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Extent of Pharmacotherapy in Covid-19: An Observational Study in a Dedicated Hospital in Bangladesh

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Article Info:

Abstract

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Objective: With the rapid increase in the rate of infection, repurposing use of many drugs like antivirals, antibiotics, LMWH, steroid, oxygen therapy were considered as an option to find promising anti-COVID therapeutics. In this study, we aim to observe the extent and variety of drugs used in different clinical categories of COVID-19 patients admitted to hospital in Bangladesh. To observe the requirement of oxygen therapy according to severity was also a prime objective to reveal the overall trend, frequency, and pattern of pharmacotherapy in a COVID-dedicated hospital.

Materials and method: A total of 1348 patients were admitted, of whom 473 were included in this single-center retrospective study. The critical group consists of 99 ICU patients, the severe group has 38, moderate was 82 and mild group 254 cases, admitted in the general ward. Hospital records of each patient were screened and information about drug and supportive therapy were collected manually by the researchers in the data collection sheet. Data express in MS excel spreadsheet and result expressed in percentage.

Results: Critical group received remdesivir (85.86%), favipiravir (27.28%), meropenem (92.93%), moxifloxacin (87.88%) dexamethasone (41.48%), Low Molecular Weight Heparin (98.99%). They also received supportive O2 therapy like High Flow Nasal Cannula (67.68%), Non-Invasive Ventilation (26.67%), and mechanical ventilator (6.06%). A severe group of patients receives the same group of drugs 97.27%, 5.26%, 60.53%, 47.37%, methylprednisolone (55.26%), and 100% LMWH. A moderate group of the patient received favipiravir (97.56%), cephalosporin (64.67%), LMWH (89.02%) and low flow O2 (97.36%) in a higher percentage. All patients of the mild group received doxycycline, ivermectin. Total 33 patients transfuse convalescent plasma.

Conclusion: Antiviral, broad-spectrum antibiotics, anti-protozoal, LMWH, corticosteroid, and oxygen therapy are the available treatment option against different clinical categories of admitted COVID-19 patients.

Keywords: COVID-19, antiviral, antibiotic, steroid, O2 therapy.

INTRODUCTION:

COVID- 19 has infected more than 74 million people and claimed over 1.6 million death cases around the world[1]. This large number of infected patients with a case fatality ratio ranges from 0.1% to 25% in different countries, demonstrates that the coronavirus disease is extremely contagious[2]. On 11th March 2020, WHO declared COVID-19, a pandemic situation. Near the time of this announcement, the first case of COVID- 19 case was reported in Bangladesh on 8th March 2020. From then to 17th December 2020, Bangladesh deals with 4,95, 841 confirmed cases and 7, 156 death[3]. Besides Bangladesh, COVID became a great concern in the densely populated South Asian region with more than 8 million confirmed cases and 1.2 million deaths up to 19th October, 2020[4].

At first, Governments of this region, taken various measures to speed dawn the spread of the pandemic, such as nationwide lockdown, quarantine curfews, restrictions on travel, and mass gatherings. Furthermore, encouraging native to practice personal hygiene and social distancing[4]. This territory is made up of some developing and under-developed countries, governments including Bangladesh loosen some toe the line, for the sake of the economy. Though the second wave of COVID-19 start to hit the region from the end of November.

SARS-COV-2 is a positive-sense, single-stranded enveloped RNA virus, contains a spike protein present on the viral surface[5]. The fusion of this spike protein of the coronavirus and the ACE_2 receptors of the cell surface facilitates its entry process. After entering into the host cells, the virus exposes their RNA; translation of RNA replication occurs and RNA replicase-transcriptase complex formed. After transcription and replication, negative-strand RNA is produced which forms structural proteins of the viruses. New viral particles of SARS-CoV-2 are formed resulting from the assembly of structural proteins and RNA in the host cell cytoplasm. Then these newly formed viral particles are released from the host cells through exocytosis, infect nearby cells. and can cause target organ infections including pneumonia, gastroenteritis, acute kidney injury, carditis etc[6].

Besides end target organ damage, the SARS-CoV-2 virus causes an indirect immune response which affects patient's morbidity and mortality. COVID-19 infected patients show high levels of pro-inflammatory mediators like IL-1β, IP-10, MCP1. Cytokine storm is thought to be linked with the severity of the disease and disease outcome[7].

People who are infected with COVID-19 are quarantined and treated in COVID dedicated health facilities. In the case of 80% of patients, SARS-COV-2 infections are self-limiting and hospital admission may not be needed, 15% of the patient with comorbidities such as diabetes, heart problems, hypertension, and obesity are more likely to develop severe pneumonia need hospital admission admitted to get proper medical care. Rest 5% of them reported developing respiratory failure, ARDS, other end-organ failure and need intensive care unit (ICU) support for a long period of time[8].

For the practical purpose of patient management, the six syndromes of COVID-19 have been categorized into mild, moderate, severe, and critical cases. Mild cases represent Influenza like illness (ILI), moderate with pneumonia (CRB 65 score 0), severe patient with severe pneumonia, sepsis, and with ARDS, septic shock developed in those, considered as critical[9].

Mild cases present with fever, cough, sore throat, malaise, headache, muscle pain without shortness of breath, or abnormal imaging. The moderate case is considered as a clinical sign of pneumonia with oxygen saturation of more than 90% at ambient air. Patients who have 30 breaths/ minute and finger oxygen saturation less than 90% at rest are considered as a severe case. Patients who are admitted in ICU with respiratory failure or any other organ failure or shock and requiring mechanical ventilation are considered a critical case[9].

No specific treatment exists for COVID-19 yet[10]. The standard practice of care focuses on treating the clinical symptoms (pyrexia, cough), and ARDS of patients with supportive care such as fluid management and auxiliary oxygen therapy. The clinical efficacy of many agents used for COVID-19 is, so far not approved yet[11].

The place and population of this retrospective, observational study is considered as one of the COVID dedicated hospitals in Dhaka city for COVID-19 patients. The findings of the study carried significant reflection of the treatment given in hospitalized COVID patients in Bangladesh. Increased hospital stay cost due to the drug, the limited amount of resources, and health professionals in a developing country like Bangladesh, this study may help to develop rational use of drugs in SARS- CoV-2 infection.

Objective:

To observe the verities and extent of drugs and oxygen therapy in the treatment of COVID-19 patients admitted to a COVID-dedicated hospital in Bangladesh.

MATERIALS AND METHOD:

All RCT-PCR positive patients who were admitted to Holy Family Red Crescent Medical College Hospital (HFRCMCH), from May 17th to September 9th, 2020, were eligible for the study. HFRCMCH located in Dhaka, Bangladesh, the major endemic area of COVID-19, is a tertiary care hospital. Holy Family Red Crescent Medical Hospital was assigned responsibility for the treatments of patients with COVID-19 by the People's Republic of Bangladesh on May 15th May 2020.

Data of individual admitted patients were collected from hospital records. Patients with RT-PCR positive reports were included in this retrospective study. Then all files were screened and patients who have a lack of information, and discontinued data excluded from the study. All the data recorded in a customized form. Patients' record files were divided into four groups, abiding by the National Guideline of Bangladesh published on 5th November 2020. One group treated as the critical case, admitted in ICU have 99 patients. The severe case has 38 patients, the Moderate group has 82 patients and the mild group includes 254 patients.

After the record, information from all four groups was expressed in an MS Excel spreadsheet, and the result was expressed in percentage.

RESULT:

Between May 17, 2020, and September 9, 2020, 1348 patients were admitted, of whom 473 were included in this retrospective study. Ninety-nine patients were treated as a critical case, thirty-eight as severe, eighty-two as moderate, and another two hundred fifty-four as the mild case.

Table 1: List of Drugs and supportive therapy in different clinical categories of COVID-19

Drugs — no./total no. (%)	Critical case (n=99)	Severe case (n= 38)	Moderate case (n=82)	Mild case (n= 254)
Anti-viral				
Remdesivir	85/ 99 (85.86%)	37/ 38 (97.37%)	01/ 82 (01.22%)	-
Favipiravir	27/99 (27.28%)	02/ 38 (05.26%)	80/ 82 (97.56%)	-
Tocilijumab	15/ 99 (15.16%)	02/ 38 (05.26%)	-	-
Bacterinub	02/ 99 (02.02%)	-	-	-
Steroid				
Hydrocortisone	17/ 99 (17.18%)	03/ 38 (07.89%)	02/ 82 (02.44%)	01/ 254 (0.39%)
Dexamethasone	41/ 99 (41.48%)	12/ 38 (31.58%)	33/ 82 (40.24%)	06/254 (02.36%)
Methylprednisolone	37/ 99 (37.38%)	21/ 38 (55.26%)	40/ 82 (48.78%)	-
Anti protozoal				
Ivermectin	13/ 99 (13.13%)	11/ 38 (28.95%)	35/ 82 (42.68%)	254/ 254 (100%)
Others				
LMWH	98/ 99 (98.99%)	38/ 38 (100%)	73/ 82 (89.02%)	-
C. plasma	31/ 99 (31.31%)	01/ 38 (02.63%)	01/ 82 (01.22%)	-
O$_2$ therapy				
Low flow	-	-	79/ 82 (97.36%)	254/ 254 (100%)
High flow	67/ 99 (67.68%)	38/ 38 (100%)	03/ 82 (03.66%)	-
NIV	26/ 99 (26.67%)	-	-	-
Ventilator	06/ 99 (06.06%)	-	-	-

Antivirals: Among antivirals, most critical (85.86%) and severe (97.37%) cases received remdesivir. whereas the moderate group of patients received favipiravir (97.57%) in the highest percentage. Tocilizumab and bacterinub used in patients admitted in ICU. (Table-1)

Other drugs: Different groups of steroids used in COVID-19 patients, among them methylprednisolone in the highest percentage (55.26% and 48.78%) in the severe and moderate group but absent in mild cases. Dexamethasone and hydrocortisone were also used in all four groups. (Table-1)

All patients in the mild group received ivermectin. The percentage is decreasing in the moderate to critical group

(42.68%. 28.95% and 13.13%). Low molecular weight heparin and convalescent plasma therapy not used in the mild group of patients. Total 33 patients received convalescent plasma, the majority (31 cases) admitted in ICU. (Table-1)

Oxygen therapy: Mild (100%) and moderate (97.36%)group of patients were on low flow oxygen. Oxygen need increased in the severe group (100%) of patients. Non- invasive ventilation and mechanical ventilator needed in ICU admitted group. (Table-1)

Each patient also received antihistamine, leukotriene receptor blocker, proton pump inhibitor, immunity booster like vitamin D, vitamin C, and zinc along with these drugs.
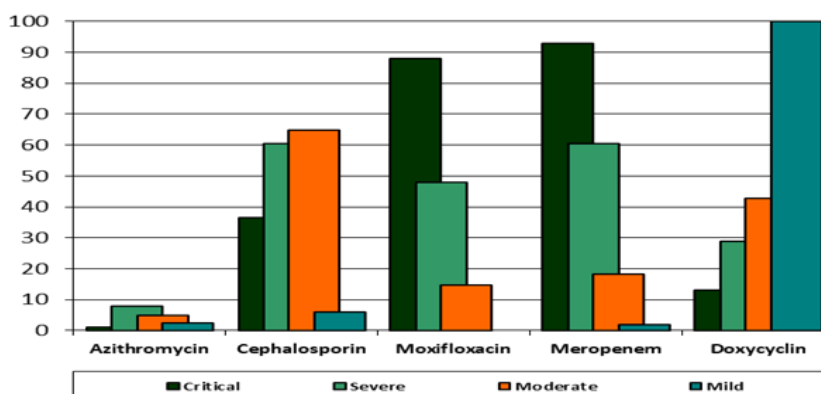

Figure-I: List of antibiotics used in different clinical categories of COVID- 19 patients

Antibiotics: All mild cases received doxycycline (100%). The rate is gradually decreasing in moderate to the critical case (42.68%, 28.95%, 13.13%). Meropenem (92.93%) highest used in critical patients admitted to ICU. Consumption rate decreasing in severe (60.53%), moderate (18.29%) and mild (1.97%) cases. No mild case patient received moxifloxacin. But the rate is quite higher in critical (87.88%) cases, then severe (47.37%) and moderate (14.63%). Cephalosporin was administered highly in moderate (64.69%)cases than in severe, critical, and mild (60.53%, 36.37%, and 5.91%). Azithromycin consumption rate quite lower than the other four antibiotics in admitted patients (1.01%, 7.89%, 4.88%, and 2.36%). (Figure-I)

Some antibiotics used in the lowest percentage like metronidazole, ciprofloxacin, levofloxacin, amoxicillin, and piperacillin-tazobactam (Pip-Taz) combination. Among them, Pip-Taz (1.01%) and levofloxacin (3.03%) were used only in critical patients. Metronidazole (2.02 %, 5.26%, 6.09%, 0.39%), ciprofloxacin (3.03%, 2.63%, 4.88%, 1.18%) and amoxicillin (1.01%, 2.63%, 1.22%, 0.39%) also given in critical, severe, moderate and mild cases respectively.

DISCUSSION:

This is one of the earliest reporting observational studies that showed several kinds of drugs used in different clinical categories of admitted COVID-19 patients in a dedicated COVID hospital in Dhaka, Bangladesh. It needs time to find proper drugs to work as potent anti- COVID agents. This study focuses on the re-purposeful use of existing drugs that are used to defeat the current pandemic situation of Bangladesh.

Critical: Ayan et al, in their retrospective study in a total of 168 ICU patients show that patients received 42.3% favipiravir 18.4% remdesivir, 57.7% methylprednisolone, 23.8% dexamethasone, 76.2% meropenem followed by 29.8% ceftriaxone, 19.8% azithromycin, and 19.4% moxifloxacin[12].

Another study in Mughda medical college, Dhaka based on ICU, observed 31.7% meropenem, 58.7% LMWH, 15.9% antiviral therapy, and 55.6% glucocorticoid consumption by the admitted patient. In the case of oxygen therapy, 15.9% patients gone through NIV and 23.8% mechanical ventilation[13]. Zhang et al, mention 45.5% receive NIV and 29.1% patient invasive mechanical ventilation[14]. In Chittagong, a total of 168 ICU patients only 8 patients transfuse convalescent plasma[12]. According to a recent study, therapeutic plasma exchange can be effective in critically ill patients if it can be applied within the first week of symptom onset[15].

In this study, antiviral drugs like remdesivir, favipiravir, tocilizumab, bacterinub, broad-spectrum antibiotics like meropenem, moxifloxacin, cephalosporin, steroid used in a critical patient admitted to ICU. Supportive oxygen therapy, NIV, mechanical ventilators were also used in this group. Total 33 patients received convalescent plasma of whom, 31 were admitted to ICU.

Severe: In an RCT, Huang et al, used remdesivir, lopinavir-ritonavir, continuous oxygen support, and corticosteroid in their 236 severe patients[16]. Cai et al, show in their study, among 85 severe cases 76.74% received antibiotics and 91.76% received antiviral[17]. Zhang et al, observed among 55 severe patients, 90.9% antiviral and 72.7% glucocorticoid therapy[14]. In this study, severe cases also received antiviral remdesivir, favipiravir, and broad-spectrum antibiotic,

steroid as like as critical patients. But they respond in high flow oxygen without ICU support.

Moderate: Cai et al shows, 233 non-severe patients received 29.79% antibiotic and 90.13% received antiviral drugs[17]. Favipiravir which was a widely considered repurposing antiviral around the world[18], was also recommended in the National Guideline of Bangladesh[9], broad-spectrum antibiotic mainly cephalosporin, steroid, and low flow oxygen received by the moderate group of patients in the present study.

Mild: In a multicenter study in Bangladesh, among 236 patients, 100% of patients received LMWH. Around 2/3 patients received steroids in different forms (dexamethasone/ methylprednisolone/ hydrocortisone) and 47% received broad-spectrum antibiotics[19]. In a large cohort study, Million et. al. has used hydroxychloroquine and azithromycin combination in France at the time of the peak of COVID-pandemic in France[20]. Also, a role of this combination therapy on the viral load of SARS-CoV-2 has been shown by La Scola et al[21]. In kishorgonj, Bangladesh clinicians were also used it[22]. In this study, a mild group of the patient received antiprotozoal drug like ivermectin, antibiotics like doxycycline and low flow oxygen. All admitted patients received immune boosters like vitamin C, D, E, and zinc.

The limitation of this retrospective study is data not reserved in the digital record system. Manual entry of data by the researcher may cause simultaneous entry of information. The strong point of the study is, its large sample size of 473 patients, duration of the study was from May to September 2020, which was the pick of the first wave in Bangladesh. it also observed in different clinical conditions of COVID-19.

CONCLUSION:

Antiviral, broad-spectrum antibiotic, anti-protozoal, LMWH, corticosteroid, and oxygen therapy were the weapon to fight against different clinical categories of admitted COVID-19 patients.

Acknowledgments:

Conflict of Interest:

None of the co-authors declared any conflict of interest regarding this article.

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