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Complete Recovery of 94 Vaccinated and Non-Vaccinated Cases from COVID-19 Treated at Home with Favipiravir, Dexamethasone, Antibiotics, and Other Supportive Medicines and Care

Asoke Kumar Roy[1], Dipanwita Ghosh[2], Avirup Roy[3], Subir Mitra[4], Nikhilesh Mitra[5] & Swapan Karmakar[6]

[1] Ex-Head, Dept. of Pathology and Cancer Screening, Chittaranjan National Cancer Institute, West Bengal, India

[2] Ex-Research Fellow, Dept. of Pathology and Cancer Screening, Chittaranjan National Cancer Institute, West Bengal, India

[3] Ex-House Physician, Institute of Medicine and Sagar Dutta Hospital, West Bengal, India

[4] Ex-Colonel, Indian Arm Force, West Bengal, India

[5] Ex-Supervisor, Ministry of Defense, Govt. of India, West Bengal, India

[6] Teacher, Boral High School, West Bengal, India

Correspondence: Asoke Kumar Roy, Ex-Head, Dept. of Pathology and Cancer Screening, Chittaranjan National Cancer Institute, West Bengal, India.

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Abstract

Objective: In 2002-2003 an extraordinary outbreak of coronavirus infection known as Severe Acute Respiratory Syndrome Corona virus or SARS CoV infection occurred in south China and eventually spread in 28 countries around the world with 8096 cases. In December 2019, Corona virus infected disease 19 or COVID-19 or SARS CoV-2 first occurred in Wuhan, South China and rapidly spread all over the world. All the leading viral disease research group and clinical Institutions have been trying hard to find an effective antiviral regime to curve the COVID-19 mortality and morbidity. The preventive vaccinations for COVID-19 are in vogue with mixed response. The objective of this study was to provide treatment for COVID-19 cases at home at the earliest with proper selection and combination of medicines to stop the mortality, morbidity and heavy hospital expenditure. ***Methods:*** All the study cases were from Kolkata, India. Considering infectivity and mortality of SARSCoV-2, primarily all the clinical history including clinical data of the cases were collected through mobile media (smart phone). The accumulated data had been recorded in history sheets which were finally completed after the recovery of the cases by personal interview or interview of the family members in case of death. The majority cases were diagnosed by RT-PCR and rest by Rapid antigen test or by symptoms. The study could be labelled as an open label study considering all the facts and figures and outcome involved in the study design of this clinical research. This study included 123 COVID-19 cases, at an age range, 10-85 Years (mean age 48·66±17·69; median age 51 years). Out of these cases, 94 cases between 22-85 years (mean age 50·44±16·83; median age 53years) were selected for home treatment up to 2 weeks with our formulated protocol consisting of Favipiravir, Dexamethasone Antibiotics (Azithromycin/ Clarithromycin or Doxycycline), Pantoprazole and Doxophylline. Out of 94 cases only two cases had experienced little fall of oxygen saturation and treated with oxygen at home and Doxophylline. All the 94 cases treated with the protocol completely recovered after two weeks without any residual symptoms. The rest 29 cases, treated outside in hospitals or clinics and designated as external cases were used for comparison. ***Results:*** Out of total of 29 COVID-19 external cases, 25 cases had taken ivermectin for COVID-19 treatment of which 19 cases recovered with various post COVID symptoms. Six cases were unresponsive to ivermectin and were admitted to hospital and out of them one patient expired. All the 94 cases,

treated at home by our protocol, had recovered completely from the disease without any residual symptoms and the recovery period was shortened. we found that, our formulated protocol for COVID-19 was an absolute success. ***Conclusion:*** From the study it is concluded that COVID-19 cases can be treated effectively at home without any casualty provided that the cases are diagnosed and treated with proper medicines at the earliest.

Keywords: COVID-19, home treatment, Favipiravir, Dexamethasone, Antibiotics

1. Introduction

All over the world people fall victim to an ultramicroscopic organism, namely Severe Acute Respiratory Syndrome Coronavirus -2 or SARSCoV-2. The coronavirus, a Ribonucleic Acid (RNA) Virus was first identified in 1960 and infects both humans and animals. (Pebody R, Zambon M & Watson JM., 2013) The animal coronaviruses are divided into 4 genera and the human coronaviruses (HCoVs) fall into 2 genera, Alpha coronavirus and Beta coronavirus. SARS-CoV and MERS-CoV (Middle East Respiratory Syndrome Coronavirus) are both Beta coronavirus. (Dennis L. Kasper & Anthony S. Fauci, 2018) In the wild, horse-shoe bat is the natural reservoir of SARS-CoV and camel is the natural reservoir of MERS-CoV, and both the SARS-CoV and MERS-CoV infection can be regarded as zoonotic disease. (Dennis L. Kasper & Anthony S. Fauci, 2018; Drosten C, Kellam P & Memish ZA., 2014)

The SARS-CoV outbreak (2002-2003) around Guangdong province of South China killed 774 and infected 8096 and the fatality rate was 9·6%. (Wong G, Liu W, Liu Y, Zhou B, Bi Y & Gao GF., 2015)

On 30th January 2020, WHO declared this novel coronavirus SARS-CoV-2 outbreak, a public health emergency of International concern (PHEIC). Till date, worldwide, 605,180,732 have been infected by COVID-19 and 6,486,169 died from it. (Worldometer)

The SARS-CoV-2 is the largest single stranded, enveloped, positive sense 30 Kb RNA virus. It binds to ACE-2 receptors on the surface of the target cell by spike protein (S-protein). (Chen N, Zhou M, Dong X, et al., 2020) The receptor binding domain of the S_1 subunit interacts with peptidase domain of ACE-2 receptors and is instrumental in recognition, binding and mediating the fusion of the virus envelope with the cell membrane. (Lu G, Wang Q & Gao GF, 2015; Kiran Panesar, 2021) The host cell cleavage action is mediated by the transmembrane protease serine sub family member – 2 (TMPRSS2). (Chen N, Zhou M, Dong X, et al., 2020; Hoffmann M, Kleine-Weber H, Schroeder S, et al., 2020) After the enzymatic cleavages the viral genome enters into the host cell. (Chen N, Zhou M, Dong X, et al., 2020) Throughout the respiratory tract the ACE receptors are found on the epithelial cells.

After an average incubation period of 1 - 14 days COVID-19 cases present with symptoms such as fever, dry cough, weakness, malaise, myalgia, headache and diarrhoea. (Dennis L. Kasper & Anthony S. Fauci, 2018) In the second week few cases with primary symptoms progress further with dyspnoea and the pulmonary function deteriorates and in severe cases lung function further deteriorates to frank Acute Respiratory Distress Syndrome (ARDS) accompanied by multi organ failure. (Dennis L. Kasper & Anthony S. Fauci, 2018)

Many medicines, some are age old drugs have been used for COVID-19 treatment. (López-Medina E, López P, Hurtado IC, et al., 2021; Cavalcanti AB, Zampieri FG, Rosa RG, et al., 2020) However, the case fatality rate could not be lowered and consequently there is an urgent need for proper antiviral medicines and treatment protocol to resist the SARS-Cov-2 onslaught.

For the acute need, a protocol was made by our team in consultation with text books of Medicine and scientific publications.

2. Methods

2.1 Source of Study Population

Formation of a Team: Considering, gravity of COVID-19 infection, a team of volunteers of six were made consisting of two Physicians, one Scientist, one Retired Army Officer, one Lawyer and one school Teacher.

Treatment protocol formulation: A treatment protocol was formed containing Favipiravir (DCGI, approved on 19.06.2020), Dexamethasone, a Proton Pump inhibitor and Antibiotics (Azithromycin/Clarithromycin or Doxycycline). Doxophylline was added to the regime to combat respiratory distress. (Dennis L. Kasper & Anthony S. Fauci, 2018; Du YX & Chen XP., 2020; Cai Q, Yang M, Liu D, et al., 2020; K.D. Tripathi, 2013; Maxine A. Papadakis, Stephen J. McPhee & Michael W. Rabow, 2019).

The protocol in detail is mentioned below.

Table 1.

Name of Medicines	Day 1 and dose	Day 2 to Day (10-14)

T. Favipiravir	3600 mg x two divided doses	1600 mg x two divided doses
T. Dexamethasone	3 mg x three divided doses after meal	Same as Day 1
T. Pantoprazole	40 mg x daily in empty stomach	Same as Day 1
T. Azithromycin or Clarithromycin Cap. Doxycycline	Azithromycin – 500 mg daily Or Clarithromycin (500 mg) x twice daily x day 1 or Doxycycline (100 mg) 1 such x twice daily	From 2nd day to 5th day Same as day 1. From 2nd day to 5th day,250 mg x twice daily Up to 5th day same as day 1
T. Doxophylline	Doxophylline-400 mgx twice daily if there is respiratory distress	Same as Day 1 up to 5th day

3. Case Definition

According to WHO guidelines SARS-CoV-2 cases were confirmed by two RT-PCR reports from two different laboratories or two different specimens collected from same person.

Study Design: Open label study with COVID-19 cases.

4. Case Selection

All treated cases (internal cases) and those cases treated outside (external cases) contacted us through mobile phone and/or video conference for consultation.

Through, smart phone patients were advised to do RT-PCR/Rapid Antigen test for COVID -19 at the earliest.

5. Treatment Support

For all the 94 internal cases of COVID-19, medicines were given as per our protocol and supplied at the residence of the cases.

A monitoring cell was formed to provide medical and other social help round the clock. Facility for oxygen therapy at home was also arranged.

6. Epidemiological Explanation and Laboratory Investigations

Clinically suspected cases of SARS-CoV-2 infection, patient's primary investigations were conducted through smart phone media using standard questionnaire such as exposure history, clinical history, family history of COVID-19 cases and laboratory investigations. The clinically suspected SARS-CoV-2 infection the respiratory samples were collected from home and the reports were made by RT-PCR confirmation or Rapid Antigen test by ICMR recognised laboratories.

In all cases, after recovery from COVID-19, written consent was taken for publication of the data.

7. Statistical Analysis

Statistical Analysis was performed with the help of Epi Info (TM) 7.2.2.2. EPI INFO is a trademark of the Centres for Disease Control and Prevention (CDC). Descriptive statistical analyses were performed to calculate the means with corresponding standard deviations (s.d.). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (χ^2) test was performed to find the associations. In the cases where one of the cell frequencies were less than 5 corrected Chi-square (χ^2) was used to find the association between variables. $p<0{\cdot}05$ was taken to be statistically significant.

8. Results

123 cases of COVID-19 with range 10 – 85 years, mean age 48·66 ± 17·69 years and the median age 51 years were included in the study. COVID 19 was prevalent in the age group of 50 years and above (51·22%). Out of these 123 cases, 56 (45·53%) were female and 67 (54·47%) were male cases.

The most common presenting symptom was fever 111 cases (90·24%), of which 107 (86·99%) had fever as their first presenting symptom ($p < 0{\cdot}00001$). Other significant presenting symptoms are Loss of smell 98 cases (79·67%), Weakness (72·36%) and Loss of Taste 82 cases (66·67%) ($p <0{\cdot}00001$). (Figure 1 and Figure 2)

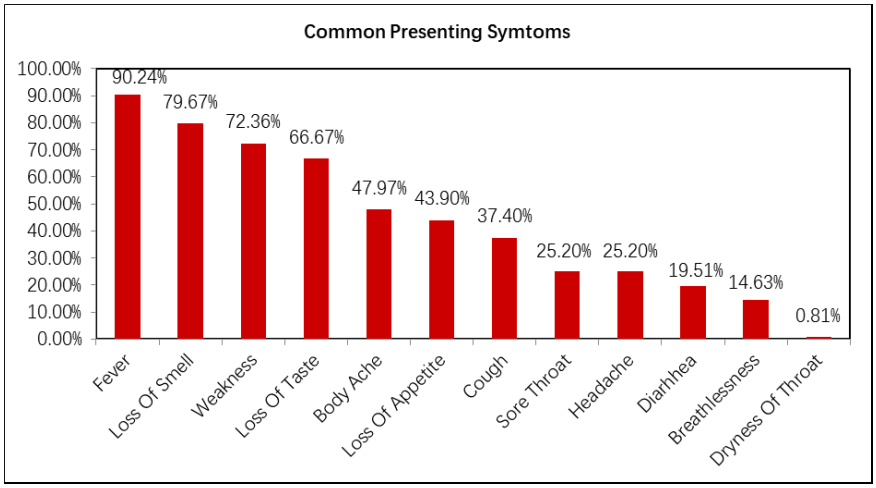

Figure 1. Bar Diagram showing Common Presenting Symptoms of COVID-19

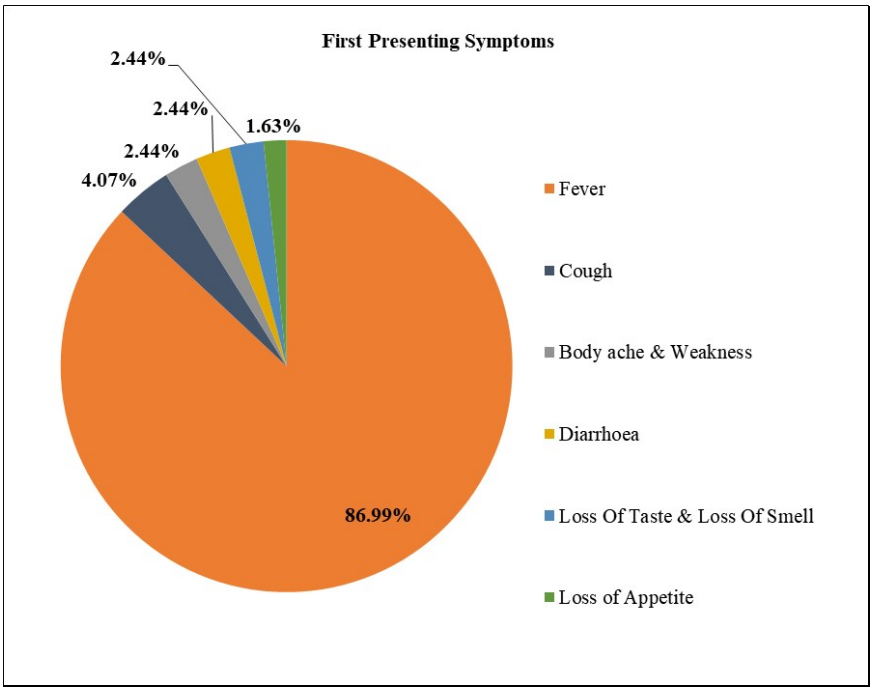

Figure 2. Pie Chart showing the First Presenting Symptoms of COVID-19

In more than 50% of the cases of loss of smell and taste appeared after 3 days of infection (50·77% and 54·39% respectively). 80 cases (65·04%) lost both smell and taste sensation at once after having the infection and was significant (p <0·00001). (Figure 3)

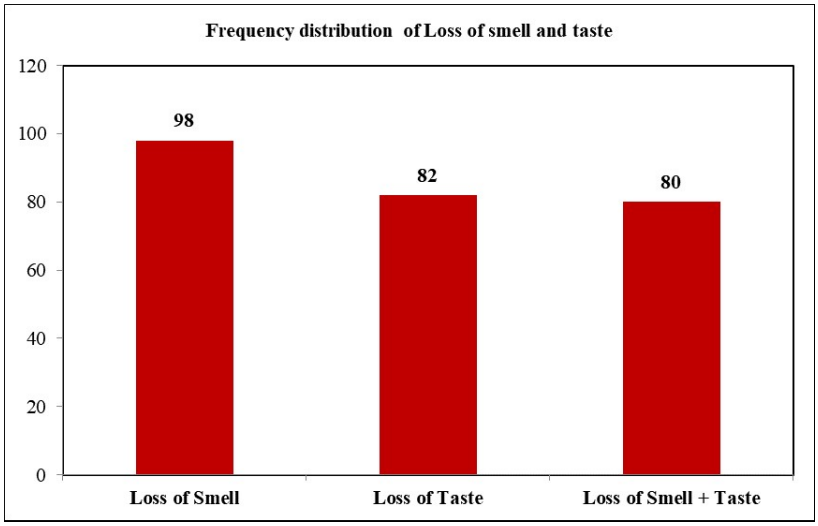

Figure 3. Bar Diagram showing Frequency Distribution Loss of smell and Loss of taste

Out of 123 cases, 120 (97·56%) cases tested for COVID-19 and the rest 3 cases were diagnosed symptomatically (had first four common symptoms of COVID-19). Of these 120 cases, 113 (94·17%) cases had done RT-PCR and remaining 7 cases (5.83%) had done Rapid Antigen Test for COVID-19 for confirmation. 107 (89·17%) cases were positive for COVID-19.

The mean and median time between symptom onset and positive test confirming SARS-COV-2 infection were 3.35 ± 3.35 and 2 days respectively.

The mean and median time between symptom onset and beginning of treatment were 4.49 ± 4.43 and 3 days respectively.

It was observed that out of 123 cases, 80 cases (65·04%) had at least one to three family members infected with COVID-19 at the same time. It was also observed that COVID-19 created panic and fear in 58 cases (47·15%). Co-morbidity was present in 45 cases (36·59%). 17 cases (37·79%) had hypertension and 17 (37·79%) cases had hypertension along with other co-morbidities. Thus, hypertension is one of the significant co-morbidity in cases of COVID-19 infection (p <0·00001). Frequency of the co-morbidities is represented in the Figure 4.

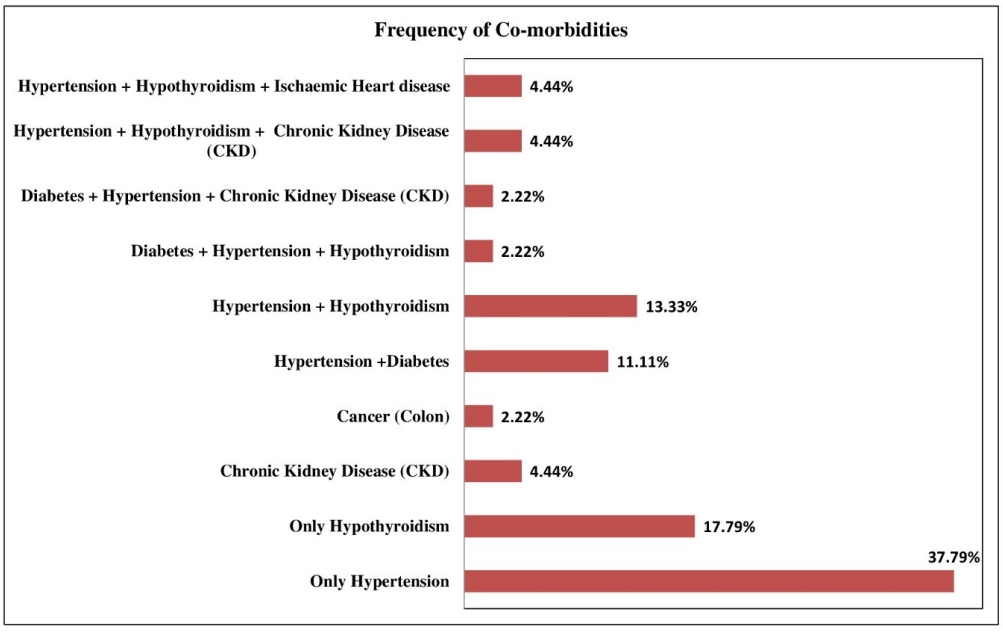

Figure 4. Bar Diagram showing Frequency Distribution of Co-morbidities

Out of 123 COVID-19 cases included in the study, 26 cases were from 2020 when vaccination for COVID-19 was not started; out of the remaining 97 cases, 38 cases (39·18%) were vaccinated for COVID-19 and out of these 38 cases 7 cases (18·42%) got infected after taking two doses of COVID-19 vaccine (Covishield).

For vaccinated patients, the median time between vaccination date and symptom onset is 22.5 days. A comparative study was done to evaluate the range of symptoms and time to symptomatic recovery in unvaccinated compared to vaccinated patients. (Table 2)

Table 2. Comparative study to see the range of symptoms and time to symptomatic recovery in unvaccinated compared to vaccinated patients

Symptomatic Recovery	Vaccinated	Unvaccinated
7 DAYS	7 (18.42%)	32 (37.65%)
10 DAYS	7 (18.42%)	16 (18.82%)
14 DAYS	5 (13.16%)	18 (21.18%)
1 MONTH OR MORE	5 (13.16%)	5 (5.88%)
LESS THAN 7 DAYS	12 (31.58%)	12 (16.47%)
21 DAYS	0 (0.00%)	1(1.18%)
1 - 4 DAYS	2 (5.26%)	1 (1.18%)
TOTAL	38	85

Out of 123 cases, 94 cases between age group 22-85 years (Mean age 50·41 ± 16·83 years; Median age 53 years) were under our standard treatment and considered as internal cases. Out of these 94 cases there were 45 females between age group 22 – 80 years (Mean age 49·07 ± 15·53 years; Median age 52 years) and 48 males between 25 – 85 years (Mean age 51·65 ± 18·02 years; Median age 55 years).

The average days between beginning of treatment and symptomatic recovery was around 7 days (35.48%)

The remaining 29 cases treated outside mostly with ivermectin (86·21%) were considered as external cases. From the comparative study between our standard treatment and external treatment it was seen that in 51·06% internal cases experienced symptomatic recovery within 7 days and only 6·38% cases took 14 days for symptomatic recovery whereas in case of external treatment 31·03% cases took more than 14 days for symptomatic recovery (Table 3)

Table 3. Comparison of Standard Treatment & External treatment for Symptomatic Recovery

	Symptomatic recovery				
	1 – 7 days	8 – 14 days	More than 14 days	Expired	Total
Standard Treatment	48	40	6	0	94
	51.06%	42.55%	6.38%	0.00%	100.00%
External Treatment	10	9	9	1	29
	34.48%	31.03%	31.03%	3.46%	100.00%

A comparative study was done between frequency of co-morbidities observed in the treatment population and the external cases. (Table 4)

Table 4. Comparison between frequency of comorbidities observed in the treatment population (Standard Treatment) and the External cases

	Co-morbidity	
Treatment	Yes	No
Standard treatment	35	59
N= 94 cases	37.23%	62.77%

External Treatment	**10**	**19**
N= 29 cases	**34.48%**	**65.52%**

Even after recovery, Chronic illness observed were respiratory distress with weakness fatigue and malaise in 9 cases (31.03%), fatigue and malaise in 8 cases (27.58%), mood change and difficulty in concentration in 4 cases (13.79%), sleeplessness in 4 cases (13.79%), feverishness (6.89%) and menstrual irregularities in 2 cases (6.89%).

Another comparative study was conducted to evaluate the effectiveness of treatment to our formulated protocol (standard treatment) with external treatment considering the Parameters like Hospitalization, Treatment failure and End point. It was observed that in case of standard treatment there was no causality or hospitalisation or treatment failure. Only 2 cases required oxygen support for a short period (moist O2 inhalation, 12 litres/min) for 4 hours for a day at home. Both the cases recovered after 5 days of starting of our treatment. However, in case of external cases, 24·14 % were hospitalized, 24·14% suffered treatment failure and turned to us with post COVID-19 complications and also there were one casualty (3·45%). (Table. 5)

Table 5. Comparison between Standard Treatment and External Treatment for Effectiveness

	Hospitalization		**Treatment Failure**		**End Point**	
Treatment	Yes	No	Yes	No	Survived	Expired
Standard treatment	0	94	0	94	94	0
N= 94 cases	0.00%	100.00%	0.00%	100.00%	100.00%	0.00%
External Treatment	7	22	7	22	28	1
N= 29 cases	24.14%	75.86%	24.14%	75.86%	96.55%	3.45%

Out of 123 cases, 39 had ivermectin for COVID-19 treatment of which 14 cases were unresponsive and shifted to our standard treatment and gradually recovered completely. 25 external cases had taken ivermectin as COVID-19 treatment out of which 19 cases responded to the treatment and recovered however, 6 cases were unresponsive and was hospitalized of which one case expired. The remaining 5 hospitalized cases recovered with hospital treatment.

9. Discussion

Since December 2019, the whole world is shattered by SARS CoV -2 or COVID-19 infection. In our study of 123 SARSCoV-2 cases, data related to age range, sex ratio, prevalence of middle age, older population, co-morbidity and presenting symptoms were almost at par with data of the patients studied by Chen N et al and Huang C et al (Chen N, Zhou M, Dong X, et al., 2020; Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al., 2020).

The studies of Chen N et al and Huang C et al and from our study it has been observed that fever is the most common symptom of SARS CoV -2 infection.

COVID-19 is a systemic disease involving all the organs of the body and the virus acts by binding with the ACE-2 receptor, present on the epithelial cell surface. ACE-2 receptor reduces the harmful action of angiotensinogen II (ANG II) and has the most important relevance to COVID-19. (Sriram Krishna S & Insel P, Loomba R., 2020) ANG II can increase inflammation and death of the cells of the alveoli which are critical for oxygen diffusion and bringing oxygen into the body.

We have also observed temporary loss of smell or taste or combined loss of smell and taste has been marked symptoms and may be considered as the indicator of the COVID-19 at the earliest.

Our observation has been supported by a previous study of the neuroscientists of Havard Medical School. (Kevin Jiang, 2020)

The Neurophysiology of anosmia in COVID-19 is unclear. (Kevin Jiang, 2020) The Sensory neurons of the olfactory nerve do not express the genes that encode ACE2 receptor protein or TMPRSS2 receptor on the contrary the structural and metabolic supporting cells around the olfactory neurons express ACE2 and TMPRSS 2 receptors encoded by corresponding gene and helps to entry of SARS CoV-2 and initiate infection and damage of these cells and may be responsible for anosmia by cutting metabolic supply line to olfactory neurons (Yang X, Yu Y, Xu J, et al., 2020).

Similarly, mechanism of loss of taste is unclear and may have link with chemosensory dysfunction and direct invasion of virus to sensory neurons via unidentified receptors.

Out of 97 cases of COVID-19, 38 cases were vaccinated for SARS CoV-2. Both vaccinated and unvaccinated cases presented with similar symptoms but the recovery period was shortened in vaccinated than unvaccinated cases. As for example, recovery period between 1- 4 days occurred in 5.26% vaccinated cases whereas it was 1.18% in unvaccinated cases. Also, the 31.58% vaccinated cases had recovery period of less than 7 days whereas it was 16.47 % in unvaccinated cases.

All the cases took Covishield vaccine for prevention of COVID-19 disease. Out of total 123 cases, 38 cases took Covishield vaccine and 7cases of them took two doses of the vaccine. Two senior Doctors, both consultant physicians, were infected after 6 months of taking the 2nd dose of Covishield vaccine. However, the protection efficacy of this adenovirus vaccine is slightly lower (70-91%) in comparison to mRNA vaccine (90-95%) (Voysey M, Clemens SAC, Madhi SA, et al., 2021; Logunov DY, Dolzhikova IV, Shcheblyakov DV, et al., 2021).

Considering the above facts linked to COVID-19 many drugs including Ivermectin and Hydroxychloroquine were introduced as an antiviral medicine with mixed response. As a result, COVID-19 related deaths could not be averted. In one study by Laing et al. (Laing R, Gillan V & Devaney E., 2017) observed that many of the underlying mechanism of ivermectin are yet to be defined, and some of this in-vitro effect of ivermectin on cells may be due toxicity of the drug. (Heidary F & Gharebaghi R., 2020)

Till date, the SARS CoV has killed over 6.3 million individuals across the world and the onslaught of it appears to be a never ending phenomenon.

On the other hand, in search of true medicines for SARSCoV-2, clinical trials are going on many antiviral agents including Remdesivir, Molnupiravir, Rivavirin, Favipiravir and protease inhibitors Lopinavir and Ritonavir. (Kiran Panesar, 2021) But out of these nucleoside analogues, Favipiravir, a pyrazine carboxamide derivative, has raised the hope of becoming most effective anti-viral agent for the COVID-19 treatment. Favipiravir inhibits viral replication by competitive inhibition of viral RNA- dependent RNA polymerase (RdRp) of RNA viruses. (Du YX & Chen XP, 2020) A clinical trial by Cai Q et al. on Favipiravir efficacy in COVID-19 in Shenzhen, China, found that the viral clearance time was significantly shorter in Favipiravir treated cases in comparison to control group. (Cai Q, Yang M, Liu D, et al., 2020) Another study by Doi et al. observed that Favipiravir administration within 1st week of SARS CoV infection substantially and rapidly clears virus from nasal secretions and also suggested that Favipiravir could be paired with Doxycycline, Azithromycin or other antivirals along with corticosteroids to prevent COVID-19 hospitalization or death in cases over 50 years or with co-morbidities. (Doi Y, Hibino M, Hase R, et al., 2020; McCullough PA., 2020)

Another publication recommends that at home, Favipiravir should immediately be used at the onset of symptoms in cases over 50 years with one or more co-morbidities along with corticosteroids. (McCullough PA, Kelly RJ, Ruocco G, et al., 2021)

In this study, Dexamethasone is included because it is a highly selective and is about 25 times more active than other corticosteroid compound (Zoorob RJ & Cender D., 1998) It has both strong anti-inflammatory and immunosuppressive effect. (Becker DE., 2013) Dexamethasone exerts anti-inflammatory effect by inhibiting pro-inflammatory gene that encodes for chemokines, cytokines (IL-1&2, IL-6, IL-8, TNF, INF-gamma, VEGF and prostaglandins), cell adhesion molecules (CAM) and the acute inflammatory molecules. (Cruz-Topete D & Cidlowski JA., 2015) Importantly, five of these cytokines are linked to SARSCoV-2 severity. (Zhong J, Tang J, Ye C & Dong L., 2020) A proton pump inhibitor, Pantoprazole, has been incorporated in this protocol to prevent steroid induced gastritis. Doxophylline, a long acting methylxanthine is included in the protocol because it does not stimulate acid secretion in comparison to other methy-xanthines and is not linked to sleep disturbances. (K.D. Tripathi, 2013)

In June 2020, immediately after availability of Favipiravir we started treatment with this regimen and it was an instant success. All the 94 cases treated at home had been symptom free within 7 days along with shortened recovery period. All the cases became RT-PCR negative after 14 days.

We have been suggesting that early diagnosis of COVID-19 cases by symptoms or by investigation is essential and should follow the immediate treatment with Favipiravir, Dexamethasone, Antibiotics, or with our protocol which can be lifesaving

10. Conclusion

We conclude that the war against COVID-19 can be easily fought and won by early detection and treatment with proper antiviral regime. The disease can also be prevented more effectively by mRNA vaccine than Adenovirus Vector borne vaccine.

Contributors

All the authors including AKR, DG, AR, SM, NM and SK contributed to either conception or design of the study, acquisition of data, or analysis and interpretation. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The corresponding author had final responsibility for the decision to submit for publication.

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We would like to acknowledge Debashis Saha of Sun for his moral support to carry out this study.

Declaration of Interests

We declare no competing interests.

Data Sharing

To guarantee the confidentiality of personal and health information, only the authors have had access to the data. The data set may be available for research upon reasonable request.

Fund Project

We have a little group of six people working for COVID-19 patients. We have no external funding.

Ethical Approval

All medicines used in the protocol were DCG, India and FDA, USA, approved and accepted by competent Authority. In all cases, after recovery from COVID-19, written consent was taken for publication of the data.

References

Pebody R, Zambon M, Watson JM. (2013). Novel coronavirus: how much of a threat? We know the questions to ask; we don't yet have many answers. *BMJ, 346*, f1301.

Dennis L. Kasper, Anthony S. Fauci, (2018). *Harrisons Infections Disease*; 3rd Edition, Indian.

Drosten C, Kellam P, Memish ZA. (2014). Evidence for camel-to-human transmission of MERS coronavirus. *N Engl J Med, 371*(14), 1359-1360.

Wong G, Liu W, Liu Y, Zhou B, Bi Y, Gao GF. (2015). MERS, SARS, and Ebola: The Role of Super-Spreaders in Infectious Disease. *Cell Host Microbe, 18*(4), 398-401.

Worldometer. https://www.worldometers.info/coronavirus/.

Chen N, Zhou M, Dong X, et al. (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet, 395*(10223), 507-513.

Lu G, Wang Q, Gao GF. (2015). Bat-to-human: spike features determining 'host jump' of coronaviruses SARS-CoV, MERS-CoV, and beyond. *Trends Microbiol., 23*(8), 468-478.

Kiran Panesar. (2021). Investigational Antivirals for Managing COVID-19. *US Pharm., 46*(2), 29-35.

Hoffmann M, Kleine-Weber H, Schroeder S, et al. (2020). SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell, 181*(2), 271-280.e8.

López-Medina E, López P, Hurtado IC, et al. (2021). Effect of Ivermectin on Time to Resolution of Symptoms Among Adults with Mild COVID-19: A Randomized Clinical Trial. *JAMA, 325*(14), 1426-1435.

Cavalcanti AB, Zampieri FG, Rosa RG, et al. (2020, November 19). Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate COVID-19, [published correction appears in N Engl J Med. 2020 Nov 19;383(21):e119]. *N Engl J Med., 383*(21), 2041-2052.

Du YX, Chen XP. (2020). Favipiravir: Pharmacokinetics and Concerns About Clinical Trials for 2019-nCoV Infection. *Clin Pharmacol Ther., 108*(2), 242-247.

Cai Q, Yang M, Liu D, et al. (2020). Experimental Treatment with Favipiravir for COVID-19: An Open-Label Control Study. *Engineering (Beijing), 6*(10), 1192-1198.

K.D. Tripathi. (2013). *Essentials of medical pharmacology*; 7th Edition.

Maxine A. Papadakis, Stephen J. McPhee, Michael W. Rabow, (2019). *Current Medical Diagnosis & Treatment, 1*, chapter 9, pp. 279.

Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. (2020). Clinical features of patient with 2019 novel coronavirus in Wuhan, China. *Lancet, 395*(10223), 497-506.

Sriram Krishna S, Insel P, Loomba R. (2020, May 14). What is ACE2 receptor ,how it is connected to

coronavirus and why might it be key to treating COVID-19, The conversion, May 14, 2020. https://theconversation.com/what-is-the-ace2-receptor-how-is-it-connected-to-coronavirus-and-why-might-it-be-key-to-treating-covid-19-the-experts-explain-136928.

Kevin Jiang, (2020, July 24). News and research, Havard Medical School.

Yang X, Yu Y, Xu J, et al. (2020). Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study [published correction appears in *Lancet Respir Med.* 2020 Apr; *8*(4), e26]. *Lancet Respir Med. 8*(5), 475-481.

Voysey M, Clemens SAC, Madhi SA, et al. (2021). Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK [published correction appears in Lancet. 2021 Jan 9;397(10269):98]. *Lancet, 397*(10269), 99-111.

Logunov DY, Dolzhikova IV, Shcheblyakov DV, et al. (2021). Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia [published correction appears in Lancet. 2021 Feb 20;397(10275):670]. *Lancet, 397*(10275), 671-681.

Laing R, Gillan V, Devaney E. (2017). Ivermectin - Old Drug, New Tricks? *Trends Parasitol., 33*(6), 463-472.

Heidary F, Gharebaghi R. (2020). Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. *J Antibiot (Tokyo), 73*(9), 593-602.

Doi Y, Hibino M, Hase R, et al. (2020). A Prospective, Randomized, Open-Label Trial of Early versus Late Favipiravir Therapy in Hospitalized Patients with COVID-19. *Antimicrob Agents Chemother, 64*(12), e01897-20.

McCullough PA. (2020). Favipiravir and the Need for Early Ambulatory Treatment of SARS-CoV-2 Infection (COVID-19). *Antimicrob Agents Chemother, 64*(12), e02017-20.

McCullough PA, Kelly RJ, Ruocco G, et al. (2021). Pathophysiological Basis and Rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) Infection. *Am J Med., 134*(1), 16-22.

Zoorob RJ, Cender D. (1998). A different look at corticosteroids. *Am Fam Physician, 58*(2), 443-450.

Becker DE. (2013). Basic and clinical pharmacology of Glucocorticoids. *AnesthProg., 60*(1), 25-32.

Cruz-Topete D, Cidlowski JA. (2015). One hormone two actions: anti and pro-inflammatory effects of glococrticoids. *Neuroimmunomodulation, 22*, 20-32.

Zhong J, Tang J, Ye C, Dong L. (2020). The immunology of COVID-19: is immune modulation an option for treatment? *Lancet Rheumatol., 2*(7), e428-e436.

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