

EXTENT OF PRESCRIBING ANTIBIOTICS AND CORTICOSTEROIDS ON COVID-19 ADMITTED PATIENTS INTO A CORONA DEDICATED HOSPITAL IN KHULNA

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Abstract:

Background: Majority of the patients infected with SARS-CoV-2 receive antibiotics and corticosteroids though its role has not yet been adequately defined. Inappropriate use of antibiotics despite bacterial co-infections may lead to global antibiotic resistance.

Aim and objectives: We aim to assess the using pattern of antibiotics and corticosteroids in different clinical categories of COVID-19 patients admitted to a hospital.

Materials and methods: This is a cross sectional study where 345 clinically diagnosed COVID 19 patients having coexisting diseases of both sexes with different age group received antibiotics and corticosteroids were included. Patients' demographic profile, treatment plan were obtained using a specially designed form. All data were compiled in Microsoft excel spreadsheet and results expressed in total number and percentage.

Results: Out of total 345 patients, male (53.62%) and female patients (46.37%) of age group between 41 to 60 years (42.89%) of different categories; mild (28.40%), moderate ((39.42%), severe (24.63%), critical (7.53%) cases were enrolled in this study. Moxifloxacin followed by ceftriaxon was most commonly prescribed antibiotic in all clinical groups with higher percentages. Other antibiotic includes meropenem, amoxicillin+ clavulanic acid, piperacillin+tazobactam, linezolid also prescribed in higher rate. Among systemic corticosteroids, dexamethasone followed by methylprednisolone, hydrocortisone was prescribed invariably with higher percentages.

Conclusion: With the rapid increase in the rate of infection, purposeful use of antibiotic and corticosteroid might be considered as a better treatment option to fight against COVID 19 patients.

Key words: antibiotic, corticosteroids, COVID 19.

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Introduction:

The COVID-19 pandemic has had a devastating impact on the healthcare system and society globally.¹ SARS-CoV-2 can lead to a wide spectrum of disease, ranging from very mild symptoms of upper respiratory tract infection

to life-threatening pneumonia, sepsis/septic shock and multiple organ failure.^{2,3} Despite the viral origin of SARS-CoV-2, antibiotics are prescribed frequently because of radiological proof of infiltrates which is the hallmarks of bacterial community-acquired pneumonia that

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requires antibiotics.^{1,4,5} Several published studies worldwide have shown that secondary bacterial infection rates increased in Covid-19 critically ill patients^{2,6} notably a high per cent (up to 94%) of antibiotic were prescribed based on experience with bacterial super infection in influenza in the treatment of COVID-19 admitted patients.^{1,2,5,6} Common bacteria include *Staphylococcus aureus*, *S. pneumoniae*, *Neisseria meningitidis*, *H. influenzae*, *Klebsiella pneumoniae* and members of the *Proteus*, *Enterobacter* and *Citrobacter* spp. etc isolated during secondary infections.⁷ Generally effective treatment for bacterial infections with broad-spectrum antibiotics is of critical importance but at the same time empiric antibiotic therapy has a greater concern due to utmost development of higher antimicrobial resistance (AMR) which can results in undesirable side effects that have a negative impact on health outcomes.^{5,7-9} World Health Organization (WHO) also concerned in this growing global health issue which will get worse due to the COVID-19 pandemic.^{8,9} WHO guidelines recommend no antibiotic therapy or prophylaxis for patients with mild or moderate COVID-19 unless signs and symptoms of a bacterial infection exist.^{9,10}

Therapeutic options with corticosteroid emerged as a steady medications which have received worldwide attention as a potentially effective treatment for COVID-19 infection.^{11,12} As the sign symptoms of COVID-19 in humans resemble those of viral pneumonia,¹³ pathogenesis due to an aberrant host immune reaction (e.g., cytokine storm) to the viral infection in all affected patients.³ Because the immune pathogenesis of pneumonia may be the same in all infected patients, immunomodulator (corticosteroid) is helpful for reducing patient morbidity and possible mortality with the early control of initial immune-mediated lung injury.³ It has been proposed that corticosteroids do not directly inhibit virus replication, and their main role is inhibiting inflammation and suppressing the intensity of immune response to COVID-19.^{3,15} Based on the anti-inflammatory action of corticosteroids, various studies have revealed the beneficial effect by blunting the severity of inflammation and preventing systemic inflammatory response, many questions like

dose of steroids, optimal timing to initiate steroid therapy or the total duration of steroid use etc still remain unclear without any conclusive evidence.^{11,16,17} Thereby further conclusive observational studies should be needed to anticipate the effectiveness and safety of corticosteroid.

Materials and Methods:

After obtaining ethical approval from institutional ethics committee, this descriptive cross sectional study conducted on three hundred forty five (345) COVID 19 positive patients admitted in the corona unit of Gazi Medical College Hospital over a five months period from February 2021 to July 2021. Consenting RCT-PCR positive patients with all age group of both sexes having co-morbidities like hypertension, diabetes, ischemic heart disease, bronchial asthma etc and received steroids and antibiotics were included in this study whereas patients with pregnancy and on lactation and those having RCT-PCR negative findings were excluded from this study. An informed written consent was obtained from each patient before recruitment and a specially designed questionnaire was used to record participant demographic profile. The six syndromes of COVID-19 have been categorized into mild, moderate, severe and critical cases by following our National Guidelines on Clinical Management of COVID-19 of Bangladesh published on 5th November 2020. Patients received steroids and antibiotics as per national treatment protocol. After collecting all the information required for the study data were collated by using Microsoft Excel 2007 spreadsheet and result was expressed in percentage.

Results:

A total of 345 COVID 19 positive patients who started antibiotics and corticosteroids from day of admission in the hospital were included in the study. Male patients 185 (53.62%) were more than female patients 160 (46.37%). Most of them were in the age group between 41 to 60 years 148 (42.89%). Hypertension (HTN) was most common coexistent disease 132 (38.26%) followed by diabetes 105 (30.43%), ischemic heart disease 60 (17.39%), bronchial asthma 48 (13.91%). All these demographic characteristics of the study population on admission are shown in Table 1.

Table-I
Demographic characteristics of the patients

Characteristics of the patients		Number of participants n= 345	Percentages (%)
Age (Years)	<20	05	1.44%
	21-40	82	23.76%
	41-60	148	42.89%
	>60	110	31.88%
Gender	Male	185	53.62%
	Female	160	46.37%
Co-morbidities	Hypertension	132	38.26%
	Diabetes	105	30.43%
	Ischemic heart disease	60	17.39%
	Bronchial asthma	48	13.91%

Sign/symptoms of different clinical categories of COVID 19 (mild, moderate, severe and critical) are showed in Table 2 where severity margin of the patient is identified by following our national guideline.

Table-II
Severity margin of the patients according to national guideline of Bangladesh.

Severity margin	Sign and Symptoms
a) Mild cases	<ul style="list-style-type: none"> The clinical symptoms are mild, and there is no sign of pneumonia on imaging. Symptoms may be: fever, cough, sore throat, malaise, headache, muscle pain without shortness of breath or abnormal imaging
b) Moderate cases	<ul style="list-style-type: none"> Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia. Respiratory distress with < 30 breaths /min Pulse oxymetry showing saturation > 90% at ambient air
c) Severe cases	<ul style="list-style-type: none"> Respiratory distress (≥ 30 breaths/ min) Finger oxygen saturation $\leq 90\%$ at rest Arterial partial pressure of oxygen (PaO₂)/fraction of inspired oxygen (FiO₂)≤ 300mmHg (1mmHg=0.133kPa)
d) Critical cases	<ul style="list-style-type: none"> Respiratory failure and requiring mechanical ventilation Shock With other organ failure that requires ICU care.

Out of 345 admitted patients in the hospital, 98 patients were treated as a mild case(28.40%), 136 patients as moderate(39.42%), 85 patients as severe(24.63%), and 26 patients treated as critical case (7.53%) which is showed in Figure 1.

Table III showed the distribution of different antibiotics in various categories of COVID 19 patients. Most frequently prescribed antibiotic in all categories of the patients was moxifloxacin. All severe (100%) and critical (100%) patients received this drug. On the other hand, moderate 125 (91.91%) and mild 86 (87.75%) cases also prescribed moxifloxacin. No

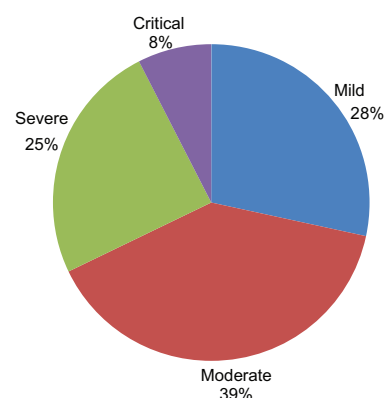


Fig.-1: Percentages of the patients on different clinical categories of COVID 19

Table III
Distribution of antibiotics in different categories of COVID 19 patients

Antibiotics	Mild n= 98	Moderate n= 136	Severe n= 85	Critical n= 26
Moxifloxacin	86 (87.75%)	125 (91.91%)	85 (100%)	26 (100%)
Meropenem	Nil	118 (86.76%)	85 (100%)	26 (100%)
Amoxicillin+ Clavulanic acid	68 (69.38%)	74 (54.41%)	Nil	Nil
Ceftriaxon	12 (12.24%)	56 (41.17%)	30 (35.29%)	17 (65.38%)
Piperacillin+Tazobactam	16 (16.32%)	28 (20.58%)	Nil	Nil
Linezolid	Nil	18 (13.23%)	20 (23.52%)	13 (50%)

mild cases received meropenem where moderate cases 118 (86.76%) and all severe (100%) and critical (100%) cases received meropenem. Another antibiotic ceftriaxon was prescribed in all categories of the patients with different percentages. Combination of antibiotics includes amoxicillin and clavulanic acid and piperacillin and tazobactam were prescribed in mild and moderate cases. Among these two combinations, amoxicillin and clavulanic acid was prescribed more. Mild 68(69.38%) cases and moderate 74 (54.41%) cases received amoxicillin and clavulanic acid combination. Piperacillin and tazobactam combination was used in mild and moderate cases with fewer percentages. 50% of the critical patients got another antibiotic named linezolid which was also prescribed in moderate and severe cases with lowest percentages.

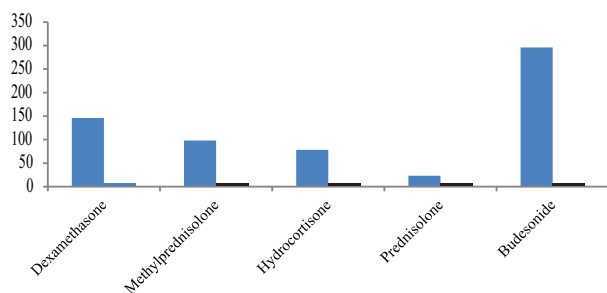


Fig.-2: *Distribution of steroids in different categories of COVID 19 patients*

Among different groups of systemic steroids, dexamethasone used in the highest percentage 146(42.31%) followed by methylprednisolone 98 (28.40%), hydrocortisone 78 (22.60%),

prednisolone 23 (6.66%). Budesonide was used commonly in the form of nebulization 296 (85.79%). This feature is shown in Figure 2.

Discussion:

This is an observational prospective type of study where total 345 patients received antibiotics and corticosteroids were recruited. Male patients 185 (53.62%) were received the drugs more than female patients 160 (46.37%). Similar findings is also found with other studies.^{4,8,16-18} Most of them were in the age group between 40 to 60 years 148 (42.89%) which is consistent with other studies done by B.J. Langford et al. , Veronese et al., Vijay et al. ^{1,17,18} A larger proportion of the recruited patients had higher rates of pre-existing co-morbidities along with COVID 19. The most common co-morbidities were hypertension 132 (38.26%) followed by diabetes 105 (30.43%), ischemic heart diseases 60 (17.39%), bronchial asthma 48 (13.91%). It is concomitant with other studies done by B.J. Langford et al., Mustafa et al., Calderon-Parra J et al., H. Alkofide et al., Bahl et al., M.Chedid et al.,^{1,2,4,12,16,19} Different clinical categories of the patient are divided into four groups (mild, moderate, severe and critical) based on severity by following our national guideline.²⁰ Patients are in mild group 98 (28.40%), moderate 136 (39.42%), severe 85 (24.63%) and critical group 26 (7.53%) who received antibiotics and corticosteroids. Patients were managed following our current guidelines.

Antimicrobial agents have been typically used empirically rather than diagnosed infection

because it is difficult to find out the actual bacterial super infections on the basis of signs and symptoms only. A study In China, data review from COVID-19 cases found that more than 70% of the patients received antimicrobial therapy, while less than 10% on an average had bacterial or fungal superinfection or coinfections.¹⁸ Antibiotic therapy has shown positive therapeutic outcomes in different clinical studies such as Hendaus et al., Guan et al., Huang et al., Chen et al.^{6,21-23} Almost all the admitted patients received antibiotics. Many of them got more than one antibiotic. Consumption rate of moxifloxacin was more than other antibiotics in all different clinical groups such as mild (87.75%), moderate (91.91%), severe (100%) and critical (100%). This fluoroquinolones (e.g. moxifloxacin) were most commonly prescribed in other studies also.^{1,2,4,19} Meropenem was second most common antibiotic prescribed in moderate (86.76%), severe (100%) and critical (100%) cases in our study followed by amoxicillin-clavulanic acid combination used in mild (69.38%) and moderate (54.41%) cases only. Ceftriaxon is the 3rd generation cephalosporin prescribed in all clinical groups with certain percentages. Use of 3rd generation cephalosporin (16.06%) was also found in another study done by Vijay et al.¹⁸ In our study additionally some antibiotics used in the lowest percentage like piperacillin-tazobactam combination used in mild (16.32%) and moderate groups (20.58%) where linezolid used in moderate (13.23%), severe (23.52%), and critical groups (50%). We found the use of Beta-lactams/beta-lactamase inhibitors, cephalosporins, linezolid, macrolides, glycopeptides, co-trimoxazole, tetracyclines etc in other clinical studies also with different percentage value.^{1,2,4,10,19} Hendaus et al., Huang C. et al., Chen et al., showed cephalosporins, carbapenems, and quinolones are good initial choices for COVID-19 patients.^{6,22,23} Notably, in this study, the frequently prescribed antibiotics are all broad-spectrum antibiotics. As such, antibiotic prescribing is significantly higher than the prevalence of bacterial co-infection. Thereby excess use of antibiotic prescriptions may tend

to increase the risk of adverse effects, and antimicrobial resistance.²⁴ Recently the World Health Organization has been changed in its guidelines regarding inappropriate use of antibiotics during the pandemic and discouraging empirical antibiotics in COVID-19.^{24,25}

All the enrolled patients in our study received corticosteroids in different doses formulations. Budesonide 296 (85.79%) was the most common corticosteroid administered in the form of nebulization followed by systemic steroids includes parenteral dexamethasone 146 (42.31%), methylprednisolone 98 (28.40%), hydrocortisone 78 (22.60%) and oral prednisolone 23 (6.66%). Another studies showed the uses of corticosteroids in varying percentages.^{15,26} Sahilu et al. revealed , the initial clinical trial results from the United Kingdom (UK) showed that dexamethasone, can be life saving for critically ill patients with COVID-19.²⁶ The WHO currently recommends against the routine use of corticosteroids in the treatment of patients with COVID-19, due to its beneficial effects for delayed viral clearance and other adverse effects such as avascular necrosis and psychosis.²⁷ Systemic corticosteroids supplementation has proved their role in lowering the circulating levels of proinflammatory mediators thus enhancing resolution of lung and systemic inflammation.^{17,26} In some studies, early use of steroids along with antiviral and broad-spectrum antibiotics showed the best result in SARS-CoV-1 but not in MERS-CoV infections.²⁸ Among the corticosteroids used in COVID-19, methylprednisolone is a short/intermediate acting glucocorticoid, while dexamethasone is a long acting steroid with steroid induced hyperglycemia lasting for more than 24 h after the last dose, with a minimal fall after an overnight fast. So all the physician must be careful about the expected worsening of hyperglycemia with the use of corticosteroids in patients with COVID-19 and should take necessary steps to prevent the adverse situation.

Although quality assessment was applied in this study, there were some limitations. Due to time constrain, therapeutic efficacy and safety can't

be measured. Adverse effects of these two categories of drug are not monitored. A follow up of 28 days was not done which might cover disease progression status. So thereby a further evidence based study is recommended to mitigate these study limitations to provide the safest therapeutic strategy for our future patients.

Conclusion:

As our study aimed to assess the use of antibiotics and corticosteroids, we found fluoroquinolones, beta-lactams, cephalosporin among antibiotics and budesonide in the form of nebulization and systemic dexamethasone, methylprednisolone among corticosteroids were the mainstream prescribed drugs to fight against the different clinical categories of admitted COVID-19 patients. We concluded our study by addressing a recommendation for long term studies which should be needed to assess the impact of the increase in antibiotic use during COVID-19 pandemic on the hospital flora and to mitigate antimicrobial resistance.

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Conflict of Interest:

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

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