Treatment Of COVID-19 In Pakistan --- Old Stratagem For New Challenges: A Multicentered Study In Pakistan

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Abstract-

Introduction: The current outbreak of COVID-19 originated in December 2019 in the city of Wuhan, China. Since no specific treatment is currently available, therefore, only isolation along with symptomatic care and oxygen therapy can prove to be fruitful. The study aims to search for possible supportive and therapeutic measures that might not be new till the development of specific treatment as the development of new drugs or potential vaccine will take time so, in the meantime, we must confide in the curative properties of already developed drugs and/or naturopathy.

Material and Methods: This Cross-sectional study was conducted in the month of April 2020 including 353 confirmed cases of COVID-19 from eight different hospitals of Pakistan. Data was collected through selfdesigned questionnaires. The analysis was done on SPSS V.21.

Results: According to study results different treatment regimens used include chloroquine, hydroxychloroquine, azithromycin, hydration, oxygen therapy, lemon syrup, and antipyretics. Lemon syrup, hydroxychloroquine, and azithromycin had effective ratios of 100, 93, and 75 respectively.

Conclusion: The most effective treatment was the combination of hydroxychloroquine and azithromycin with the recovery rate of 97%.

Keywords: COVID-19 treatment; drugs effective for COVID-19; treatment strategy for COVID-19 in Pakistan.

I. INTRODUCTION:

The current outbreak of COVID-19, cause of which was later identified as coronavirus originated in December 2019 in the city of Wuhan, China, [1]. With its rapid spread all over the world, the WHO declared COVID-19 as a pandemic on March 12th, 2020, [2]. As a respiratory infectious disease, COVID-19 spreads mainly by respiratory droplets, respiratory secretions, and also through direct contact,[3]. While, initial data suggests that this virus has an incubation period of three to seven days,[4]. These findings are based on limited data of patients, that too of an emerging pandemic. This disease presents itself with a wide range of diverse clinical symptoms ranging from asymptomatic patients to septic shock and multiorgan failure,[5]. The most common symptoms include fever, fatigue, and dry cough,[6]. Since no specific anti-viral medication or vaccine is currently available, therefore, current management relies on isolation along with symptomatic care and oxygen therapy. No specific treatment for COVID-19 has been found. Only supportive therapeutic strategies are being used for infections and mainly the focus has been on prevention of transmission,[5]. Studies suggest that the management of patients with mild infection involves only supportive care including oxygen therapy, nutritional supplements, and acetaminophen. On the other hand, severe and critical patients are dealt with using high flow oxygen, convalescent plasma, and organ function support, Certain medications including [5,6]. hydroxychloroquine (an analogue of chloroquine) are being studied and used to possibly treat Covid-19 patients. The clinical safety profile of hydroxychloroquine is better than that of chloroquine and has relatively lesser concerns regarding drugdrug interactions, [7,8].

The emergency that the world faces today demands that we develop urgent and effective, protective as well as therapeutic measures. If not so, governments will not be able to minimize both, deaths from COVID-19 and the economic impact of viral spread. Hence, this study aims to search for possible supportive and therapeutic measures that might not be new to the world of science. The development of new drugs or potential vaccine will take time so, in the meantime, we must confide in the curative properties of already developed drugs and/or naturopathy.

II. MATERIALS AND METHODS:

A. Study design:

This descriptive, cross-sectional study was conducted in April 2020, during which 353 confirmed cases of COVID-19 from eight different hospitals of Pakistan i.e. Sheikh Zayed Hospital, Rahim Yar Khan, Civil Hospital, Bahawalpur, Jinnah Hospital, Lahore, Nishtar Hospital, Multan, Agha Khan University Hospital, Karachi, District Head Quarters Hospital, Peshawar, Sheikh Zayed Hospital, Quetta, and RHC Aga Khan, Gilgit Baltistan were included in the study population. Data was collected using a self-designed structured questionnaire distributed to doctors of

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above-mentioned hospitals with a response rate of 100%.

B. Data Analysis:

A descriptive analysis of the study variables was performed using SPSS v.21.0. Data were normally distributed. Cronbach's alpha of the questionnaire was calculated for 80 responses to assess its reliability in our population. It was 0.818 indicating high inter-scale reliability. Effect ratio was used to check the efficacy rate of each treatment. A graph was designed using MS Excel.

III. RESULTS

Data was collected from 8 different hospitals of Pakistan including four hospitals from Punjab, one from Sindh, one from Khyber Pakhtunkhwa, one from Baluchistan and one from Gilgit Baltistan. The total positive cases of COVID-19 in these hospitals were 353 till 20th April 2020. 167 patients had a travel history of the pandemic area. The recovery rate is 92.46% while the death rate is7.54% for 199 closed cases as shown in fig 1 and table I below:



Fig 1: Primary and secondary cases.

Table I: Frequency

Total cases	353
Recovered cases	184
Deaths reported	15

The data of individual hospitals showed that by far the most effective drug regimen was a combination of chloroquine and azithromycin. Rest of the data is given in Table 2 below along with the treatment: **Table II:** Complete data of individual hospitals

		Cases			
Hospital	Total positive cases	with travel	Cases recovered	Deaths reported	Treatment given
Sheikh Zayed Hospital, Rahim Yar Khan	25	15	05	02	Chloroquine
Civil Hospital, Bahawalpur	42	37	09	03	Chloroquine, Azithromycin, Paracetamol
Jinnah Hospital, Lahore	100	20	97	03	Hydroxychloroquine and Azithromycin.
Nishtar Hospital, Multan	35	08	20	01	No treatment
Agha Khan University Hospital, Karachi	100	60	30	04	Treatment for lung infections, increased immunity
District Head Quarters Hospital, Peshawar	15	12	10	00	Hydroxychloroquine
Sheikh Zayed Hospital, Quetta	25	08	02	02	Good hydration and oxygenation 02 patients who recovered were using lemon syrup
RHC Aga Khan, Gilgit Baltistan	11	07	11	00	Hydration and antipyretics

The efficacy rate of each treatment was calculated using the effect ratio formula i.e. total no of the recovered patient taking that drug/ total no of patients taking that drug * 100 on SPSS V.21. the most effective therapy was lemon syrup; hydroxychloroquine and azithromycin being next to it respectively. The details of the results are shown in Table III below.

Table III: Efficacy rate of each treatment

Therapy/Treatment given	Total no. of patients who were given therapy	Total no. of patients taking therapy and got better	Effect ratio
Chloroquine	67	14	21
Azithromycin	142	106	75
Hydration	36	13	36
Oxygenation	25	2	8
Lemon syrup	2	2	100
Hydroxychloroquine	115	107	93

IV. DISCUSSION:

In the current study, a total of 353 cases from eight different hospitals in Pakistan were included. All the patients showed positive results on PCR based COVID-19 testing. The current study shows a total of 167 patients out of 353 (47.3%) had travel history from an epidemic area which shows potent transmission capability of the virus which is transmitted through large droplets generated during coughing and sneezing by symptomatic as well as asymptomatic patients. Infection is acquired either by inhalation of these droplets within one meter of a person who has COVID-19 or touching surfaces contaminated by them and then touching the nose, mouth, and eyes,[9]. Safety measures, such as face masks and other personal protective equipment are recommended for prevention.

According to the current study, the recovery rate is 92.46% while the death rate is7.54% for 199 closed cases. This result is by the overall data of Pakistan showing similar recovery (92%) and death rate (8%),[10]. China shows a recovery rate of 94% and a death rate of 6% both of which are more than the results shown in the current study,[11]. However, the results in Italy and Spain demonstrate variation displaying a lower recovery rate, 70%, and 80% respectively, but greater death rates, 30%, and 20%, [12,13].

Treatment for COVID-19 is essentially symptomatic and supportive. The eight hospitals included in the study utilized various methods for treatment including the use of antipyretics, hydration, hydroxychloroquine, chloroquine. oxygenation, antibiotics such as azithromycin, and lemon syrup. Treatment principles include maintaining hydration and nutrition and controlling fever and cough,[14]. Two hospitals, Sheikh Zayed Hospital Quetta and RHC Aga Khan Gilgit Baltistan gave only symptomatic treatment showing an effective ratio of about 36% for hydration and 8% for oxygenation therapy. Oxygenation includes the delivery of oxygen through, face masks, nasal cannulas, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation. In a case series of 99 hospitalized patients with COVID-19 infection from Wuhan, oxygen was given to 76% and antibiotics to 71%,[15]. Another study by Li et al. shows a mortality of 50% with Extracorporeal membrane rate oxygenation,[16]. This shows that oxygenation therapy is somewhat effective but it should be provided on time for effective patient management.

Fever is the most common symptom in COVID-19 patients and is being treated with antipyretics, acetaminophen is the most common and is being used as a first-line antipyretic,[17]. Chloroquine, being used in two of the eight hospitals, shows a 21% effect ratio. It is an antimalarial agent that inhibits pH-dependent replication in viruses and was found to be effective in SARS-CoV2 infection, [18,19]. In 2020, Gao et al. studied the effect of chloroquine and hydroxychloroquine in the treatment of COVID-19 in over 100 patients, showing that chloroquine

phosphate is effective in preventing the exacerbations of pneumonia and shortening the disease course depicting that chloroquine is somewhat effective for the treatment of COVID-19,[20]. The results of the current study also show the effectiveness of hydroxychloroquine, which is being used in two of eight hospitals included in the study with the effect ratio of 93%. Another clinical trial found that hydroxychloroquine has higher potency at inhibiting the SARS-CoV2 virus. The suggested dosing from this study was an oral dose of hydroxychloroquine 400 mg BD for the first day and then 200 mg BD for the following four days,[8]. The use of hydroxychloroquine with azithromycin in Jinnah Hospital, Lahore shows a 97% recovery rate which is the highest rate among all the treatment modalities making this significant treatment method against COVID-19. A study by Gautret et al. on French confirmed COVID-19 patients depicts similar results showing substantial association of hydroxychloroquine with viral load reduction in COVID-19 patients and reinforcement of its effect by azithromycin,[21]. Another study further depicts the role of azithromycin for the prevention of severe respiratory tract infections when administrated to patients suffering from a viral infection, [22]. In Sheikh Zayed hospital Quetta, lemon syrup along with hydration and oxygenation was found to be effective for the two patients taking it. This depicts a positive relationship between the use of lemon svrup and the recovery of patients. The results do not show how this mechanism occurs and the researchers could not find any other study depicting this effect. Further studies are needed to determine the effect of lemon syrup.

Corticosteroids and antivirals have not been used in any of the eight hospitals but various other researches describe their use in COVID-19 infection. According to Lei et al., the treatment of 51 COVID-19 patients with traditional Chinese medicine, interferon, Lopinavir, Ritonavir, and short-term corticosteroids was effective and resulted in the recovery of 50 patients,[23]. On the other hand, while studying 416 COVID-19 patients, Shang et al. reported that globulin corticosteroid therapy and gamma administration had prolonged hospitalization and increased mortality, [24]. These two studies show a questionable relationship in the use of corticosteroid treatment for COVID-19 infection. In the antiviral treatment of hospitalized adult patients with severe Covid-19, no benefit was observed with lopinavirritonavir treatment showing that treatment with only antiviral agents shows no notable effect, [25]. But the combination treatment of antiviral agents with other medications depicts a prominent response as depicted in a study by Lei et al,[23].

The limitations of our study include the nonavailability of individual patient data and limited longterm outcome follow-up. The strength of our study is that it provides information regarding various treatment regimens being used in different setups and their effect ratio. It also opens the door for further research on how various therapies are related to COVID-19 treatment.

A total of 353 cases of COVID-19 have been reported in the above-mentioned hospitals of Pakistan till 20th April 2020, out of which 47.3% had a travel history of the epidemic area showing that the rest of 52.7% cases were secondary cases. Out of 199 closed cases, 92.46% recovered from the disease while only 7.54% died due to COVID-19. Different strategies were used in different setups including hydroxychloroquine, chloroquine. azithromvcin. hydration, oxygen therapy, and antipyretics mainly. While two patients in Quetta who got recovered from the disease were found using lemon syrup along with good hydration and oxygenation which was being administered to all the patients showing that lemon syrup somehow is effective (with the effect ratio of 100); however, further researches are required to exactly know the efficacy and role of lemon syrup in COVID-19 treatment. In Nishtar Hospital, Multan no specific treatment or therapy was given to the patients. Drugs that were used in most of the cases in different settings include azithromycin, hydroxychloroquine, and chloroquine with effective ratios of 75, 93, and 21 respectively. The most effective treatment was the combination of hydroxychloroquine and azithromycin which was used in Jinnah hospital Lahore with a 97% recovery rate.

I. RECOMMENDATIONS

The current study reports various treatment modalities used in different hospitals all over Pakistan and their efficacies. We would like to recommend that patients COVID-19 be treated with hydroxychloroquine and azithromycin to cure the infection limiting the spread of COVID-19 in the world until the development of a new drug. The lemon syrup can also be used in patients as it is a natural product having no side effects and results in the recovery of patients. Further works are needed to determine if these compounds could be useful as chemoprophylaxis.

II. ACKNOWLEDGEMENT

None

III. CONFLICTS OF INTEREST

The authors declare no conflict of interest.

IV. References

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