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# OBSERVATIONAL STUDY ON CLINICAL FEATURES, TREATMENT AND OUTCOME OF COVID 19 IN A TERTIARY CARE CENTRE IN INDIA - A RETROSPECTIVE CASE SERIES

General Medicine

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## ABSTRACT

Till date, no proven therapy exists for treatment of SARS-coV-2 infections which has been declared a pandemic by WHO in March, 2020. **OBJECTIVE:** This study will attempt to explore the demographic profile and outcome in the patients receiving multidisciplinary, personalised approach including use of Broad Spectrum Antivirals - Ivermectin, anti-inflammatory and antioxidants roles of Statins and N-acetyl-cysteine along with Standard of Care (SOC) in hospitalised COVID19 patients in a tertiary care centre. **SETTING:** Inpatient department (designated COVID ward) **PARTICIPANTS:** COVID-19 patients with laboratory confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections in the year 2020 between June 14- 28, 2020 Main outcome measures: The outcome of Interests are : a. Studying the demographic profile of COVID 19 cases b. Study the treatment outcomes in terms of death or discharge in patients receiving Ivermectin+N-acetyl-cysteine+Statin along with Standard of care.**RESULTS:** 148 patients were included in the study. All of them had confirmed COVID19 infection by the rtPCR method. Average age of the patients was 57.57 years ( Range = 17 - 88), 49% were male, 51% female. 81% of the patients had at least one or more comorbidities. Most common comorbidities included diabetes( 32%), Hypertension (27%),Ischaemic Heart Disease (8%). The in hospital, Case Fatality Rate was 1.35 %. The remaining 146 were discharged from the facility after an average 12 days duration of stay. **CONCLUSIONS:**. Triple therapy with Ivermectin, N-acetyl-cysteine and Atorvastatin along with standard of care is safe and effective in SARS-coV-2 infection.

## KEYWORDS

SARS-CoV-2, COVID-19, Treatment, NAC, Ivermectin, Atorvastatin

## INTRODUCTION

Since December 2019, the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which started as an outbreak in Wuhan, China has spread rapidly as a pandemic around the world,[1] causing multi organ dysfunction most prominent of which are coronavirus disease 19 (COVID-19) pneumonia, acute respiratory distress syndrome (ARDS), cardiac injury, liver and renal injury, thrombosis including Pulmonary Embolism and Stroke, and death[2]

Although the exact pathophysiology behind COVID19 infection is still unknown, it is primarily known to affect the Respiratory System although other systems including Neurological manifestation are recently coming to light.[3] Structural and functional analysis showed that the spike for SARS-CoV-2 also bound to ACE2 [4][5][6] whose expression was high in lung, heart, ileum, kidney and bladder . In the lung, ACE2 was highly expressed on lung epithelial cells. Patients with severe diseases were reported to have increased plasma concentrations of proinflammatory cytokines, also called a cytokine storm including interleukin (IL)-6, IL-10, granulocyte-colony stimulating factor (G-CSF), monocyte chemoattractant protein 1 (MCP1), macrophage inflammatory protein (MIP)1α, and tumor necrosis factor (TNF)-α .[7][8].

Treatment of SARS-cov-2 is still unknown and mostly symptomatic although clinical application of principles of antiviral therapies are being investigated. A valid method in this pandemic situation is repurposing older drugs. One of the most controversial drugs during the current SARS-CoV-2 pandemic is the well-known oral antimalarial drug hydroxychloroquine (HCQ), routinely used in the treatment of autoimmune diseases like rheumatoid arthritis or lupus. However, all studies that used HCQ with rather contradictory results.

Recently perhaps the most promising treatment strategy has been to use Corticosteroids, in particular Dexamethasone in the RECOVERY trial in reducing mortality.[9] Other treatment strategies have been to use Low Molecular Heparin to prevent thrombotic complications arising from endothelial dysfunction. [10]

Based on these evidences, Government of India has issued Standard of Care guidelines in managing mild, moderate and severe COVID19 infection which incorporates the use of Oxygenation, restricted fluid therapy, use of anticoagulation either Unfractionated Heparin (UFH) or Low molecular weight heparin (LMWH) and corticosteroid in the form of either Methylprednisolone or Dexamethasone.

This retrospective cohort study aims to describe the demographic profile of hospitalised patients in a tertiary care centre in India and their treatment outcomes when along with Standard of Care, personalised medicine targeting the various pathophysiology of COVID19 was provided. These include the use of antivirals, anti-inflammatory and antioxidants - Ivermectin, Atorvastatin and N-acetylcysteine.

Ivermectin is already known to have broad-spectrum anti-viral activity *in vitro* [11-14]. It inhibits SARS-CoV-2 in vitro , with a single dose to Vero-hSLAM cells 2 h post infection with SARS-CoV-2 and achieves ~5000-fold reduction in viral RNA at 48 h. Hence, Ivermectin warrants a second look to evaluate its possible benefits. [15] Based on the promising in vitro data, single dose Ivermectin 12mg was added to standard of care.

As a cure remains elusive, the current management of patients with COVID-19 infection focuses mostly on supportive care with the most severe cases often requiring mechanical ventilation and standard care for ARDS patients of any cause. However, increasingly data is coming to light that ARDS in COVID19 differs from other causes in multiple ways. [16] ARDS in COVID 19 is very sensitive to PEEP as it has relatively good lung compliance despite poor oxygenation, there is lack of pulmonary vasoconstriction and significant shunting, and thrombotic microangiopathy[17][18][19]. Some authors suggest that vascular endothelial dysfunction plays a vital role in the pathogenesis of COVID-19 infections [17]. Thus it is postulated that statin treatment

may improve endothelial and vascular function in these patients.

In fact, such a combination of statin/ARB treatments has been used previously in some centres during the Ebola outbreak in West Africa [20]. Thus a similar approach has been suggested by Fedson et al [21] for COVID 19 patients. Statins are known for their pleiotropic anti-inflammatory, antithrombotic and immunomodulatory effects. Based on pathophysiology and understanding of its associated coagulopathy, endothelial dysfunction, and dysregulated inflammation., researchers proposed that statins might mitigate the effects of COVID-19 infection in selected patients. Hence, the decision was taken to add low dose Atorvastatin 10 mg was added to SOC.

Another promising drug due to its antioxidant property was N-acetyl-cysteine. N-acetylcysteine (NAC) is a precursor of glutathione [22] and acts as a powerful antioxidant and free radical scavenger in the body. There have been several clinical trials investigating the use of NAC in respiratory illness in humans. Intravenous NAC has been used clinically for the treatment of ARDS [23]. In both *in vivo* and human trials, nebulized NAC may improve arterial oxygen tension [24], [25]; and attenuate pulmonary fibrosis [26], and ARDS [27].

Thus in this tertiary care hospital adjuvant treatment with Ivermectin + Atorvastatin + NAC was undertaken along with Standard of Care. This study aims to describe the demographic profile and treatment outcomes.

## METHODS:

**Study design and patient selection :** This study was done in the inpatient department of designated COVID19 facility of Medical College Kolkata. Hospital records of patients admitted between 14.06.2020 - 21.06.2020 were accessed and daily round data along with severity of disease, medication received and treatment outcome were noted for all patients ( n = 148 ).
This is a retrospective case series aimed at describing patient profile and treatment outcome of patients admitted with COVID 19 infection.

## PATIENTS:

All patients were rt-PCR confirmed COVID-19 inpatients older than 18 years at diagnosis were included in the analysis as treatment group.

All patients received Standard of Care based on severity as per MOHFW, India Clinical Guidelines [28] and along with that were given Ivermectin single dose, Atorvastatin 10mg daily and injection N-acetyl-cysteine, irrespective of disease severity.

## PROCEDURE AND TREATMENT :

Patient data was collected from written health records in the year 2020. Demographic data, as reported by the patient, and a current medical history of hypertension, diabetes, obesity, cardiovascular disease, heart failure, stroke, asthma, COPD, other lung disease, kidney disease, liver disease, autoimmune disease, history of cancer, thyroid disease were collected.

The following vital signs, if available, were collected and documented: heart rate (beats per minute), breaths per minute (BPM), systolic and diastolic blood pressure (mmHg), body temperature (°C), oxygen saturation measured by pulse oximetry (O2 %), body weight (kg), and/or body mass index (BMI).

Based on clinical parameters each patient was designated a severity of Mild, Moderate or Severe as per Mohfw guidelines [28].

## RESULTS:

148 patients were included in the study. All of them had confirmed COVID19 infection by the rtPCR method. Average age of the patients was 57.57 years ( Range = 17 - 88), 49% were male, 51% female. 81% of the patients had at least 1 or more comorbidities. Most common comorbidities included diabetes( 32%), Hypertension (27%),Ischaemic Heart Disease (8%). Other comorbidities included COPD/BA (3%), Chronic Kidney Disease (6.7%), Chronic Liver Disease (2%) and immunocompromised states including HIV and cancer (6%).

Based on the Clinical severity assessment guidelines [28] 5% patients had severe disease, 27.5% had moderate disease and 67.5% had mild disease.

None of these patients were lost to follow-up for the defined outcome. Only 2 of the 148 patients treated with Standard of Care + Ivermectin + Atorvastatin + N-acetyl-cysteine, expired. The in hospital, Case Fatality Rate was therefore, 1.35 %, which was well below the national average. [29] The remaining 146 patients were discharged from the facility after an average 12 days duration of stay. No notable adverse events related to drugs occurred in any of the subjects during this study.

## DISCUSSION:

COVID - 19 till date has no proven effective treatment. Symptomatic therapy along with that pathophysiology based treatment protocols have been adopted by the government. Our observations in this study demonstrate there is a role for further disease modulation based therapy using broad spectrum antiviral - Ivermectin, pleiotropic effects of Atorvastatin and the lung protective and antioxidant of N-acetyl-cysteine. This triple therapy along with standard of care has demonstrated a lower case fatality rate without any notable adverse events and can be considered as adjuncts to successful therapy for COVID 19. However, its observational, non randomised nature prevents a causal conclusion and warrants further investigation through larger Randomised Controlled Trials.

## FUNDING

No cost was borne by patients or investigators for this study. The drugs were available via the hospital supply.

## ETHICAL CLEARANCE

Institutional ethical committee clearance was obtained prior to study.

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**CONFLICT OF INTEREST** - NONE

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