

Judicious use of medications in COVID-19 patients and its outcome

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Abstract

Background: COVID-19 is associated with the respiratory disorder in humans which has been declared as a global epidemic and pandemic in the first quarter of the year 2020. COVID-19 is known to cause severe pneumonia and multiple complications. Multiple protocols and management strategies are currently being developed worldwide to overcome this issue. However, in resource-limited settings like India which deal with a huge population base, it is critical for the doctors to be well equipped to speedily identify and treat patients who require admission and critical care. Hence the attempt has been made in this study to identify and compare the various treatment modalities in patients care at a district level. **Methods:** The present retrospective cohort study was carried out amongst 106 patients with confirmed COVID-19 admitted at tertiary care hospital. The data was retrieved from hospital records of 106 patients admitted between April 2020 to March 2021. The data was analysed including the patient demographics, characteristics, the antibiotics used, steroids administered, clinical interventions and clinical outcomes according to the treatment protocol. **Results:** Majority 52(49.0%) of the patients were below the age of 40 years. Majority 48(67%) patients recovered within 10 days of hospital with the use of Piperacillin and Tazobactam combination and majority 45/71(63%) patients recovered within 10 days of hospital with the use of Inhalation and IV combination. Majority 48(45%) patients recovered with oxygen less than 5 lit/min. **Conclusion:** The present study concluded that patients with combination of inhalation and IV steroids along with cover of higher antibiotics recovered early and without secondary infection and almost significant number of patients needed more than 5 liter of oxygen that means corona virus affects seriously irrespective of age, sex and other comorbidities and this disease needs a serious attention.

KEY WORDS: COVID, Corona, Steroids, Oxygen, Antibiotics.

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INTRODUCTION

COVID-19, or more popularly known as Novel Corona Virus, is associated with the respiratory disorder in humans which has been declared as a global epidemic and pandemic in the first quarter of the year 2020 by the World Health Organization¹. In December 2019, COVID-19 was first identified in Wuhan, China, as a respiratory tract

infection causing symptoms, such as fever, chills, dry cough, fatigue, and shortness of breath.² This atypical viral pneumonia has disabled the world, causing catastrophic health and economic losses. The novel coronavirus belongs to the family of SARS and MERS-CoV, but the impact of the former is more crippling as illustrated by the exponential increase in infectious cases.³ As of mid-April 2020, the infection has spread to over 185 countries, infected more than two million people and resulted in over 127,000 deaths globally⁴. The first case of the COVID-19 pandemic in India was reported on January 30, 2020.⁵ COVID-19 in majority of the population (80%) presents as an asymptomatic or mild infection. However, the disease is known to cause severe pneumonia and multiple complications, especially in certain high-risk groups. These remaining 20 per cent of infected patients will need admission and hospital care, including five per cent of them who require intensive care and ventilator support.⁶ Multiple protocols and management strategies are

currently being developed worldwide to overcome this issue. However, in resource-limited settings like India which deal with a huge population base, it is critical for the doctors to be well equipped to speedily identify and treat patients who require admission and critical care. This will ensure proficient utilization of resources and facilities available without overburdening the existing healthcare system.⁷

Hence the attempt has been made in this study to identify and compare the various treatment modalities in patients requiring hospital admission, ICU care in an ICU set up at a district level.

A wide range of drugs that have earlier been approved for other indications as well as several investigational drugs are being studied through clinical trials for benefit in COVID-19.⁸ While patients with no prior comorbid conditions had a case fatality rate of 0.9 per cent, it was notably higher among those with specific underlying comorbidities, making these population groups high-risk and more vulnerable to severe COVID-19.⁹ Supplemental oxygen therapy is the first line in the treatment of hypoxemic respiratory failure.¹⁰ Before the COVID-19 pandemic, noninvasive oxygen therapies, such as, high-flow nasal oxygen (HFNO) and/or noninvasive positive-pressure ventilation (NPPV), were increasingly used in hypoxemic patients due to their proven benefits on minimizing the need for endotracheal intubation.¹¹ The recent multinational Surviving Sepsis Guideline in COVID-19, recommends giving steroids in patients with severe COVID-19 on mechanical ventilation with ARDS, in order to reduce the destructive inflammatory immune response (based on very minimal evidence though), and to treat suspected adrenal insufficiency associated with sepsis, particularly in those with refractory shock, although this guideline advises against the use of corticosteroids in COVID patients in non-ARDS respiratory failure on mechanical ventilation.¹² Dexamethasone, a corticosteroid, has shown benefits in critically ill patients with COVID-19, reducing the mortality by about one-fifth or one-third in patients requiring oxygen or ventilator support, respectively.¹³ The management of severe COVID-19 cases includes immediate oxygen therapy and monitoring, it may be necessary to proactively prevent complications and secondary infections, treat underlying diseases and provide organ function support.¹⁴ Treatment of co-infections relies on empirical antimicrobial therapy to treat all likely pathogens causing severe acute respiratory infection (SARI) and sepsis. Patients suspected

to have COVID-19 should be administered appropriate empirical antimicrobials within 1 h of identification of sepsis.¹³ There is no current evidence to recommend any specific treatment for patients with confirmed COVID-19. While a variety of antiviral agents, including antiviral peptides (e.g. favipiravir) and corticosteroids have been used in COVID-19 patients, their role and mode of action has yet to be established.¹⁵ Hence, an attempt has been made in this study to compare use of supplemental oxygen, steroids and use of antibiotics in hospitalized covid patients in an ICU setup at a district level. The present study was conducted to see the outcome of judicious use of various medications in COVID-19 patients.

MATERIAL AND METHODS

The present retrospective cohort study was carried out amongst 106 patients with COVID-19 admitted at tertiary care hospital and those patients who were discharged to home were taken into the study in various arms. The data was retrieved from hospital records of 106 patients admitted between April 2020 to March 2021. The data was screened for any errors. The data of 106 patients was analyzed including the patient demographics, characteristics, the antibiotics used, steroids administered, clinical interventions and clinical outcomes according to the treatment protocol. The standard treatment protocols from authorities were followed along with institutional guidelines and personal patient care experience. Appropriate statistical testes are applied.

Exclusion criteria: Patients needing NIV and ventilatory support were referred to higher centres and they were excluded.

Based on the data the patients were categorized in groups,

Groups depending on antibiotics used-

Group 1- Injection. Tazobactam and Piperacillin 4.5 gm IV 3times daily for 10 days

Group 2 - Injection. Tazobactam and Ceftriaxone 1.5 gm IV 2 times daily for 10 days

Groups depending on type of steroids used-

Group 1 – Injection Dexamethasone 8 mg IV od and inhalation by Budesonide for 10 days

Group 2 - Only Injection Dexamethasone 8 mg IV od for 10 days

Groups depending on flow of oxygen required-

Group 1 – 1 to 5 lit/min of oxygen flow

Group 2 - 6 to 10 lit/min of oxygen flow

Group 2 - 11 to 15 lit/min of oxygen flow

RESULTS

Table 1: Distribution of patients according to Gender

Gender	No. of patients
Male	76 (71.7%)
Female	30 (28.3%)

Table no. 1 shows that in the present study majority 76(71.7%) were males and 30(28.3%) were females.

Table 2: Distribution of patients according to Age-Group

Age-Group	No. of patients
Total	106 (100%)
21-30	18(16.9%)
31-40	34(32.1%)
41-50	20(18.9%)
51-60	18(16.9%)
60-70	14(13.2%)
>70	02(1.9%)
Total	106(100%)

Table no. 2 shows that in the present study majority 52(49.0%) of the patients were below the age of 40 years followed by 20 (18.9%) between 41 to 50 years of age.

Table 3: Distribution of patients according to antibiotics used and duration of stay in hospital

Antibiotics/ Recovery	<10 days	11 – 20 days	> 20 days	Total
Piperacillin + Tazobactam	48/71 (67%)	21/71 (30%)	02/71 (3%)	71
Ceftriaxone+ Tazobactam	08/35 (22%)	20/35 (57%)	07/35 (21%)	35

Table no.3 shows that majority 48/71(67%) patients recovered within 10 days of hospital with the use of Piperacillin and Tazobactam combination. While only 08/35(22%) recovered within 10 days of hospital with the use of Ceftriaxone and Tazobactam combination. The difference was statistically significant.

Table 4: Distribution of patients according to method of steroids used and duration of stay in hospital

Steroids/ Recovery	<10 days	11 – 20 days	> 20 days	Total
Inhalation + IV	45/71 (63%)	22/71 (31%)	04/71 (6%)	71
IV	11/35 (31%)	19/35 (54%)	05/35 (15%)	35

Table no. 4 shows that majority 45/71(63%) patients recovered within 10 days of hospital with the use of Inhalation and IV combination as compared to 11/35 (31%) patients only on IV steroids. The difference was statistically significant.

Table 5: Distribution of patients according to flow of oxygen per minute used and duration of stay in hospital.

Flow of O ₂ / Recovery	<10 days	11 – 20 days	> 20 days	Total
1 – 5 lit/min	37/48 (77%)	10/48 (20%)	01/48 (3%)	48 (45.28%)
6 – 10 lit/min	10/25 (40%)	14/25 (56%)	01/25 (4%)	25 (23.58%)
11 - 15 lit/min	09/33 (33%)	17/33 (51%)	07/33 (16%)	33 (31.13%)

Table no. 5 shows that majority 45(45.28%) patients recovered with oxygen less than 5 lit/min followed by 25 (23.58%) patients recovered with oxygen between 6 to 10 lit/min and 33 (31.13%) requiring more than 10 lit/min. The difference was statistically significant.

Table 6: Distribution of patients with morbidity or without morbidity at the time of discharge.

Recovery	Without Morbidity	With Morbidity
Total	75 (70.75%)	31 (29.25%)

Table no. 6 shows that majority 75 (70.75%) of patients recovered without having any morbidity and 31(29.25%) patients suffered from some kind of morbidity as mentioned in discussion.

DISCUSSIONS

The present study was conducted on the data retrieved from the hospital files and reports of 106 COVID patients. The present study shows that majority 76(71.7%) were males and 30(28.3%) were females. Also, in the present

study majority 52(49.0%) were below the age of 40 years followed by 20 (18.9%) between 41 to 50 years of age. In the present study, 48/71 = 67% who were on Piperacillin/ Tazobactam recovered within 10 days vs 8 out of total 35 patients who had received ceftriaxone tazobactam equal to

22% recovered within first 10 days. The difference was statistically significant. At 10 to 20 days and after 20 days improvement was similar in both the groups. other drugs also contributing factors for recovery at various stages which also we tried to compare in this retrospective study. Role of antibiotics was to prevent the secondary infection. This could contribute to recoveries in patients at various stages. As antibiotics were used for initial 10 days only, probably further prolongation of antibiotics course is not required usually as shown in the study. Antibiotics may be necessary part of the therapy in addition to other therapies for rapid recovery and to prevent secondary infections as steroid is one of the important line of treatment being used in the disease. In a study by Ga Eun Park¹ (2021)¹⁶ In log rank test, the piperacillin/tazobactam group tended to have a better clinical outcome than the ceftriaxone and clindamycin group (Log rank $P < 0.001$). in multivariate analysis, clinical failure was more frequent in the ceftriaxone plus clindamycin group than in the piperacillin/tazobactam group (HR 3.316; 95% CI, 1.589–6918, $P = 0.001$). They concluded that treatment with piperacillin/tazobactam was more effective than that with ceftriaxone plus clindamycin in patients with early NV-HAP.

In the present study, it was observed that majority 45/71(63%) of the patients recovered within 10 days of hospital with the use of Inhalation and IV combination as compared to 11/35(31%) patients only on IV steroids. The difference was statistically significant. At 10 to 20 days 22 of remaining 26 patients from the first arm i.e. 84% improved and discharged vs 19 of remaining 24 patients i.e. 79% patients were discharged home in the 2nd arm or steroid only arm. after 20 days 4/4 in the first arm vs 5/5 in the second arm were recovered and discharged home i.e. All the remaining patients improved and discharged home. While during 1st 10days improvement was significantly higher In IV steroid and inhalational steroid arm. combined therapy might have halted disease progression as compared to patients from steroid only arm. After 10 days recovery may be part of healing phase and natural course of illness that's why in the both arms improvement was similar. Again comparable improvement in after 20 days was seen. Both IV steroid plus inhalational steroid and IV steroid only helped in recovery but in former management seems to reduce the hospital stay at early course of illness. In a study by Jong Hoon Hyun(2021)¹⁷ found that among patients with severe COVID-19, early use of corticosteroids showed favorable clinical outcomes which were related to a reduction in the length of hospital stay. In a study by Awadhesh Kumar Singh (2020)¹⁸ Of the 5 studies (4 retrospective studies and 1 quasi-prospective study) conducted for evaluating the role of corticosteroids, 3 studies have shown benefit, while 2 studies shown no

benefit and there was a suggestion of significant harm in critical cases in one sub-study. RECOVERY trial is the only randomized controlled trial that has shown a significant reduction of death by 35% in ventilated patients and by 20% amongst patients on supplemental oxygen therapy with the dexamethasone, although no benefit was observed in mild cases. In a study by Sanjay Ramakrishnan (2021)¹⁹ Early administration of inhaled budesonide reduced the likelihood of needing urgent medical care and reduced time to recovery after early COVID-19. In the present study, it was found that majority 45(45.28%) of the patients recovered with oxygen less than 5 lit/min followed by 25(23.58%) patients recovered with oxygen between 6 to 10 lit/min and 33(31.13%) requiring more than 10 lit/min. Out of 48 patients on < 5 lit/min oxygen at 10 days 37(77%) recovered and out of 25 patients on 6 – 10 lit/min of oxygen at 10 days 10 (40%) recovered and out of 33 patients on 11 – 15 lit/min of oxygen at 10 days 9 (33%) recovered. As the oxygen requirement was increased, it increased stay in the hospital significantly 58/106 = 54% patients needed >5lit to 15 lit of oxygen that points towards significant number of patients irrespective of age and sex develop serious viral pneumonia as we all have been seeing the serious covid cases over more than 1 year now Oxygen requirement is dependent on the lung damage. Which can be assessed very well with CT scan score but as the study was carried out in resource limited scenario, CT was not possible in all the patients in this study and groups were not compared on CT severity score. Rather oxygen requirement was monitored closely in this study which correlated very well with stay of patients in the hospital. Patients requiring less than 5lit/min of oxygen improved very well within time frame of 10 days . But as the oxygen requirement increased the stay in the hospital increased. The difference was statistically significant. Although other combined therapies /drugs is also equally contributing factor for recovery of patients. In a study by Gregory L. Calligaro (2020)²⁰ in a resource-constrained setting, HFNO for severe COVID-19 HRF is feasible and more almost half of those who receive it can be successfully weaned without the need for mechanical ventilation. In the present study we did not use HFNO, NIV or mechanical ventilatory supports in any of these patients. In the present study, it was observed that majority 75 (70.75%) of the patients recovered without having any morbidity and 31(29.25%) patients suffered from some kind of morbidity as mentioned in discussion.

SUMMARY

In the present study amongst 106 patients' data, we can conclude that patients on combination of inhalation and IV steroids along with cover of higher antibiotics Piperacillin + Tazobactam recovered early and without secondary

infection. Good clinical monitoring in resource limited condition may help in reducing the cost as we monitored patients on the basis of requirement of oxygen rather than CT severity score. Corona virus Disease can lead to serious pneumonia irrespective age, sex differences so needs strict attention. Resources need to be increased while managing such deadly pandemic.

LIMITATIONS

The study was carried out on stored hospital data in resource limited condition. The sample was less, hence study with larger sample size need to be carried out. The guidelines kept on changing from time to time, it was challenge to formulate therapies at any point of pandemic. The virus and pandemic itself is new to all. As we mentioned for diagnosis of severity of lung damage can be very well assessed by CT scan score but it could not compared as it was not possible to do CT scans in all patients and we couldn't compare the data accordingly but definitely it was very well correlated with good clinical monitoring. All the patients couldn't receive IV (Remdesivir) or oral antivirals. So we couldn't compare these factors for outcome (reducing or increasing) stay of patients in the hospital. Patients needing NIV and ventilatory support were referred to higher centres and they were not compared in this study. We couldn't take into consideration other comorbidities as diabetes mellitus, hypertension etc and their effect on outcome of patients.

REFERENCES

- World Health Organization(2020). Coronavirus disease (COVID-19) Pandemic, WHO. Accessed from <https://www.who.int/emergencies/diseases/novel-coronavirus-2019> on 31st March 2020
- Lai C.-C., Shih T.-P., Ko W.-C., Tang H.-J., Hsueh P.-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *Int. J. Antimicrob. Agents.*2020;55:105924.
- Liu Y., Gayle A.A., Wilder-Smith A., Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J. Travel Med.* 2020;27.
- COVID-19 dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). Available from: <https://arcg.is/0fHmTX>, accessed on April 15, 2020.
- Ministry of Health and Family Welfare, Government of India COVID-19 India dashboard. 2020. <https://www.mohfw.gov.in/> Retrieved from.
- World Health Organization. Novel Coronavirus (2019-nCoV) Situation Report - 46. Geneva: WHO; 2020.
- George M. Varghese, Rebecca John et al., Clinical management of COVID-19 *Indian J Med Res* 151, May 2020, pp 401-410 DOI: 10.4103/ijmr.IJMR_957_20.
- Centers for Disease Control and Prevention. Information for clinicians on therapeutic options for COVID-19 patients. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html>, accessed on March 23, 2020.
- The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) - China, 2020. *China CDC Week* 2020; 2 : 113-22.
- Rali AS, Garies T, Narendra D, Patel P, Guntupalli K. High-flow nasal cannula: COVID 19 and beyond. *Indian J Respir Care* 2020;9:134-40.
- Chawla R, Dixit SB, Zirpe KG, Chaudhry D, Khilnani GC, Mehta Y, et al. ISCCM guidelines for the use of non-invasive ventilation in acute respiratory failure in adult ICUs. *Indian J Crit Care Med.* 2020;24:S61-s81.
- Alhazzani W., Moller M., Arabi Y.M., Loeb M., Gong M.N., Rhodes A. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19) *Intensive Care Med.* 2020;46:854-887.
- WHO. Clinical management of severe acute respiratory infection when COVID-19 is suspected.2020. [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected)
- Chen N, Zhou M, Dong X. et at.. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395: 507-13.
- Singhal T. A review of coronavirus disease-2019 (COVID-19). *Indian J Pediatr* 2020; 87: 281-6.
- Ga Eun Park, Jae-Hoon Ko, Hyun Kyun Ki. Clinical Benefits of Piperacillin/Tazobactam versus a Combination of Ceftriaxone and Clindamycin in the Treatment of Early, Non-Ventilator, Hospital-Acquired Pneumonia in a Community-Based Hospital. *International Journal of General Medicine* 2020;13:705-712.
- Jong Hoon Hyun, Moo Hyun Kim, Yujin Sohn, Yunsuk Cho, Yae Jee Baek, Jung Ho Kim et al.. Effects of early corticosteroid use in patients with severe coronavirus disease 2019. *Hyun et al.. BMC Infectious Diseases* (2021) 21:506.
- Awadhesh Kumar Singh, Sujoy Majumdar, Ritu Singh, Anoop Misra. Role of corticosteroid in the management of COVID-19: A systemic review and a Clinician's perspective *Diabetes and Metabolic Syndrome. Clinical Research and Reviews* 14 (2020) 971e978.
- Sanjay Ramakrishnan, Dan V Nicolau Jr, Beverly Langford, Mahdi Mahdi, Helen Jeffers, Christine Mwasuku et al.. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial *Lancet Respir Med* 2021;9: 763-72.
- Gregory L. Calligaroa, Usha Lallac, Gordon Audleyd, Phindile Ginaa, Malcolm G. Millerb, Marc Mendelsone et al.. The utility of high-flow nasal oxygen for severe COVID-19 pneumonia in a resource-constrained setting: A multi-center prospective observational study. *E Clinical Medicine* 28 (2020)100570.

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