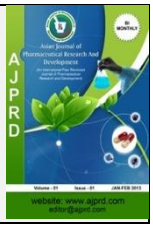
Available online on 15.12.2021 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research



Open Access

Review Article

Various Symptoms, Prevention and Treatments of Corona-virus (Covid-19)

Amol G. Jadhao*, Vaishali B. Magar

Department of Pharmaceutics, Gawande College of Pharmacy, Sakharkherda, Buldana, Maharastra, India

A B S T R A C T

Corona means "crown," and examined nearly, the round virus has a "crown" of proteins called peplomers jutting out from its center in every direction. These proteins help the virus identify whether it can infect its host. The severe acute respiratory syndrome has caused an alarmimg situation of the worldwide. The first detection, in Decmber2019, there have been no effective drug therapy options for treating the SARS-CoV-2 pandemic. And healthcare professionals are using some drug like remdesivir, favipiravir, chloroquine, hydrochloroquine, azithromycin, paracetamol, steroids, multivitamins, ivermectin, tocilumab, NSAIDs, treatment with monoclonal antibodies and convalescent plasma etc. of treatments. The condition known as severe acute respiratory syndrome (SARS) was also linked to a highly infectious coronavirus. The SARS virus has since been included and found to be successfully curable. The disease is caused by the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2), previously referred to as the 2019 novel coronavirus (2019-nCoV). The symptoms is typically rapid, ranging from hours to days after infection. Symptoms include fever, cough and, often, sore throat, headache, Sneezing, shortness of breath, wheezing, or difficulty in breathing. Reduce their anxiety level effectively when they are in the events of stress by using reasonable coping styles. Early studies of the out-break focused on the novel coronavirus gene and structure modeling, host and clinical case analysis. Currently, hundreds of registered clinical trials are underway, most of which are assessing antiretroviral agents, anti-inflammatory or immunosuppressant therapies, and passive antibody treatments.

Keywords: Remdesivir, Favipiravir, Coronavirus, SARS-CoV-2, COVID-19, Convalescent plasma, Monoclonal Antibodies.

A R T I C L E I N F O: Received; 18 May. 2021; Review Complete; 24 Sept. 2021 Accepted;07 Nov. 2021 Available online 15 Dec. 2021

Cite this article as:

Cheekti DK, Kumar PVT, Dhage R, Gappa S, Sahoo B, *In Vitro* Characterization of Nasal Spray to Asses Bioequivalence, Asian Journal of Pharmaceutical Research and Development. 2021; 9(6):90-97. **DOI:** http://dx.doi.org/10.22270/ajprd.v9i61028

***Address for Correspondence:**

Bikash Sahoo, Director, Orbicular Pharmaceutical Technologies Pvt Ltd, R&D Center, Plot No: 53, ALEAP Industrial Estate, Behind Pragati Nagar Colony, Kukatpally, Hyderabad – Telangana, India.

INTRODUCTION:

A pandemic on March 11, 2020. It is worth mentioning that at that stage the infection rates of asymptomatic infections were relatively high, and infections among children and young adults were relatively low. Hence, having future incidence prediction tools like mathe-matical modelling is vital in forecasting the spread of COVID-19 to ultimately protect the healthcare systems in different countries all over the globe.[1]

The source was traced to a seafood market in Wuhan but the cause was still a mystery. By January 7th, a new strain of coronavirus was identified and named; SARS-COV-2 (severe acute respiratory syndrome coron virus. By January 31st, there were over 9000 cases reported globally. The rate at which the new virus was spreading started to cause panic, and the WHO declared a "global emergency". By March, more than 11 countries had been affected by the virus, and the pandemic status was declared. Many countries subsequently imposed containment measures including nation-wide shutdowns. These included schools, universities, and med cal schools.[2] Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), continues to spread globally and cause massive societal disruption and death. As of August 3, 2020, COVID-19 has been responsible for >18 million cases and approximately 690,000 deaths worldwide. The United States is in the midst of a substantial surge of new cases, and despite months of effort, few treatment options with proven efficacy for COVID-19 are available. Currently, hundreds

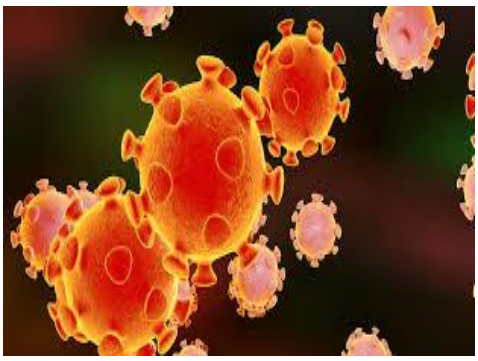
of registered clinical trials are underway, most of which are assessing antiretroviral agents, anti-inflammatory or immunosuppressant therapies, and passive antibody treatments.[3]

The high risk of anxiety disorders was noted among university and college students before the pandemic started. Studies revealed that anxiety has been diagnosed in 12–43% of college and university students. Therefore, it is important for students' psychological development to adjust and reduce their anxiety level effectively when they are in the events of stress by using reasonable coping styles. Early studies of the out-break focused on the novel coronavirus gene and structure modeling, host and clinical case analysis. The China National Health Commission has released guidelines to promote psychological crisis intervention for patients, people under medical observation, medical workers, and public during the COVID-19 outbreak since Jan 6, 2020.[4]

The patients' clinical data were obtained from our hospital's medical records, including patient demo-graphics, histologic subtypes, Ann Arbor stage, baseline complete blood count (CBC), the International Prognostic Index (IPI) score,[10] and chemotherapy regimens. Variables including the number of chemotherapy cycles, number of dose-adjustments, nadir ANC values, records of FN, and FN-related hospitalization were extracted; This study was conducted in accordance with the Declaration of Helsinki. Study protocols were approved by the institutional review board of the Peking Union Medical College Hospital. Written informed consent was obtained from all patients before the collection of patients'information.[10]

The COVID-19 pandemic makes us vividly aware of the major global imbalances and challenges that we collectively face today (Sakketa and Koebner, 2020; Sumner et al., 2020). As we witness too often, a crisis – whether economic, political, environmental or social – tends to hit the poorest, weakest and most marginal the hardest, laying bare the most acute societal and political weaknesses of countries around the world; But while COVID-19 may be pulling back our veneers of societal normalcy and stability, it did not create the weaknesses that it is exposing. Prior to the COVID-19 crisis, asymmetric relations between local and global power structures were on the rise. Coronaviruses are a family of viruses that can cause respiratory illness in humans. They get their name, "corona," from the many crown-like spikes on the surface of the virus. Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and the common cold are examples of coronaviruses that cause illness in humans. The virus is distinguished by its rapid flare-up in which the infection transmits through close contact with the persons who is already infected.4–8 Knowledge, attitude, and practice (KAP) survey is a crucial suitable method for assessing existing programmers and evaluating effective behavioral change strategies in the community. Currently, few studies are demonstrating the level of awareness among students in Saudi Arabia. This is probably the first research to evaluate KAP of the Saudis applied medical undergraduate students in the Abha, Asir region concerning COVID-19. Medical and para-medical students are vulnerable to infection of COVID-19 since their training in the hospitals let them to be in close contact to the infected patients. COVID-19 manifestations were categorized as mild, moderate, and severe according to guidelines. Patients who underwent assisted ventilation were also registered and stratified. Full general examination was done regarding vascular and endocrine systems, neurological evaluation, and evaluation for autoimmune diseases or coagulation disorders. [21,17,18]

Materials and Methods:



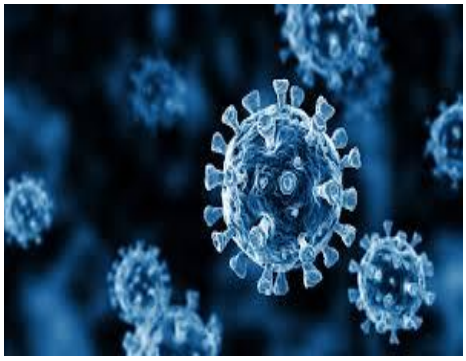


Figure 1: Novel Corona Virus.

This prospective, ongoing study analyzed data from the eight Houston Methodist hospitals from March 28, 2020, through July 6, 2020, with the approval of the Houston Methodist Research Institute ethics review board and with informed patient or legally authorized representative con-sent.

Patients:

Severe disease was defined as one or more of the following: shortness of breath (dyspnea), respiratory rate 30/minute, blood oxygen saturation 93% (on room air), partial pressure of arterial oxygen/fraction of inspired oxygen ratio <300, and/or pulmonary infiltrates >50% within 24 to 48 hours (of screening assessment). Life-threatening disease was defined as one or more of the following: respiratory failure, septic shock, and/or multiple organ dysfunction or failure.[4]Consecutive outpatients

attending the Emergency Room of the Clínica Universidad de Navarra (Pamplona, Spain) with symptoms compatible with COVID-19, no more than 72 h of fever or cough and a positive PCR for SARS-CoV-2 were enrolled. Patients with positive IgG against SARS-CoV-2, comorbidities considered risk factors for severe disease or COVID-19 pneumonia at baseline were excluded.[5]

At San Gerardo Hospital, ASST-Monza, Italy, we analyzed in a retrospective study patients with severe COVID-19 pneumonia who were receiving high-flow oxygen at the moment of enrollment and who had died or were discharged at the time of data collection. Our results can contribute to the general overview regarding the role of these agents in severe COVID-19 pneumonia, suggesting an interesting, even not statistically significant, evidence of the effectiveness of tocilizumab treatment in this dis-ease and sow a seed of reflection about their use in future waves of pandemic. We compared two cohorts of patients selected from those included in the STORM trial [NCT04424992]. The target population was adult with COVID-19 pneumonia diagnosed by nasopharyngeal swab and chest radiography admitted to our hospital before March 20, 2020 and treated with local standard of care.[13]

Population and Sampling:

All adults (≥18 years) who were volunteers to participate after informed consent was given have participated. The sample size was calculated using a single population proportion formula based on a previous study from China[17] using the following assumptions: 95% confidence level, and α = level of significance (5%), and margin of error (d) =0.05, design effect of 2, and non-response 10%. The sample was calculated using Epi-info version 7 and the maximum sample size used in this study was 693. From 20 kebeles of Gondar town, 6 kebeles were selected randomly using the lottery method. A multi-stage sampling technique was employed, Eligible participants completed a web-based survey that collected data on their demographics, current knowledge of COVID-19, stigma related to COVID-19, and relevant symptoms over the last 24 hours. (Table 1).[14,19]

Table.1: Sample Size Calculation using Epi-information

Sr. No.	Variable	Prevalence	Sample Size
1.	Depression	16.5	466
2.	Anxiety	28.8	693
3.	Stress	8.1	228

The questionnaires were anonymous and each IP address can only be filled in once to ensure the confidentiality and reliability of data. The questionnaire package consisted of three components: basic conditions of students, subjective feelings related to the epidemic situation and 20 practical situation questions in the Self-Rating Anxiety Scale (SAS). In this study, we investigated 18,294 college students, who were from 31 provinces, mainland China.[4]

Study Setting and Design:

A community-based cross-sectional study design was conducted in the Awi zone from July 28 to August 27, 2020. This zone is one of 11 zones of the Amhara Regional State, Northwest Ethiopia. Injibara is the administrative center of the Awi zone and is located 452 km north of Addis Ababa and 129 km South of BahirDar (City of Amhara Region). The zone has 9 districts and three admin-istrative towns. The zone is bordered in the west by Benishangul-Gumuz Region, on the North by West Gondar Zone, and the East by West Gojjam Zone. According to 2007 census data conducted by Central Statistical Agency, this zone had a total population of 1,322,693, of whom 64, 8295 were men and 674,397 were females.

Symptoms of Covid-19:

COVID-19 symptoms vary among individuals, from asymptomatic infection to serious respiratory failure. Fever, cough, fatigue, slight dyspnoea, sore throat, headache and conjunctivitis are common symptoms of the disease. Gastrointestinal involvement, with diarrhoea, nausea and vomiting, was reported in a lower percentage of cases. Hypothesized that SARS-CoV-2 could have neuroinvasive potential, since viral entry into the central nervous system may contribute in some patients to development of respiratory failure. The reported hyposmia and hypogeusia experienced by individuals with COVID-19 could also indicate a potential neurotropismof this virus. The neuroinvasive capacity of SARS-CoV-2 remains poorly understood. Mortality due to COVID- 19 appears to be lower than that of SARS-CoV (10%) and MERS-CoV (35%). However, it is still too early to evaluate the actual mortality rate of the disease, considering the rapid spread of COVID-19. Old age, ischaemic heart disease, hypertension, diabetes mellitus, chronic lung disease, cancer and patients receiving immunosuppressive medicines are the major risk factors for poor outcomes.[23] The symptoms of which range from asymptomatic course to pneumonia, acute lung and multiorgan failure and death. In order to develop a meaningful therapy strategy, different medications are used off label. One of this is remdesivir, a precursor of a nucleotide analogus that inhibits viral RNA polymerase.[15]

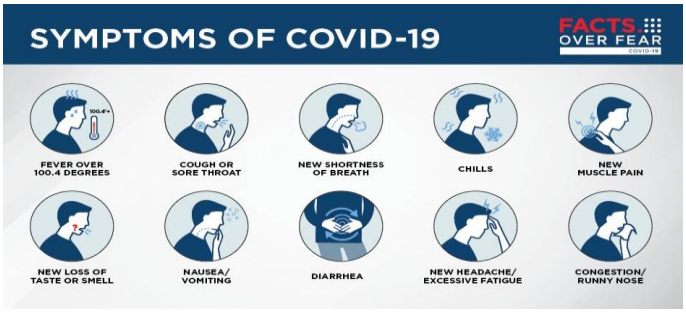


Figure 2: Symptoms of Covid-19

Prevention & Treatment:

Figure 3: Prevention of Corona-virus.

Remdesivier:

Remdesivir, the Food and Drug Administration issued an Emergency Use Authorization on May 1, 2020 (modified on August 28, 2020), to permit the use of remdesivir for treatment in adults and children hospitalized with suspected or laboratory-confirmed Covid-19. Remdesivir has also received full or conditional approval in several other countries since that time. However, given high mortality despite the use of remdesivir, it is clear that treatment with an antiviral drug alone is not likely to be sufficient for all patients. Current strategies are evaluating remdesivir in combination with modifiers of the immune response. A variety of therapeutic approaches including novel antivirals, modifiers of the immune response or other intrinsic pathways, and combination approaches are needed to continue to improve outcomes in patients with Covid-19.[12] Remdesivir was initially available through individual compassionate use requests. This pathway was halted for the majority of patients due to the overwhelming numbers of requests and the need to focus on clinical trials. Remdesivir access was then limited to these clinical trials and expanded access programs.[13] Finding antivirals that reduce mortality from severe respiratory viral infections has proven challenging. Phase 3 trials of baloxavir and pimodivir for severe influenza were unsuccessful. Lopinavir–ritonavir and hydroxychloroquine are not efficacious in treating Covid-19.[14] Mechanism of Action: Remdesivir is a monophosphoramidate prodrug of remdesivir- triphosphate (RDV-TP), an adenosine analog that acts as an inhibitor of RNA-dependent RNA polymerases (RdRps). Remdesivir-TP competes with adenosine-triphosphate for incorporation into nascent viral RNA chains.[11]

Favipiravir:

Favipiravir, previously known as T-705, is a prodrug of a purine nucleotide, favipiravir ribofuranosyl-5′-triphosphate. The active agent inhibits the RNA polymerase, halting viral replication. Most of fa-vipiravir's preclinical data are derived from its influenza, Various dosing regimens have been proposed based on the type of infectious indication. Dosing variations are likely due to the lower favipiravir EC_{50} values described against influenza compared with Ebola and SARS-CoV-2. Doses at the higher end of the dosing range should be considered for the treatment of COVID-19. Favipiravir is currently available in Japan for the treatment of influ-enza, but not available in the United States for clinical use. Limited clinical experience has been reported supporting the use of favipiravir for COVID-19. In a prospective, randomized, mul-ticenter study, favipiravir (n = 120) was compared with Arbidol (n = 120) for the treatment of moderate and severe COVID-19 in-fections. Differences in clinical recovery at day 7 were observed in patients with moderate infections (71.4% favipiravir and 55.9% Ar-bidol, *P* = .019). No significant differences were observed in the se-vere or severe and moderate (combined) arms.[73] These data sup-port further investigation with RCTs of the efficacy of favipiravir for the treatment of COVID-19.[16]

Chloroquine and hydroxychloroquine:

Hydroxychloroquine and chloroquine inhibit SARS-COV-2 bind- ing to the ACE-2 receptor. These drugs can be engulfed into endo- somes and lysosomes, which will lead to increased pH in these cellular compartments, which in turn impedes membrane fusion. Finally, hydroxychloroquine and chloroquine decrease cytokine release, which could help mitigate the cytokine storm that can occur in SARS-CoV-2-infected patients. Hydroxychloroquine has been postulated to be less toxic than chloroquine. Chloroquine promotes the cytoso- lic uptake of zinc, which has an antiviral effect by disrupting RdRP activity. Azithromycin has also been proposed as an adjunct to hydroxychloroquine/chloroquine therapy, but it has not been rigorously tested. Regarding car-diac risks of 4-aminoquinolines, studies have found prolongation of QTc interval. In a study conducted by, one out of eleven patients had to terminate treatment with hydroxy- chloroquine early because of the QTc risk. In a study by Borba out of 81 patients were diagnosed with a pro- longed QTc interval following treatment with hydroxychloroquine.[6] Covid-19 has affected tens of millions of individuals across the globe and upended the lives of countless others. Despite advances in supportive care and treat- ment, mortality remains high, and prevention of infec- tion continues to be crucial.1 Early on in the pandemic, hydroxychloroquine was suggested as

a possible pre- vention- method or treatment for covid-19, given evidence of in-vitro inhibition of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [8].

Azithromycin:

The first participant was recruited to principle on April 2, 2020. The azithromycin group enrolled participants between May 22 and Nov 30, 2020, by which time 2265 participants had been randomly assigned, 540 to azithromycin plus usual care, 875 to usual care alone, and 850 to other interventions. 2120 (94%) of 2265 participants provided follow-up data and were included in the Bayesian primary analysis, 500 participants in the azithromycin plus usual care group, 823 in the usual care alone group, and 797 in other intervention groups. 402 (80%) of 500 participants in the azithromycin plus usual care group and 631 (77%) of 823 participants in the usual care alone group reported feeling recovered within 28 days. We found little evidence of a meaningful benefit in the azithromycin plus usual care group in time to first reported recovery versus usual care alone (hazard ratio 1·08, 95% Bayesian credibility interval [BCI] 0·95 to 1·23), equating to an estimated benefit in median time to first recovery of 0·94 days (95% BCI –0·56 to 2·43).[7]

Paracetamol:

As SARS-CoV-2 uses ACE2 on the surface of human cells for infection [5], we examined whether paracetamol alters the risk of infection by SARS-CoV-2 by modulating ACE2 levels. Human Calu-3 and Caco-2 cell lines have been shown to be highly susceptible to infection by SARS-CoV-2 pseudo-virus [5], though the levels of ACE2 in these cell lines have not been reported. Thus, we began by analysing levels of ACE2 protein in these cells; the lung adenocarcinoma cell line A549 was used as a control because it has been shown to be more resistant to infection by SARS-CoV-2 pseudo-virus [5]. Overall, levels of ACE2 in Caco-2 (p value = 0.0190) and Calu-3 (p value = 0.5172, non-significant) cells were higher than those in A549 cells (Figure 3). Therefore, we decided to use Caco-2 cells for our next set of experiments.

Next, we treated Caco-2 cells with paracetamol (concentration range between 0.1 and 5 mM) or ibuprofen (concentration range between 0.05 and 2 mM) for 24 h and assessed levels of ACE2 mRNA and protein by real-time qPCR and Western blotting, respectively. [10]

Steroids:

Corticosteroids have been used in quite a few studies with COVID-19 without any pre-adjudication to look at the outcomes dedicated to the steroid therapy. Most of these studies had a small cohort size and had a high degree of heterogeneity regarding the choice of steroids, the dose and timing of the steroids, and had a co-prescription of broad-spectrum antibiotics and antivirals. Corticosteroids it is short acting drug had been tried in a few studies with SARS-CoV-1 and MERS-CoV infections. Two studies of patients with SARS-CoV-1 and influenza A (H1N1) viral pneumonia showed that the use of systemic corticosteroids was associated with reduced mortality in critical patients. Methylprednisolone was used in a significant number of studies followed by hydrocortisone, prednisolone and dexamethasone. In MERS-CoV, steroid treatment was associated with an adverse outcome with higher 90-day crude mortality, methylprednisolone it is intermediate acting drug, particularly when used in high dosage (up to 1000 mg/day) did show some survival benefit and some degree of reduction in incidence of ARDS and early discharge from the hospital.[8]

Multi-vitamins:

Among all participants, 64% did not take vitamin C supplements during the 6 months before the pandemic; however this percent decreased to 50% after the pandemic. Only 7.7% and 5.6% of the participants were taking vitamin C supplements on daily and weekly base,respectively, during the 6 months before the pandemic, however they significantly increased ($p<0.001$) to 16.4% and 9.1% after the pandemic (Table 1). It was found that, 55.6% of the participants did not take vitamin D supplements during the 6 monthsbefore the pandemic; however, this percent decreased to 51.5% after the pandemic. Regarding supplementation of Zinc, it was observed that, 83.5% of the participants did not take zinc supplements during the 6 months before the pandemic; howeverthis percent decreased to 74.4% after the pandemic. On the other hand,4% and 2.9% of the participants were taking zinc supplements either daily or weekly during the 6 months before the pandemic, however they were significantly increased ($p<0.001$) to 8.8 and 5%, respectively, after the pandemic (Table 1).When it came to the multivitamin supplements, it was noticed that there was no big difference between those taking them before and after the pandemic. [9]

Ivermectin:

Classification: Antiparasitic

Rationale for Use: Inhibits the replication of SARS-CoV-2 in cell cultures; however, pharmacokinetic and pharmacodynamic studies suggest that doses up to 100-fold higher thanthose approved in humans would be necessary to achieve the plasma concentrations necessary for the antiviral effect detected *in vitro*.

Mechanism of Action: Ivermectin inhibits the host alpha/beta-1 nuclear transport proteins, which are a part of a key intracellular transport process that viruses use to enhance infection by suppressing the host antiviral response.

The NIH covid-19 treatment guidelines recommend against the use of ivermectin,except in a clinical trial.

The available clinical data on the use of ivermectin to treat covid-19 are limited.[13]

Tocilizumab:

Patients treated with tocilizumab received the experimental treatment (8 mg/kg up to a maximum of 800 mg per dose, with an interval of 12 hours for a maximum of two doses) within the TOCIVID-19 trial,[10] a multicenter single-arm open-label Phase 2 study. Our study was based on an individual matched design done in variable proportion in

which each patient treated with tocilizumab on March 21 and 22, 2020 was matched with patients treated with the standard of care according to: age, sex, duration of symptoms from onset to hospitalization, WHO clinical score severity at the day of the first tocilizumab administration (WHO, 2020) and days from admission to tocilizu-mab administration. Forty-four patients receiving the local standard of care (consisting in hydroxychloroquine 200 mg BID, ceftriaxone 2 g QD, azithromycin 500 mg QD, acetylcysteine 600 mg BID) were found to match the 31 patients treated with tocilizumab, with a variable ratio ranging from 1 to 3 each. An inferential approach suitable to account for variable matching was adopted.[15]

NSAIDs:

The NIH covid-19 treatment guidelines recommend there be no difference in the use of antipyretic treatments (e.g., acetaminophen or NSAIDs) between patients with or without covid-19. Patients taking NSAIDs for comorbid conditions should continue therapy as previously directed by their prescriber. ESICM and SCCM Surviving Sepsis Campaign recommendations suggest acetaminophen for temperature control in critically ill adults with covid-19 who develop fever. The FDA continues to investigate the use of NSAIDs in patients with covid-19 symptoms. Concern for potential worsening of covid-19 symptoms has been suggested, but confirmatory clinical data is lacking at this time. There is an anecdotal published letter that suggests a link between ibuprofen and increased ACE2 expression that may lead to worse outcomes in covid-19 patients.[13]

Treatment with Monoclonal Antibodies:

Even though more than 75 monoclonal antibodies have been licensed for use by the US Food and Drug Administration, only 3 are used to treat or prevent infectious diseases respiratory syncytial virus, anthrax, and 'Clostridioides difficile'. Two different monoclonal antibody products have been shown to be effective in reducing mortality from Ebola virus disease, especially if used during early onset of infection. One of these was a combination of 3 monoclonal antibodies, while the other was a single monoclonal antibody. The successful treatment of an aggressive fatal virus supports the potential of monoclonal antibodies for the treatment of COVID-19. Therapeutic trials will include treatment of patients with SARS-CoV-2 infection, with varying degrees of illness, to block disease progression. Given the long half-life of most monoclonal antibodies (approximately 3 weeks for IgG1), a single infusion should be sufficient. Most patients with SARS-CoV-2 infection (in the absence of advanced age or co morbidities) will recover without treatment, albeit at variable rates, emphasizing the need to study monoclonal antibodies in patients most likely to benefit from early monoclonal antibody therapy.[16]

Convalescent plasma:

Convalescent plasma (CP) therapy, a classic adaptive immunotherapy, has been applied to the prevention and treatment of many infectious diseases for over a century. Convalescent plasma is being considered as a viable treatment for SARS-CoV-2 infections because it can provide short-term, immediate immune protection. Previously, it was discovered that neutralizing antibodies were able to bind spike-receptor binding proteins on the surface of SARS-Cov and Middle East Respiratory Syndrome (MERS) viruses. The antibodies in Convalescent plasma bind to the SARS-Cov-2 viruses, inhibiting them from binding to cells, Convalescent plasma, compared to remdesivir and hydroxy- chloroquine or chloroquine, has demonstrated the least severe side effects. In seven studies of convalescent plasma for SARS-CoV-2 infections, six of them showed improvement in patient conditions after treatment and one study showed no improved outcomes conducted a multicenter a study on 46 COVID-19 patients, mean age 63 years with bilateral infiltrates on chest X-ray in 36 patients. Forty three patients were alive and 3 patients (6.5%) died within 7 days. The PaO2/FiO2 improved by 112 units in survivors, chest radiogram severity decreased in 23%, ferritin and LDH decreased. Administration of plasma from persons who have recovered from COVID-19 provides antibodies to the recipient, which may neutralize the virus and reduce disease progression. Potential benefits include improvement in symptoms, reduced need for supplemental oxygen or mechanical ventilation, and reduced mortality.[13]

Amphotericin B:

Amphotericin B is a polyene antifungal agent with a broad range of activity against yeasts and molds, as well as the protozoan parasite *Leishmania* spp. LAmB binds to ergosterol in the fungal cell membrane leading to ion leakage and cell death. The initial formulation was amphotericin B deoxycholate (DAmB), which was developed in the 1950s. For many decades DAmB was the only antifungal agent available for the treatment of invasive fungal diseases. Because of the increasing prevalence and changing microbiological spectrum of invasive fungal infections, some form of amphotericin B still provides the most reliable and broad spectrum therapeutic alternative. However, the use of amphotericin B deoxycholate is accompanied by dose-limited toxicities, most importantly, infusion-related reactions and nephrotoxicity. Severe coronavirus disease (COVID-19) is currently managed with systemic glucocorticoids. Opportunistic fungal infections are of concern in such patients. While COVID-19 associated pulmonary aspergillosis is increasingly recognized, mucormycosis is rare. We describe a case of probable pulmonary mucormycosis in a 55-year-old man with diabetes, end-stage kidney disease, and COVID-19. Amphotericin B (Am B) which belongs to the polyene group has a wide spectrum in vitro and in vivo antimicrobial activity against fungi and parasites, but resistance to Am B is rare despite extensive use. If you are giving this medication to yourself at home, learn all preparation and usage instructions from your health care professional. Before using, check this product visually for particles or discoloration. If either is present, do not use the liquid. Learn how to store and discard medical supplies safely. [24]

Conclusion & Discussion:

Conclusions: This study shows that among the whole of vitamins, roles of vitamins A, C, D, and E are more defined and may be more effective on the immune system and emphasizes the importance of vitamins in the prevention of viral infections, including COVID-19, and sufficient vitamin intake is highly recommended to prevent viral infections like COVID-19. Communities' negligence in preventive measures is the major obstacle to break the spread of the virus. This finding revealed that 20.2% of the study participants were ready on COVID-19 preventive measures. The study found that the prevalence of good knowledge for COVID-19 prevention measures was found to be 76.6%, which implies that a majority of the communities had adequate knowledge towards covid-19.[11]

In this study, nearly one-third (32.0%), about a quarter (25.8%), and one in every seventh study participants had depression, anxiety, and stress, respectively. Being female and ever smoking negatively affect depression. On the other hand, a history of medical illness, the number of people in close contacts between 1 and 2, and ever smoking are contributing factors for anxiety.

RESULT:

Patient of characteristics 94 patients assessed, 50 did not meet eligibility criteria, 20 declined to participate and 24 were randomized. All randomized patients received the corresponding study product and completed 28 days of follow-up (Fig. A)

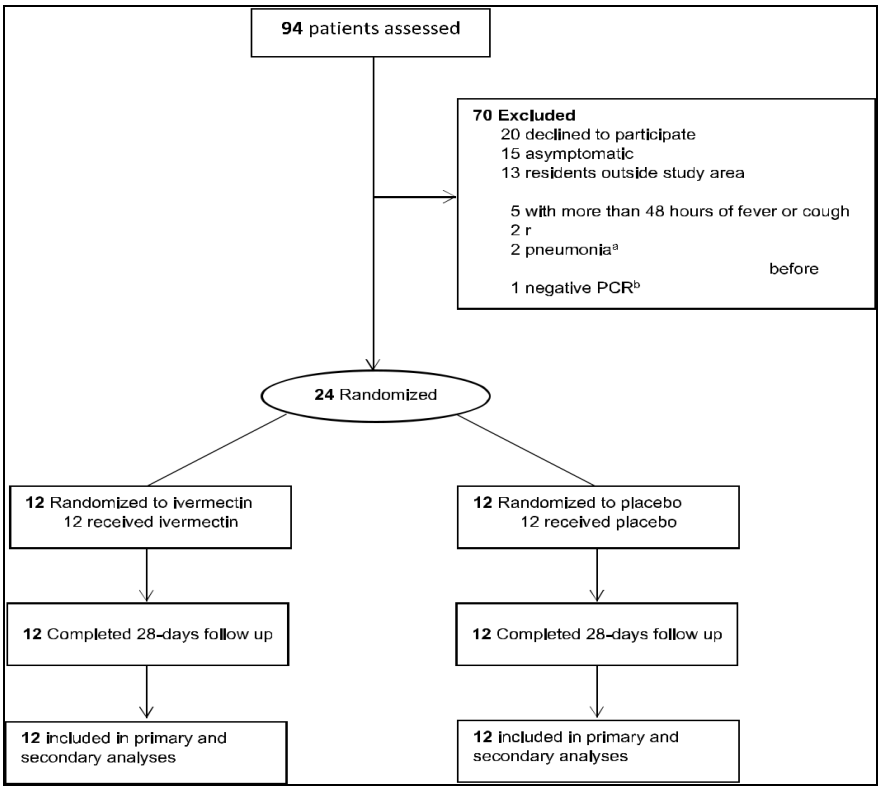


Figure: A. Enrollment and patient flow. One presented with pneumonia in the ER and one had a compatible X-ray during screening. Formally screened based on epidemiological and clinical suspicion but had a negative PCR.

The patients received remdesivir on day 11 of disease; day 12 saw her condition improve. She was able to be withdrawn from oxygenation, and oxygen saturation was 19%.[18]

REFERENCE:

1. Walid Al-Zyoud, Thelal Oweis , Haytham Al-Thawabih The Psychological Effects of Physicians' Communication Skills on COVID-19 Patients, in Dovepress research, patient Preference and Adherence 2021:15 677–690.
2. Nirav Nimava, Shruti Singh, *et al* Online Medical Education in India – Different Challenges and Probable Solutions in the Age of COVID-19, in Dovepress research, advances in Medical Education and Practice 2021:12 237–243.
3. Eric Salazar, y Paul A. *et al.* Treatment of Coronavirus Disease 2019 Patients with Convalescent Plasma Reveals a Signal of Significantly Decreased Mortality, in Elsevier, Immunopathology And Infectious Diseases The American Journal of Pathology, 2020; 190(11).
4. Wantong Han1, Lingzhong Xu1, Aimin Niu, Online-Based Survey on College Students' Anxiety During COVID-19 Outbreak in Dovepress reaearsch, Psychology Research and Behavior Management 2021; 14 385–392.
5. Carlos Chaccoura, Aina Casellasa, Andres Blanco-Di Matteo, The effect of early treatment with ivermectin on viral load, symptoms and humoral response in patients with non-severe COVID-19: A pilot, double-

blind, placebo-controlled, randomized clinical trial in Elsevier, 2589-5370/© 2021.

6. Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care, WHO Guidelines epidemic and pandemic diseases, Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections page no. XIV.
7. Sultan Ayoub Meo, Syed Ziauddin A. Zaidi, Trisha Shang,*et al.* Biological, molecular and pharmacological characteristics of chloroquine, hydroxychloroquine, convalescent plasma, and remdesivirfor COVID-19 pandemic: A comparative analysis, Journal of King Saud University – Science 32, 2020; 3159–3166.
8. Mukhtar H. Ahmed1 & Arez Hassan, Dexamethasone for the Treatment of Coronavirus Disease (COVID-19) : a Review, COVID-19, SN Comprehensive Clinical Medicine.
9. Duaa Mohamed Bakhshwin1 and Abdulaziz Bakhshwin, Impact of the Emerging COVID-19 Pandemic on the Consumption of Multivitamins (C, D and Zinc) by the Saudi Arabian Population, Journal of Pharmaceutical Research International, 33(26B): 11-20, 2021;Article no.JPRI.67426ISSN: 2456-9119.
10. Nuno Santos Leal, Yizhow Yu, Yuwen chen, Giogio Fedele and Luis Miguel Martins, Paracetamol Is Associated with a Lower Risk of COVID-19 Infection and Decreased ACE2 Protein Expression: A Retrospective Analysis,*COVID* 2021, *1*(1),218229; https://doi.org/10.3390/covid1010018.
11. Hydroxychloroquine in the prevention of COVID-19 mortality Published Online November 5, 2020 https://doi.org/10.1016/ S2665-9913(20)30390-8 See Articles,2021; 31:9.
12. Daniel Adane1 Alex Yeshaneh 1 Biresaw Wassihun 2 Addisu Gasheneit3, Level of Community Readiness for the Prevention of COVID-19 Pandemic and Associated Factors Among Residents of Awi Zone, Ethiopia: A Community-Based Cross-Sectional Study in Dovepress, Risk Management and Healthcare Policy, 2021:14 1509–1524.
13. Sören Jeppesen & Jason Miklian, Introduction: Research in the Time of Covid-19, Forum for Development, Routledge Taylor and francies group, 2020; 47(2):207–217,
14. Tim Smith, PharmD, BCPS; Jennifer Bushek, PharmD; Aimée LeClaire, PharmD, BCPS; Tony Prosser, PharmD, COVID-19 Drug Therapy by Clinical Drug Information Clinical Solutions Elsevier publication, Updated October 23, 2020.
15. Leila Jahanshahlua, Nima Rezaeic, Monoclonal antibody as a potential anti-COVID-19, Biomedicine & Pharmacotherapy, https://doi.org/10.1016/j.biopha.2020.110337.
16. Gopala Koneru, Gaber El-Saber Batiha, Abdelazeem M Algammal, *et al* BCG Vaccine-Induced Trained Immunity andCOVID-19: Protective or Bystander? Infection and Drug Resistance from Dovepress, 2021:14 1169–1184.
17. Serena Capici,Luca Sala, Stefania Galimberti,*et al* The Role for Tocilizumab in COVID-19 Patients: Reflections on Monza Cohort Data, Infection, rapid communication from Dovepress, Infection and Drug Resistance 2021:14 1389–1392.
18. Temesgen Yihunie Akalu, Kassahun Alemu Gelaye, Mulat Addis Bishaw, Depression, Anxiety, and Stress Symptoms and Its Associated Factors Among Residents of Gondar Town During the Early Stage of COVID-19 Pandemic, , from Dovepress, Risk Management and Healthcare Policy 2021:14 1073–1083.
19. P. BrouquiA. Giraud-Gatineau D. Raou, Critical reappraisal of remdesivir investigational trials in COVID-19, New Microbes and New Infections, A mini review, 2020; 38(11).
20. Sanders JM, Monogue ML,Jodlowski TZ,Cutrell JB, Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19) A Review of JAMA, 01 May 2020; 323(18):1824-1836.
21. Mohamed Adam, Moawia Gameraddin, Magbool Alelyani, Assessment of Knowledge, Attitude, and Practice Concerning COVID-19 Among Undergraduate Students of Faculty of Applied Medical Sciences at King Khalid University, Abha, Kingdom of Saudi Arabia: A Cross-Sectional Surveyed Study, Advances in Medical Education and Practice 2021:12 789–797.
22. Dalia Tohamy, Mohamed Sharaf, Khaled Abdelazeem, A Research paper of Ocular Manifestations of Post-Acute COVID-19 Syndrome, Upper Egypt Early Report, Journal of Multidisciplinary Healthcare 2021:14 1935–1944.
23. Eric William Hall ; Nicole Luisi ; Maria Zlotorzynska ;Willingness to Use Home Collection Methods to Provide Specimens for SARS-CoV-2/COVID-19 Research: Survey Study, Journal of Medical Internet Research, 2020 Sep; 22(9): e19471, Published online 2020 Sep 3. doi: 10.2196/19471, PMCID: PMC7473702, PMID: 32790639.
24. Deepak Garg . Valliappan Muthu . Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature, https://doi.org/10.1007/s11046-021-00528-2(0123456789().,-volV)(01234567.