

# Treatment of COVID-19 Patients at a Medical College Hospital in Bangladesh

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## ABSTRACT

**Background and aim:** Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has induced a sense of panic around the world as the disease is highly contagious and has been spreading in full swing during last 5 months causing millions of COVID-19 patients and hundreds of thousands of deaths. Bangladesh, a country of 170 million people, is not an exception regarding COVID-19; it has reported several thousand COVID-19 patients with several hundred of deaths. This observational study has been planned to assess the scope and limitation of management strategy against COVID-19 patients in a medical college hospital of Bangladesh with available drugs in a real-life situation.

**Materials and methods:** All patients in this cohort ( $N: 33$ ) were positive for SARS-CoV-2 by polymerase chain reaction (PCR) and they attended the hospital with variable presenting symptoms those ranged from cough and fever to respiratory distress and pneumonia. As per the protocol, the patients were regularly evaluated for several parameters of COVID-19-related pathology. Before discharge, they were checked for SARS-CoV-2 for 2 consecutive times. The management strategy included standard of care (SoC) and administration of hydroxychloroquine and azithromycin, available in Bangladesh.

**Results:** Out of total 33 patients, 1 patient died at day 4 day after admission. Two patients developed severe complications and were referred to tertiary hospital in Dhaka (2 and 3 days after admission), the capital of Bangladesh, where they recovered and were discharged from hospital after being SARS-CoV-2 negative. The rest 30 patients were discharged from the medical college hospital after being negative for SARS-CoV-2 in two subsequent assessments and improvement of their COVID-related symptoms. The average hospital stay of these patients was 14.5 days with a range of 10–24 days.

**Conclusion:** It seems that most of the COVID-19 patients may be adequately managed by standard of care management with drug support. However, early diagnosis and hospitalization with adequate care may be important variables for better survival. These factors may be properly ensured if the patient burden remains at a palatable level in forthcoming days in Bangladesh.

**Keywords:** Bangladesh, Coronavirus disease 2019, Therapy.

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## INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an acute infection of the respiratory tract that emerged in late 2019 in China and then progressed to different countries around the world and caused considerable morbidity and mortality.<sup>1,2</sup> These facts ultimately led WHO to declare COVID-19 a pandemic.<sup>3</sup> Although the etiological agent of COVID-19 is known, proper insights about its epidemiology, virology, pathogenesis and management strategy are yet to be developed; making it one of the most notorious public health problems in the world.

COVID-19 may exhibit a variety of clinical presentations. Some COVID-19 patients remain asymptomatic, but they are capable of transmitting the virus.<sup>4</sup> A second group of COVID-19 patients express mild symptoms, some of which are indistinguishable from normal flu and some of them develop moderate symptoms<sup>5,6</sup> of considerable concerns. Finally, some patients develop severe complications like respiratory distress and pneumonia resulting in death.<sup>7–9</sup> More information is now piling about diverse nature of COVID-19 presentations.

The mechanisms underlying pathogenesis of COVID-19 are still elusive and more times will be required to get proper insights about major cellular and molecular events relating to diverse pathogenesis of COVID-19.<sup>10–12</sup> Although COVID-19 is induced by

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severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathological processes are possibly regulated by interactions of viruses with host immunity. The disease usually starts with mild symptoms such as cough and fever with other allied symptoms of COVID-19. Some of the patients with mild symptoms experience a sudden deterioration of their condition either in the later stage of the disease or in the process of recovery. If the patients proceed to acute respiratory distress syndrome (ARDS) and multiple-organ failure rapidly, death becomes the usual outcome. Whether the patient is recovered or dead, host immunity to the virus seems to play a cardinal role with many other auxiliary factors.

As the numbers of patients with COVID-19 has passed 4 million mark and the numbers of death are over 300,000 in the world, strategies are needed to block further transmission of SARS-CoV-2 infection and management of COVID-19 patients. To achieve this goal to suitable extents, the activities of the health care delivery system may be centered under T3; test, tracing and treatment, as proposed by WHO.<sup>13</sup>

Bangladesh, a country of 170 million people, detected its first case of COVID-19 on 8th March 2020 and the first fatality was recorded on 18th March 2020. The numbers of patients with morbidity and fatality due to COVID-19 have been increasing since then and about 5–15% tested for SARS-CoV-2 are positive for the virus and many of these patients need hospitalization. The management of patients with COVID-19 remains a challenge for the entire world.<sup>14</sup>

Although severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is primarily considered as a respiratory virus, emerging data indicates that COVID-19 involve several body tissues and organs. And, the virus of COVID-19 imparts its effect on many tissues, some are distal to the respiratory system. As of today, no antiviral drug effective for COVID-19 has been documented. Several investigators have used different antiviral drugs developed for other coronavirus or EBOLA, anti-inflammatory drugs, and immune modulators.

This observational study presented here has been accomplished in real-life situation in a medical college hospital of Bangladesh. We used a comparatively cheaper management strategy. Almost all patients in this cohort were treated by a combination of hydroxychloroquine and azithromycin with standard of care management.

## MATERIALS AND METHODS

### Patients

The study was conducted at Kishoreganj, about 110 km from Dhaka, the capital of Bangladesh. It is one of the 64 districts of the country. This is a single center study and observational in nature. The study is of prospective type. The study was approved by the hospital authority and informed consent was taken from all patients if and when necessary. The study was conducted on the basis of a pre-prepared data sheet. The protocol was formed in such a manner that various vital signs, basic hematological data, parameters of liver and kidney functions, levels of oxygen saturation, and different important electrolytes could be checked during admission and at different time points. All patients of this study were tested for SARS-CoV-2 in nasal swab and all of them were positive for SARS-CoV-2. The criteria for discharge was being negative for SARS-CoV-2 in 2 consecutive assessments, usually 24 hours apart and with improvement of symptoms and signs of COVID-19. This is a generalized guideline of COVID-19 management of Bangladesh.

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In some cases when the patients developed severe complications, those were referred to tertiary COVID-19 hospital in Dhaka. A total of 33 patients could be finally analyzed on the basis of inclusion and exclusion criteria.

### Therapeutic Regimen

All patients received standard of care (SoC) management as per recommendation of the attending physician based on their clinical conditions and pathological evaluations. These included antipyretic drugs to control fever, pain killers for alleviating pain, oxygen for controlling respiratory distress and saline for maintaining proper hydration. One drug regimen that included hydroxychloroquine and azithromycin was given to all patients. Hydroxychloroquine was given at a dose (400 mg, twice daily on first day, followed by 200 mg, thrice daily from day 2 to 10). Azithromycin was given at a dose of 500 mg on first day, followed by 250 mg daily for 4 days.

### Study Design

The patients were properly assessed about vital signs, and physical examination was done at admission. Also, all new symptoms and aggravation of pre-existing symptoms were monitored. Peripheral blood was taken from each patient to check complete blood picture, levels of hemoglobin, creatinine, bilirubin, and alanine aminotransferase (ALT) to develop insights about the condition of vital organs. X-ray of chest and ECG were accomplished as and when necessary. Oxygen saturation was monitored regularly and all preparations were adopted to provide oxygen supply.

### Statistical Analysis

The data have been shown as mean and standard deviation as well as median and range. For the statistical analysis, paired t test was used for normally distributed data. When the distribution was skewed, the Wilcoxon signed-rank test was used. A *p* value of less than 0.05 was regarded as statistically significant.

## RESULT

Out of 33 patients with COVID-19, 25 were male and 8 were female. The age of the patients varied from 18 to 65 years with a mean age of 36.6 years. In this cohort, some patients had co-morbidities in addition to be positive for SARS-CoV-2, as shown in Table 1. Hypertension was reported by nine, whereas diabetes mellitus was seen in five patients. Two patients also gave history of ischemic heart disease and one patient had chronic obstructive pulmonary disease. The history of drug intake at the time of admission has been shown in Table 1.

The presenting symptoms of the patients were variable. Twenty-two patients had fever and 24 patients were suffering from cough. Breathing difficulty was seen in eight patients. Also, some patients reported symptoms such as chest tightness, myalgia, anosmia, and loose motion (Table 2).

**Table 1:** General information, comorbidities and drug history intake of COVID-19 patients

| Variables      |                                       | Number        | Percentage        |       |
|----------------|---------------------------------------|---------------|-------------------|-------|
| Demographics   | Total                                 | 33            | 100               |       |
|                | Sex                                   | Female        | 8                 | 24.25 |
|                |                                       | Male          | 25                | 75.75 |
|                | Age (years)                           | Mean $\pm$ SD | 36.36 $\pm$ 12.47 |       |
| Median (range) |                                       | 32 (18–65)    |                   |       |
| Co-morbidities | Diabetes mellitus                     | 5             | 15                |       |
|                | Hypertension                          | 9             | 27                |       |
|                | Ischemic heart disease                | 2             | 6                 |       |
|                | Chronic obstructive pulmonary disease | 1             | 3                 |       |
| Drug history   | Bronchodilator, anti-hypertensive     | 1             | 3                 |       |
|                | Anti-diabetic drug                    | 5             | 15                |       |
|                |                                       | 3             |                   |       |

**Table 2:** Presenting clinical complaints of patient with COVID-19 on the day of admission

| Variables            | Number | Percentage |
|----------------------|--------|------------|
| SARS-CoV-2 positive  | 33     | 100        |
| Fever                | 22     | 68         |
| Cough                | 24     | 73         |
| Breathing difficulty | 8      | 24         |
| Chest tightness      | 4      | 12         |
| Myalgia              | 5      | 15         |
| Loose motion         | 4      | 12         |
| Anosmia              | 1      | 3          |

All patients were examined properly during admission and all requisite investigations were also accomplished. The data of investigational parameters have been in Table 3.

Different vital signs and parameters of blood for assessing overall conditions of the patients were checked regularly. The data of various parameters during admission and day of discharge or day of referral has been given. Two patients were referred to tertiary hospital of Dhaka. One of them had SpO<sub>2</sub> of 73% and the other had 88% and they had evidence of pneumonia in chest X-ray. At the referral hospital, they received extensive management and discharged from there after recovery. Only, one patient with COVID-19 in our cohort died at this hospital after he developed pneumonia. This patient also had inferior myocardial infarction during admission. Out of 33 patients, 30 patients were discharged after being negative for SARS-CoV-2 for two times, 24 hours apart. The comorbidities did not have any adverse effect on the survival or progression of COVID-19 at this hospital.

## DISCUSSION

This is an observational study in a real-life situation in which comparatively cheaper management approaches revealed hopeful outcome. The patients received hydroxychloroquine and azithromycin and 30 out of 33 patients recovered within a mean period of 14 days. There have been only one mortality and only two referrals. The referred patients also survived at their tertiary hospital.

**Table 3:** Clinical and pathological features of patient with COVID-19

| Variables                   |                | Day of admission     | One week after admission |
|-----------------------------|----------------|----------------------|--------------------------|
| Respiratory rate (BPM)      | Mean $\pm$ SD  | 26.46 $\pm$ 4.25     | 26.03 $\pm$ 5.07         |
|                             | Median (range) | 26 (22–40)           | 24 (22–45)               |
| Pulse rate (BPM)            | Mean $\pm$ SD  | 77.42 $\pm$ 7.32     | 76.46 $\pm$ 5.67         |
|                             | Median (range) | 76 (70–98)           | 74 (68–90)               |
| SpO <sub>2</sub> (%)        | Mean $\pm$ SD  | 98.21 $\pm$ 2.03     | 97.46 $\pm$ 5.15         |
|                             | Median (range) | 99 (92–100)          | 99 (73–100)              |
| Hemoglobin (g/dL)           | Mean $\pm$ SD  | 12.89 $\pm$ 1.74     | 13.03 $\pm$ 1.74         |
|                             | Median (range) | 12.75 (9–15.5)       | 13 (10–16.5)             |
| WBC (mm <sup>3</sup> )      | Mean $\pm$ SD  | 9,564 $\pm$ 2,832    | 8,078 $\pm$ 1,298*       |
|                             | Median (range) | 9,000 (5,600–20,000) | 7,800 (6,200–1,100)      |
| Neutrophil (%)              | Mean $\pm$ SD  | 72.23 $\pm$ 6.05     | 68.33 $\pm$ 6.35*        |
|                             | Median (range) | 71 (62–87)           | 68 (56–84)               |
| Platelet (mm <sup>3</sup> ) | Mean $\pm$ SD  | 274.86 $\pm$ 60.39   | 308.7 $\pm$ 39.14*       |
|                             | Median (range) | 280 (180–380)        | 320 (220–390)            |
| Bilirubin (mg/dL)           | Mean $\pm$ SD  | 0.89 $\pm$ 0.26      | 0.74 $\pm$ 0.25*         |
|                             | Median (range) | 0.9 (0.3–1.3)        | 0.7 (0.4–1.2)            |
| SGPT/ALT (U/L)              | Mean $\pm$ SD  | 45.05 $\pm$ 18.75    | 44.30 $\pm$ 20.00        |
|                             | Median (range) | 43.5 (16–78)         | 38 (15–91)               |
| Creatinine (mg/dL)          | Mean $\pm$ SD  | 1.05 $\pm$ 0.44      | 0.88 $\pm$ 0.26          |
|                             | Median (range) | 1.1 (0.4–2.5)        | 0.9 (0.4–1.8)            |
| Sodium (mEq/L)              | Mean $\pm$ SD  | 131.09 $\pm$ 2.99    | 132.56 $\pm$ 3.89        |
|                             | Median (range) | 131.5 (124–136)      | 133 (120–140)            |
| Potassium (mEq/L)           | Mean $\pm$ SD  | 4.60 $\pm$ 0.50      | 4.69 $\pm$ 0.34          |
|                             | Median (range) | 4.7 (3.4–5.1)        | 4.8 (3.7–5.5)            |
| Chloride (mEq/L)            | Mean $\pm$ SD  | 95.86 $\pm$ 2.40     | 98.78 $\pm$ 7.34         |
|                             | Median (range) | 96 (90–100)          | 98 (92–134)              |

SpO<sub>2</sub>, oxygen saturation; WBC, white blood cell; S. ALT, alanine transaminase; AST aspartate transaminase; SD, standard deviation

Statistical significance was considered when *p* value was <0.05 and shown as \* mark

Several lines of therapy have been developed for management of COVID-19 patients. Some of them seems to be useful at the initial stage of the diseases, whereas other can be effective in advanced stages. Also, some countries have reported about ventilation of several patients.

The combination of hydroxychloroquine and azithromycin have been used for treating COVID patients around the world with differential outcome. In a large cohort study, Million et. al. has used these drugs combination in France and reported that use of these drugs in COVID patients were safe and induced low mortality at the time of peak of COVID-pandemic in France.<sup>15</sup> Also, a role of this combination therapy on viral load of SARS-CoV-2 has been shown by La Scola et al.<sup>16</sup> Taken together, use of these drugs are rationale and evidence-based, however, some studies have provided logics against their use. The study presented here that was properly monitored has unmasked a favorable outcome.

This is one of the prevailing studies that showed that even without a direct antiviral drug the death can be contained to minimum. This scenario may contrast with thousands deaths in developed countries those used several drugs along with several sophisticated maneuvers. The causes underlying this cannot be responded with the present know how about virology and mechanism of pathogenesis of COVID-19. Also, several other factors

indicate that SARS-CoV-2 virus that spread in Europe and USA vs Bangladesh may be different in some features, which need to be clarified in future.<sup>17-19</sup> Also, the age and other general profiles of the patients may have influenced the outcome. Data supporting this concept is on rise as several thousand COVID-19 patients have died in Europe and USA, the fatality is still low in Asian and African countries. COVID-19 is a disease induced by a virus, SARS-CoV-2, but the pathogenesis is mainly controlled by host immunity. Although unaware of the real mechanisms, it would be tempting to consider that host immunity may be different among human races in the context of COVID-19, however, more information would be required to substantiate these hypotheses.

The major limitation of the study is small sample size of only 33 patients; however, this is acceptable as observational study. The next, there has been no control group in this study. In fact, this is not a possible scenario in a pandemic situation. The time is not suitable for assessing comparative benefits of different groups. Moreover, this is not a comprehensive study for management of COVID-19 in Bangladesh or any other country as the disease itself manifest with diverse pathological features.

However, we strongly recommend for a large cohort study with bigger sample size and proper control group using different drug regimen. The main idea of this communication is to show that COVID-19 should not initiate a state of panic. The next, if the patients are diagnosed early and provided with hospital-based management, the outcome may be favorable. This can be optimized by different public health measures and precautions for pandemic by policy makers. The concept of our study may be applied for management of COVID-19 patients in other developing and resource-constrained countries of Asia and Africa.

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