**Article**

Comparative **Clinical management, treatment pattern and medications of COVID-19 practiced at Dhaka city in Bangladesh: a randomized cross-sectional study**

Tabassum Jannat1,2, Md. Moklesur Rahman Sarker3,4\*, Safaet Alam5, Mst. Luthfun Nesa6, Selina Akhter7

### Abstract

Before introducing of COVID-19 vaccines the management of COVID-19 was mainly performed by repurposing of existing drugs and adopting the traditional practice. Later on vaccine immunization was introduced in addition to repurposing of drugs and traditional practice. The present study aimed to identify the treatment pattern of COVID-19 along with the traditional practices followed in Bangladesh and justify their purposes of use. For this purpose, a randomized cross-sectional prescriptive study was conducted among COVID-19 survivors who received treatment from hospitals or staying at home to collect their prescriptions, other medical records, and interview on to discuss on different aspects of their disease conditions and treatment. The patients’ prescriptions and interview reports were used to identify mostly used classes of drugs, their frequency and other traditional practices followed by the patients suggested by doctors. These prescriptions were then analyzed to establish a treatment pattern followed by the common people of Bangladesh. The data were collected from a total of 184 participants (age between 18 years to 80 years old) of COVID-survivors of both sexes residing in different locations of Dhaka city in Bangladesh during 10 March 2021 to 30 July 2021. Among the 184 participants, 123 were from non-hospitalized and 61 from hospitalized patients. The numbers of male COVID-19 patients were higher than that of female. We found that COVID-19 patients were treated with several classes of medications. The major classes of medicaments used were antiviral drugs (Ivermectin, Remdisivir, Favipiravir), antibiotics (Azithromycin, Doxycycline, Amoxicillin+Clavulanic acid, Cefuroxime, Cefixime, Moxifloxacin, Gemifloxacin, Levofloxacin, Meropenem), anticoagulants (Rivaroxaban, Enoxaparin, Betrixaban), and nutritional supplements (Vitamin C, Vitamin D, Vitamin B complex, Zinc, Multivitamin, Daflon, Pancreatin, Calcium+Amino acid). Traditional healing practices were also followed by patients at home including inhalation of water vapor, consumption of spiced tea, physical exercises, and gurgling with hot water with verbal suggestion or without the suggestion of the physicians. The treatment pattern of COVID-19 was mostly symptomatic. Although the treatment pattern and the type of repurposing drugs were mostly followed WHO and country guidelines, the frequent use of antibiotics and corticosteroids were not in compliance with the above guidelines. The COVID-19 treatment pattern practiced in Bangladesh was mostly found to be symptomatic which was aligned with the guidelines of WHO and drug administration of Bangladesh except the use irrational and frequent use of antibiotics and corticosteroids.

**Keywords**: Commercial drug, Formulated drug, Fexofenadine hydrochloride, Quality control parameters, Quality of medicine

1Department of Pharmacy, University of Asia Pacific, 74/A Green Road, Dhaka, Bangladesh; 2Griffith Institute for Drug Discovery, Griffith University, Queensland, Brisbane, Australia; 3 Department of Pharmacy, Gono University (Bishwabidyalay), Nolam, Mirzanagar, Savar, Dhaka- 1344, Bangladesh; 4Pharmacology and Toxicology Research Division, Health Med Science Research Limited, 3/1 Block F, Lalmatia, Dhaka 1207, Bangladesh; 5Drugs and Toxins Research Division, BCSIR Laboratories Rajshahi, Bangladesh Council of Scientific and Industrial Research, Rajshahi 6206, Bangladesh; 6Department of Pharmacy, State University of Bangladesh, 77 Satmasjid Road, Dhanmondi, Dhaka 1205, Bangladesh; 7Department of Public Health, Faculty of Allied Health Science, Daffodil International University, Dhanmondi, Dhaka 1207, Bangladesh

**\* Correspondence:** Namer………….., Designation……………….. Affiliation…………………………….

 Email: …………………; Phone: ……………………………

### Introduction

# Coronavirus, known as SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2), is a deadly virus that turned out to be a devastating outbreak all over the world. It became highlighted on 31st December 2019 as the China health authority alerted WHO (world health organization) about a new type of severe pneumonia of very different etiology in the main city of Hubei Province of China, Wuhan. The cases had been reported since December 8, 2019, and many patients worked at or lived around the local Huanan Seafood Wholesale Market although other early cases had no exposure to this market (Lu et al., 2020). On January 07, a novel corona virus, originally abbreviated as 2019-nCoV by WHO, was identified from the throat swab sample of patient (Hui et al., 2020). This pathogen was later renamed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the Coronavirus Study Group (Gorbalenya et al., 2020), and the disease was named coronavirus disease 2019 (COVID-19) by the WHO.

# As of 30 January 2020, 7736 confirmed and 12,167 suspected cases had been reported in China and 82 confirmed cases were detected in 18 other countries (Burki et al., 2020). In the same day, WHO declared the SARS-CoV-2 outbreak as a Public Health Emergency of International Concern (PHEIC) (Burki et al., 2020). As of 13 December 2021, coronavirus was spread in 222 countries and territories with 269,468,311 confirmed cases of COVID-19 and 5,304,248 deaths (WHO, 2021). Bangladesh is not also an exception. On 8 March 2020, the first case of COVID-19 was confirmed in Bangladesh. Between 8 March and 15 May 2020, according to the Directorate General of Health Services (DGHS) on behalf of the Ministry of Health in Bangladesh, there were 20,065 COVID-19 confirmed cases by rt-PCR including 298 related death cases where the case fatality rate (CFR) was 1.48%, highest confirm case was identified on 15 May which was 1202 and highest death was figured out on 13 May, 2020 (Hossain et al., 2020). The pandemic of COVID-19 badly affected in Bangladesh likewise other countries. The government tried its best to tackle this devastating situation. According to WHO Bangladesh report, there were 1,579,710 confirmed cases of COVID-19 with 28,031 deaths in Bangladesh between 03 January 2020 to 13 December 2021 COVID-19, 2021).

Later on vaccines from various sources were introduced in Bangladesh and the number of COVID-19 cases and death rate due to COVID-19 were reduced significantly. Yet, parallel treatment for COVID-19 infected patients was practiced with the repurposing of

drugs and other treatment mentioned earlier. However, diversity of SARS-CoV-2 and frequent change of new variants was a great challenge towards the effectiveness of vaccines [8]. Furthermore, adequate production, allocation, storage conditions and affordable prices for purchasing were some of the major challenges in the way of sufficient production, supply, and chain management and to ensure its efficacy and safety (Polack et al., 2020; Folegatti et al., 2020; Wouters et al., 2021; Hossen et al., 2020).

# Prior to sufficient availability and supply of COVID-19 vaccines, the only treatment options for COVID-19 patients was repurposing of drugs. The recovery rate of COVID-19 patients could be increased by applying several evidence-based repurposed antiviral drugs that slow down the replication of SARS-CoV-2 and/or decrease disease symptoms (Hossain et al., 2021). According to NIH guidelines, the recommended repurposing drugs that could be used in COVID-19 patients were Remdisivir, Dexamethasone (alternatively prednisolone or methylprednisolone could be used) and Baricitinib, used evaluating the conditions of the patients. WHO recommended differently towards the treatment procedure. Remdisivir, hydroxychloroquine, azithromycin were recommended for the COVID-19 patients. Later on, Remdisivir and hydroxychloroquine were withdrawn from the suggested guideline, the later was suspected to cause various heart diseases (Lepere et al., 2021; Alam et al., 2021). According to NIH guidelines, Remdisivir can be considered administering to inpatient hospital with constant monitoring in severe cases, though renal insufficiency is a major point of contraindication in this usage (NIH, 2021). The treatment pattern in Bangladesh was represented in the website of the directorate general of health services (DGHS), Government of the Peoples’ Republic of Bangladesh, where several drugs were recommended for the treatment purposes of COVID-19 patients. Based on the severity and symptoms, the drugs such as, Paracetamol, Chloroquine, Remdisivir, Corticosteroids, Favipiravir, Tocilizumab, Interleukin, etc. were recommended in this guideline (NIH, 2021; Rahman and Rahman, 2020)..

In Bangladesh, the prevention and treatment of COVID-19 was managed by a blend of repurposing of drugs, immunization, oxygen and ventilation support and by applying traditional practice and intake of vitamins and other supplements. However, enough research has not been conducted so far to present a clear picture on the clinical practice, treatment pattern and medications used for the management of COVID-19 patients in Bangladesh as well as nobody has justified those practice with the standard practice and guidelines given by WHO and/or followed by other developed countries of the world. That’s why the present study was carried out to investigate the medicaments of COVID-19 patients living in Dhaka city in Bangladesh including repurposing and conventional medicines and justify the rationality of the medicines used based on diagnosis, symptoms and underlying co morbidities as well as to compare the WHO and DGHS guidelines.

### Materials and Methods

## Study subjects, consent, and ethical aspect

## The study participants were representative (184 COVID-19 patients of age 18-80 years) of COVID-19 survivals living at Dhaka city in Bangladesh. The study subjects (COVID-19 patients) were randomly selected from different COVID-19 hospitals, clinics as well as who received treatment staying at home. The consent of the patients was obtained before conducting the study. The objectives, significance, risk and benefits, etc. of the study were explained to the patients before getting their consent for participation in the study. The COVID-19 survivals who could provide written prescription of physicians and willingly agreed to participate were included in the study. An ethical approval for the study protocol was obtained from the institutional review board (IRB) for human ethics of the State University of Bangladesh before conducting the study (Protocol approval no: 2020-12-15/SUB/H-ERC/0002).

## Collection of data

After getting informed consent, the patients were asked to provide a photocopy or picture of their prescriptions along with other medical reports (if available). Additionally the patients were also asked about the medicines they have taken (according to or without prescriptions provided by health care practitioners), the dose and dosage regimen of the medicines, and the management policies followed by them throughout the treatment period. Besides, the severity of their diseases, complications, and other questions relating to COVID-19 and it’s treatment were asked for better clarification and evaluation of the justification of their prescriptions. The prescriptions were collected physically as well as through online platform (email, messenger, whatsapp, etc.). Interview/discussion with the patients were performed face to face as well as by phone call or audio/video call using messenger, whatsapp, imo, viber or online zoom meeting.

The data were collected from prescriptions and discussion with 184 COVID-19 survivors (hospitalized

## and non-hospitalized). The data collection period was from 10 March 2021 to 30 July 2021. The name and personal information of the patients were kept confidential and the patients were coded with patients ID starting from P-01 to P-184. Among the study subjects, 61 patients were hospitalized and received treatment in hospital, and 123 patients received COVID-19 treatments staying at home as per the prescriptions of physicians. The collected data of medicaments and other traditional practice which were advised to follow by the physicians as a part of their treatment procedure have been summarized in Table 1 and Table 2.

### Results

## Demographic characteristics of the patients

## Among total 184 patients, 61.4% was male and 38.6% female (Figure 1a). In case of 61 hospitalized patients, male patients were more (55.7%) than female ones (44.3%); and among the 123 non-hospitalized patients, male patients were 64.2% and female patients were 35.8% (Figure 1A). We have divided the patients in two groups according to age. Among 184 patients, 59.8% patient was below 40 years and 40.2% above 40 years. When we considered only hospitalized patients, 49.2% was below 40 years and 50.8% was above 40 years. For non-hospitalized patients, 65% was below 40 years and 35% was above that age. These data has been summarized in Figure 1B.

**Clinical management of COVID-19 patients in Bangladesh**

*COVID-19 confirmation test*

All the patients of this study were tested positive in the confirmed COVID test by various recognized national and private organizations solely designated for tests.

*Biochemical tests/ analysis*

Several biochemical tests were suggested like CBC with ESR, serum ferritin, D-Dimer, Chest X-ray and HRCT which was acknowledged by patients while conversation and observation of treatment records.

*Physical observation*

COVID-19 patients’ symptoms were noted and listed (Table 3). Common symptoms include fever, headache, body ache, chest tightness, cough, sore throat breathing difficulty etc. Comorbidities for instance hypertension, diabetes, insomnia, kidney disease etc. were also identified through diagnosis.



*Oxygen saturation*

Typical problem arisen from COVID pneumonia was hypoxia which means low oxygen saturation level in blood. It was one of the major complications of COVID-19 that the oxygen saturation drops all of a sudden in COVID patients. So, every patient was suggested to monitor his/her oxygen saturation level on a regular basis regardless of staying at home or hospital.

*Ventilation*

Severe patients were transferred to ICU and under ventilation. Those who were unable to breathe were under artificial methods to assist breathing (ventilator).

*Treatment*

Various drugs were prescribed both for symptomatic and prophylactic treatment to the patients according to their age, symptoms and stage of infection.

*Treatment procedure of COVID-19 patients in Bangladesh*

Moving forward towards the treatment procedure, several classes of drugs were found including antiviral, antibiotic, antipyretic, antitussive, corticosteroid, mucolytes, anxiolytic, anticoagulant, antihistamine, vitamin and mineral supplements, and bronchodilators. Occasionally monoclonal antibody, antidiabetic, antihypertensive, antiprotozoal and cholesterol-lowering agents were also prescribed summarized in Table 1.

**Categories of drugs used for the treatment of COVID-19 patients**

*Repurposing of antiviral drugs*

Among the antiviral drugs, Ivermectin, Remdisivir and Favipiravir were used. The topmost and only antiviral drug prescribed in non-hospitalized patients was Ivermectin having a frequency of 56 prescriptions out of 122 (46%) (Fig. 2A). In the case of hospitalized patients, Ivermectin and Remdisivir were in 17 and 25 prescriptions respectively (28% and 41% respectively) whereas Favipiravir use was very low consuming 1 prescription (2%) (Fig. 2B).

*Repurposing of antibiotics*

During COVID pandemic, the mostly commonly used antibiotics were Azithromycin (class: Macrolide), Doxycycline (class: tetracycline), Amoxicillin and Clavulanic acid combination (class: Penicillin), Cefuroxime, Cefixime (class: cephalosporin), Moxifloxacin, Gemifloxacin and Levofloxacin (Fluoroquinolone) and Meropenem (class: carbapenem). Considering the use of antibiotics, Azithromycin was prevalent (28%, 17 prescriptions), followed by Penicillin and Fluoroquinolone (23%, 14 prescriptions), Meropenem (16%, 10 prescriptions), Doxycycline (11%, 7 prescriptions) and Cephalosporin (7%, 4 prescriptions) - all for hospitalized patients (Fig. 2B). For non-hospitalized ones, Azithromycin was mostly prescribed covering 46 prescriptions (37%), while Fluoroquinolone, Doxycycline, Cephalosporin and Penicillin were in 5, 38, 8 and 2 prescriptions respectively (4%, 28%, 7% and 2% respectively) (Fig. 2A).

**Table 1:** **Medicaments followed by non-hospitalized patients diagnosed with COVID-19 at Dhaka city in Bangladesh**

|  |  |  |
| --- | --- | --- |
| Name of Drug Classes | No. of Prescriptions | Percentage (%) |
| Antiviral | Ivermectin | 56 | 46 |
| Favipiravir | 6 | 5 |
| Antihistamine | 56 | 46 |
| Bronchodilator | 24 | 20 |
| Montelukast | 46 | 37 |
| Immunosuppressant | 1 | 1 |
| Antitussive | 16 | 13 |
| Antibiotics | Penicillin | 2 | 2 |
| Fluoroquinolone | 5 | 4 |
| Azithromycin | 46 | 37 |
| Tetracycline | 35 | 28 |
| Cephalosporin | 8 | 7 |
| Nutritional supplements | Vitamin C | 73 | 59 |
|  | Vit D | 33 | 27 |
|  | Zinc/Zinc + Vit B | 57 | 46 |
|  | Multivitamin | 4 | 3 |
|  | Amino acid-Calcium/Calcium | 2 | 2 |
| Antiparasitic | Metronidazole | 5 | 4 |
| Mucolytes | 1 | 1 |
| PPI | 12 | 10 |
| Anxiolytics | 3 | 2 |
| Antihypertensive | 5 | 4 |
| Anticoagulant | 20 | 16 |
| Antipyretic | Paracetamol | 94 | 76 |
| Antiemetic | Domperidone | 4 | 3 |

*Antihistamines*

Mostly used antihistamine was Fexofenadine; however Rupatadine and Ebastin were occasionally prescribed. Antihistamines were prescribed in 21 cases (34%) of hospitalized patients (Fig. 2b). One of the highest prescribed drug classes are Antihistamine (46%) found in 56 prescriptions of non-hospitalized patients (Fig. 2a).

*Anticoagulants*

The main anticoagulant drugs used were Rivaroxaban and Enoxaparin; however, Betrixaban was also given in few cases. In the case of hospitalized patients, anticoagulants were used most frequently covering 34 prescriptions among 61 prescriptions (56%) (Fig. 2b). For non-hospitalized ones, anticoagulants were prescribed in 20 cases (16%) (Fig. 2a).

*Bronchodilators*

Montelukast was the most commonly used bronchodilator. Other used bronchodilators include Salbutamol, Salmetrelol and Fluticasone combination, Bumetanide, Budesonide and Doxophylline. Montelukast was one of the most popular drugs being in 32 prescriptions (52%) whereas other Bronchodilator use was in 23 cases (38%) in hospitalized patients (Fig. 2b).