FiO2 <300 mm Hg, or lung infiltrates >50%. In moderate covid-19 pneumonia, patients show evidence of lower respiratory disease during clinical assessment or imaging and they have saturation of oxygen (SpO2) ≥94% on room air. Patients with estimated glomerular filtration rate less than 30 mL/ min, raised Alanine aminotransferase (ALT) or Aspartate aminotransferase (AST) more than five times of the upper limit, features of cardiomyopathy, ECG changes, Absolute neutrophil count (ANC) less than 1000/μL, platelet count less than 50,000/μL at screening and patients with body weight less than 40 kg were excluded from the study. Thorough clinical evaluation was done in all cases. Routine investigations were done including CRP, LDH, and serum ferritin on first day. D-Dimer test and IL6 were also done in selected cases. Routine Chest X-ray and HRCT thorax were done in all cases having either unilateral or bilateral lung infiltrates. ECG was done in all cases and 2D-ECHO was done in selected cases before starting drugs like Remdesivir. Proper informed consent was taken from all patients and their guardians. Depending on their clinical and radiological criteria, patients were treated with various modalities of drugs approved under EUA. We had three groups of patients. Approval obtained on 28.03.2020 for undertaking the study & on 29.12.2020 for sending the manuscript for publication.

- Group I (Moderate)- Who received Remdesivir alone
- Group II (Moderate)- Who received Remdesivir and CP
- Group III (Severe)- Who received Remdesivir, CP, and TCZ.

In Group I, we had 255 cases (male-176, female-79). Remdesivir was given in the dose of 100 mg twice a day on first day followed by 100 mg once a day for 5 days to 10 days.

In Group II, there were 139 patients (105 male and 34 female) who received CP along with intravenous Remdesivir. CP was given to patients in whom PaO2/FiO2 ratio varies between 200 and 300, respiratory rate more than 30/minute, or oxygen saturation less than 90% on room air and when the treating clinician predicted a high risk of progression to severe or life-threatening stage. However, pregnant/breastfeeding women, patients with known hypersensitivity to blood products, those who received pooled immunoglobulin in last 30 days, and critically ill patients were excluded from plasma therapy. First dose of CP was 200 ml infused over 2–4 hrs and a second dose of 200 ml was transfused after 24 hours, if no adverse effects were seen.
In Group III, we had 38 patients (32 male and 6 female) who received TCZ along with Remdesivir and CP. This was given to patients with severe disease and MODS requiring ICU care with either NIV or invasive ventilator support. TCZ was given at a dose of 400 mg iv stat (total two doses) for CRS (cytokine release storm). In addition to drugs under EUA all patients also received iv antibiotics, ivermectin, Low Molecular Weight Heparin (LMWH), Steroids, Vitamin C and Zinc supplements along with oxygen, NIV or invasive ventilation as and when required.

Patients were closely monitored for vitals, oxygen saturation, respiratory rate, and any complications. Hematological, biochemical, and radiological parameters were also monitored frequently as per our institutional protocol, which is guided by Indian Council of Medical Research (ICMR) and Government of India Ministry of Health and Family Welfare (MoHFW). Detail analysis of patients including presenting clinical symptoms, co-morbidities like hypertension, diabetes and ischemic heart disease, hypothyroidism, COPD (Chronic Obstructive Pulmonary Disease), malignancy, radiological assessment, and computed tomography (CT) severity score were done. Relevant laboratory parameters like NLR (Neutrophil Lymphocyte Ratio), CRP, ALT, AST, serum ferritin, and D-dimer were also analyzed. Patients outcome in the form of improvement in clinical symptoms, length of stay, time to turn negative, and in-hospital mortality was recorded. Survival rate was calculated as the percentage of people in this study who survived, got discharged, and went home. Statistical analysis was done by using SPSS version 26.

Results

We had a total of 448 patients who were included in our study, out of which 326 were male and 122 were female with a male to female ratio of 2.7:1 [Figure 1]. Their age varied between 16 and 91 years with an average age of 51.4 years with a SD of ± 6.4 [Figure 2]. About 271 patients were initially enrolled to receive Remdesivir but 16 patients did not receive full dose of the drug because six patients developed severe sinus bradycardia and 10 had altered liver function tests after the first dose of remdesivir and were excluded from study. The remaining 255 patients (57%) received only Remdesivir (176 male, 79 female), 139 patients (31%) received Remdesivir along with two units of CP (105 male and 35 female), and 38 received triple therapy (combination of Remdesivir, CP and TCZ (32 male and 6 female) [Figure 3].

Patients in all the three groups presented with complaints of varying degrees of fever, cough, chest pain, weakness, and breathlessness. Hypertension and diabetes were the dominant co-morbid conditions in these patients who received EUA drugs. In patients who received the triple drug combination, diabetes mellitus and hypertension together comprised 44%. In patients who received Remdesivir along with CP, the same two disorders constituted 43%. In patients who received Remdesivir only, diabetes and hypertension together comprised 92% [Figure 4]. Other co-morbid conditions like hypothyroidism, COPD (Chronic obstructive pulmonary diseases) and IHD (Ischaemic Heart Disease) constituted 1–9% of cases. Most patients had either one (39.9%) or two, or more (55.7%) of the coexisting conditions. Hypertension was the commonest (47%) followed by type 2 Diabetes Mellitus (43.3%).

Clinical symptoms significantly improved in Group I along with an increase of hemoglobin saturation within 2 days of
therapy. Several parameters improved like increased lymphocyte counts and decreased CRP. Radiological examination also showed varying degrees of absorption of lung lesions within 5 days. In group II, though there was clinical well-being the radiological parameters worsened in 35% of cases. The mean length of stay in patients belonging to group I was 13.88 days with a SD of +/- 8.71 days. In Group II too, it was 13.88 days with SD of +/- 8.73 and in Group III, it was 14.23 with SD of +/- 9.06 days [Figure 5]. Viral load was undetectable within 7 days after transfusion in 21 (15%) patients in group II versus 105 (41%) in group I and five (13%) in group III.

The survival rate in group I was 78%, 44% in Group III and only 13% (five patients) in Group III [Figure 6]. The mortality rate was 22% in group I, 56% in group III, and 87% in group III. Maximum mortality was seen between 60 and 80 years of age, and with two or more than two associated co-morbid conditions. No treatment-related complications were observed in group I. All of them tolerated the drug well. About 45% of patients felt clinically better after the second dose of remdesivir. 5% of cases who received CP had minor transfusion reactions, and one patient had TRALI (Transfusion related acute lung injury) and three patients had TACO (Transfusion associated circulatory overload), which was managed aggressively. Asymptomatic transaminitis was seen in 14 (36%) patients. Overall, our patients tolerated Remdesivir, CP, and TCZ well.

**Discussion**

Andrews et al.[13] reported the first case of coronavirus-2 (SARS CoV-2) in Kerala, India on January 27, 2020. Then on the number of positive cases has been increasing in an alarming manner. Death occurs mainly due to bilateral pneumonia, respiratory failure, and thrombotic complications attributed to immune-mediated inflammatory damage. After the approval of EUA drugs by FDA, several studies were done all over the world to predict the safety and effectiveness in treating covid-19 cases.

The success rate varied widely with some studies showing high efficacy versus no benefit in some others. Remdesivir, a broad-spectrum antiviral medication was found to be superior to placebo in ACTT-1 clinical trials. The mortality in this study was 15% with Remdesivir whereas in our series it was 21%, which was a little higher. Another double-blind, placebo-controlled multicentric trial by Yeming Wang et al.[6] from China found that intravenous Remdesivir did not significantly improve the time to clinical improvement, mortality, or time to clearance of virus in patients with serious COVID-19 compared with placebo. But in our study, there was improvement in clinical well-being and the time to clearance of the virus. In the SOLIDARITY trial,[13] there was a trend towards reduced mortality with Remdesivir among patients requiring low-flow or high-flow oxygen at baseline, but not among those requiring mechanical ventilation that is similar to our observation.

CP is a source of antiviral neutralizing antibodies along with anti-inflammatory cytokines, and other immunomodulatory proteins, which might have a role in improving systemic inflammatory response syndrome as shown in the study by Rojas et al.[14] In the pre-vaccine era, CP was used to treat viral diseases such as poliomyelitis, measles, mumps, and influenza and more recently Ebola virus disease. Ever since the publication of the first case series from China, multiple observational studies have been published reporting the association between CP
and reduced mortality, decrease in length of hospital stay, and viral load in patients with Covid-19. In our study, the mean length of stay in group I and II was 13.88 days with a SD of +/− 8.71 and 8.73 days. However, in group III the mean length of stay was 14.23 days with a SD of =/− 9.06 days. The PLACID (PLAsma Convalescent InDia) trial conducted by the Indian Council of Medical Research (ICMR) showed lack of survival benefit though there were improvements in symptoms like oxygen saturation level and faster viral clearance, which was similar to our observation—the success rate being only 44%. Due to study limitations, it is difficult to predict whether this success rate is because of CP or remdesivir because the patients received both modalities of therapy. CP was not associated with a reduction in progression to severe covid-19 or all-cause mortality. A recent Cochrane review including 20 studies (one randomized controlled trial, three controlled non-randomized studies of intervention, 16 non-controlled non-randomized studies of intervention), concluded that the effectiveness of CP in improving mortality or clinical improvement is uncertain in patients with Covid-19. The most recent RECOVERY trial has included a randomised comparison of CP versus usual care alone. The Independent Data Monitoring Committee (DMC) held a routine meeting on Thursday 14 January to review the available safety and efficacy data and closed the recruitment to the CP arm of the RECOVERY trial as there has been no convincing evidence of the effect of CP on clinical outcomes in patients admitted to hospital with COVID-19.

Like the study by Zhang et al., Channappanavar R and Perlman S also documented that cytokine release storm leads to destruction of alveolar epithelial cells, thereby releasing proinflammatory cytokines like IL-1β, IL-6, and tumor necrosis factor, which is the leading cause of organ dysfunction and mortality in covid-19 pneumonia. A study by Zhou et al. had identified increased IL-6 levels as one of the laboratory markers associated with high mortality. In our series, 67% of cases who expired had increased IL-6 levels, which is similar to the above mentioned study. TCZ, a monoclonal antibody, directed against the IL-6 inhibitor is the most common agent used for treatment of SARS CoV-2 pneumonia with evidence of CRS (Cytokine release Storm) followed by Anakinra and Itolizumab in China, France, and Italy, and it has shown a survival benefit in these patients. Patel et al. showed improved survival, reduced ICU, stay and ventilatory support in patients treated with TCZ. But in our series, the survival rate was poor (13%); only five patients survived out of 38 patients treated with TCZ. Though there was viral clearance after 8–10 days they succumbed to multi-organ failure. The high mortality rate probably attributed to more associated comorbid conditions, old age, advanced disease, and less number of patients and given to only the most severe cases. Results from the BACC Bay trial also found TCZ not to be effective in preventing intubation or death in hospitalized patients with moderate COVID-19 disease, which was similar to our study. This study being observational in nature has its own limitations. Testing, triaging, and aggressive treatment is the cornerstone in managing covid-19 cases. The family physicians play an important role in testing, triaging, and timely referral of the cases to higher center thereby helping in early diagnosis and management.

Success rate of various drugs under EUA varies in different studies. We observed 78% success rate with Remdesivir, 44% with CP, and only 13% with the combination of three [Remdesivir, CP and TCZ]. The success rate is poor in patients having two or more co-morbid conditions and in multi-organ failure.

**Conclusions**

Though the success rate of various drugs under EUA varies in different studies from all over the world, the data to support their use are encouraging as part of its ongoing efforts to fight COVID-19. The U.S. Food and Drug Administration even broadened the scope of the existing EUA for Remdesivir to include treatment of all hospitalized adult patients irrespective of their severity. We observed a 78% success rate with Remdesivir, 44% with CP and only 13% with the combination of three [Remdesivir, CP, and TCZ]. The last result was perhaps dismal because the patients were serious and in multi-organ failure. Therefore, EUA drugs should be used in all cases of moderate to severe pneumonia.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Zhu H, Wei L, Niu P. The novel coronavirus outbreak in Wuhan, China. Glob Health Res Policy 2020;5:6. doi: 10.1186/s41236-020-00135-6.

2. U. S. Food and Drug Administration Approves Gilead’s Antiviral Veklury (Remdesivir) for Treatment of COVID-19. Gilead Sciences, Inc. 22 October. 2020, 23:2020. Available from: https://in.news.yahoo.com/u-food-drug-administration-approves-200200390.html.

3. Cantini F, Goletti D, Petrone L, Najafi Fard S, Niccoli L, Foti R. Immune therapy, or antiviral therapy, or both for COVID-19: A systematic review. Drugs 2020;80:1929‑46.

4. NIH Clinical Trial Shows Remdesivir Accelerates Recovery from Advanced COVID-19 (Press release). National Institute of Allergy and Infectious Diseases. 2020. Accessed: April 2020. Available from: https://www.niaid.nih.gov/news-events/
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nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19. [Last accessed on 2020 Apr 29].

5. Kolata G. Federal Scientists Finally Publish Remdesivir Data. The New York Times. Available from: https://www.nytimes.com/2020/05/23/health/coronavirus-remdesivir.html. [Last accessed 2020 May 25].

6. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, et al. Remdesivir in adults with severe COVID-19: A randomised, double-blind, placebo-controlled, multicentre trial. Lancet 2020;395:1569-78.

7. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the treatment of COVID-19 - Final report. N Engl J Med 2020;383:1813-26.

8. Agarwal A, Mukherjee A, Kumar G, Chatterjee P, Malhotra P, PLACID Trial Collaborators. Convalescent plasma in the management of moderate COVID-19 in adults in India: Open label phase II multicentre randomised controlled trial (PLACID Trial). BMJ 2020;371:m3939. doi: 10.1136/bmj.m3939.

9. Li L, Zhang W, Hu Y, Tong X, Zheng S, Yang J, et al. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe COVID-19: A randomized clinical trial. JAMA 2020;324:460-70. doi: 10.1001/jama.2020.10044.

10. Zhang C, Wu Z, Li JW, Zhao H, Wang GQ. Cytokine release syndrome in severe COVID-19: Interleukin-6 receptor antagonist tocilizumab may be the key to reduce mortality. Int J Antimicrob Agents 2020;55:105954. doi: 10.1016/j.ijantimicag.2020.105954.

11. Channappanavar R Perlman S. Pathogenic human coronavirus infections: Causes and consequences of cytokine storm and immunopathology. Semin Immunopathol 2017;39:529-39.

12. Andrews M A, Areekal B, Rajesh K. First confirmed case of COVID-19 infection in India: A case report. Indian J Med Res 2020;151:490-2.

13. WHO Solidarity Trial Consortium, Pan H, Peto R, Henao-Restrepo AM, Preziosi MP, Sathiyamoorthy V, et al. Repurposed antiviral drugs for Covid-19-Interim WHO solidarity trial results. N Engl J Med 2021;384:497-511

14. Rojas M, Rodriguez Y, Monsalve DM, Acosta-Ampudia Y, Camacho B, Gallo JE, et al. Convalescent plasma in COVID-19: Possible mechanisms of action. Autoimmun Rev 2020;19:102554. doi: 10.1016/j.autrev.2020.102554.

15. Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA 2020;323:1582-9.

16. Abolghasemi H, Eshghi F, Cheraghalii AM, Imani Fooladi AA, Bolouki Moghadam F, Imanizadeh S, et al. Clinical efficacy of convalescent plasma for treatment of COVID-19 infections: Results of a multicenter clinical study. Transfus Apher Sci 2020;59:102875. doi: 10.1016/j.transci.2020.102875.

17. Hegerova L, Gooley TA, Sweerus KA, Maree C, Bailey N, Bailey M, et al. Use of convalescent plasma in hospitalized patients with COVID-19: Case series. Blood 2020;136:759-62.

18. Xia X, Li K, Wu L, Wang Z, Zhu M, Huang B, et al. Improved clinical symptoms and mortality among patients with severe or critical COVID-19 after convalescent plasma transfusion. Blood 2020;136:755-9.

19. Joyner MJ, Bruno KA, Klassen SA, Kunze KL, Johnson PW, Lesser ER, et al. Safety update: COVID-19 convalescent plasma in 20,000 hospitalized patients. Mayo Clin Proc 2020;95:1888-97.

20. Piechotta V, Chai KL, Valk SJ, Doree C, Monsef I, Wood EM, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: A living systematic review. Cochrane Database Syst Rev 2020;7:CD013600. doi: 10.1002/14651858.CD013600.pub2.

21. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 2020;395:1054-62.

22. Patel A, Shah K, Dharsandiya M, Patel K, Patel T, Patel M, et al. Safety and efficacy of tocilizumab in the treatment of severe acute respiratory syndrome coronavirus-2 pneumonia: A retrospective cohort study. Indian J Med Microbiol 2020;38:117-23.