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Review Article

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Comparison of Covid-19 Treatment Strategies: A Systematic Review

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Abstract

The novel coronavirus (COVID-19) which had its first outbreak in Wuhan, China went on to create a global health crisis. From contemplating the disease as a mere virus to formulating systematic strategies to contain the same, most of the countries had to revamp their healthcare systems. While some countries were able to cease the proliferation of the virus, others failed to do the same.

This study in particular aims to evaluate the planned resistance of selected countries (U.S.A, France, India, and Brazil) against COVID-19 in both pharmacological and non-pharmacological aspects and solidarity trial of treatment of COVID -19 by WHO, to come up with a universal treatment guideline that can be followed by countries worldwide.

Keywords: COVID-19, Treatment Strategies, Solidarity Trial.

1. Introduction

In the year 2019, the world was yet to face deadly combat against an unseen enemy, something which it had never fought before. Wuhan located in central China's Hubei province reported an unusual case of viral pneumonia on December 31st, 2019. This caught the attention of WHO's country office in China and led to the activation of a series of support teams on 9th January 2020. The outbreak was later stated to be caused by SARS-CoV-2 which caused COVID-19.

The main symptoms included fever, dry cough, shortness of breath, and in some cases, it would present as acute respiratory distress syndrome (ARDS). The hunt for a potential drug therapy to manage this disease was still ongoing meanwhile the desperateness to it was manipulated by emotions rather than rational decisions and scientific evidence.

Pharmacological and non-pharmacological measures are taken by countries across the world to overcome the issues faced by this deadly disease. Different treatment protocols are followed by different countries based on the studies conducted by groups, some more effective than others. There is a huge gap in the information of successful universal guidelines because of individual and uncoordinated studies by the countries.

This study is supported by guidelines and strategies of countries such as the U.S.A, France, India, and Brazil which have proved to be successful and a solidarity trial of COVID-19 by WHO. The main objective of this study would be to make a universal guideline that could be followed all over the globe. This would help in better decision-making by healthcare workers based on the best available and tested guidelines and strategies.

2. Objectives

General Objective

• To come up with a universal treatment guideline for COVID-19 patients both pharmacologically and non-pharmacologically from different treatment guidelines given by selected countries and solidarity trials by WHO.

Specific Objectives

• To enumerate COVID-19 treatment strategies of selected countries and solidarity trial by WHO.
• To compare treatment strategies utilized among the selected

countries and solidarity trials by WHO.

Research Question

How can we come up with universal guidelines to treat COVID-19 patients both pharmacologically and non-pharmacologically from different treatment guidelines given by selected countries and solidarity trials by WHO?

3. Limitation

These findings are related to the guidelines for healthcare facilities and communities, as updated until May 2021, however some guidelines may have been continuously updated beyond this date, some information was unable to be obtained from the government guidelines due to restricted accessibility even though it was provided by news outlets or other medias, fliers, newspaper which were not included here. This study only used government guidelines accessible by the public, which may have limited the scope of the study's usable information. Also, it compares aggregate groups and not individuals in exposure and disease occurrence.

4. Operational Definition of Terms

• **Treatment Strategy** - A treatment plan or policy which specifically focuses on recovery from a particular disease by addressing the characteristics of the disease and also describes the process of achieving an individual treatment plan goals.

• **Pharmacological Treatment -** Treatment of a disorder or disease using drugs/medications. In the treatment of COVID-19, the medications are used to minimize the intensity of the disease, reduce recovery time, and increase overall survival from the disease.

• **Non- Pharmacological Treatment** - management of disease using supportive care, surgery, radiation, or other modes instead of the use of medication. In the treatment of COVID-19, supportive treatments like mechanical ventilation, supplemental oxygen administration are used for patients with low oxygen saturation to enhance the survival rate.

• **Solidarity Trial -** solidarity trial is a large international clinical trial to help find an effective treatment for COVID-19, launched by world health organizations and partners. Countries which took part include Afghanistan, Argentina, Bahrain, Canada, Djibouti, Egypt, France, Islamic Republic of Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Norway, Oman, Pakistan, Occupied Palestinian Territory, Qatar, Saudi Arabia, Somalia, South Africa, Spain, Sudan, Switzerland, Syrian Arab Republic, Tunisia, Thailand, United Arab Republic and Yemen.

5. Methodology

Our study design is a systematic review. The data were taken from articles that were available on the internet. selected articles were reviewed to compare the pharmacological and non-pharmacological treatment strategies in the U.S.A, France, India, and Brazil and the solidarity trial of COVID-19 by WHO. PRISMA checklist criteria are used as the method to address the research question. The search terms used were COVID-19, treatment strategies, and solidarity trial. After eliminating duplicate articles, full-text articles were reviewed and relevant articles were listed down and were further analyzed.

Final articles were reviewed to extract the pharmacological and non-pharmacological treatment strategies of COVID-19 patients.

The data was analyzed by the statistician and presented in the form of Graph/Pie Chart/Pyramid.

PICO

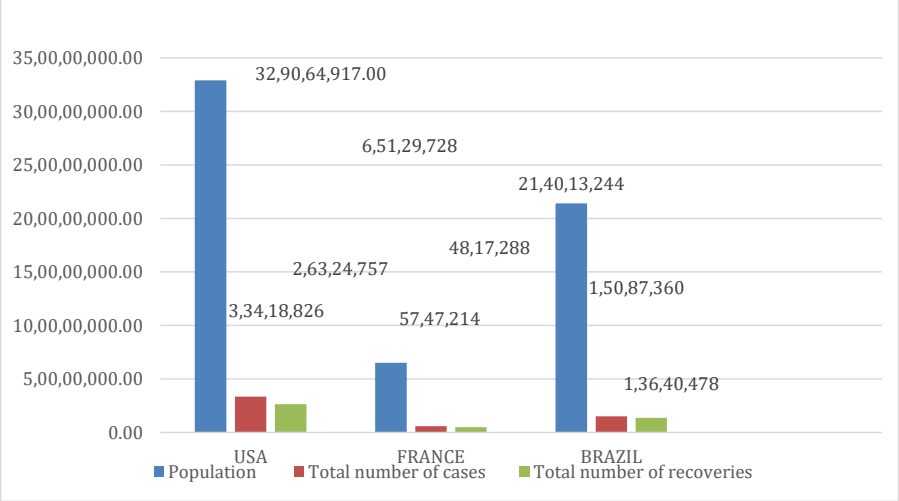
Population - Countries with 5 million or more COVID-19 cases and 4 million or more total recoveries and WHO solidarity trial.
Intervention - Study the pharmacological and non-pharmacological treatment strategies of COVID-19.
Comparison - Pharmacological and non-pharmacological treatment strategies of COVID-19 followed by the selected countries and solidarity trial.
Outcome - Standardized treatment strategies.

Inclusion Criteria

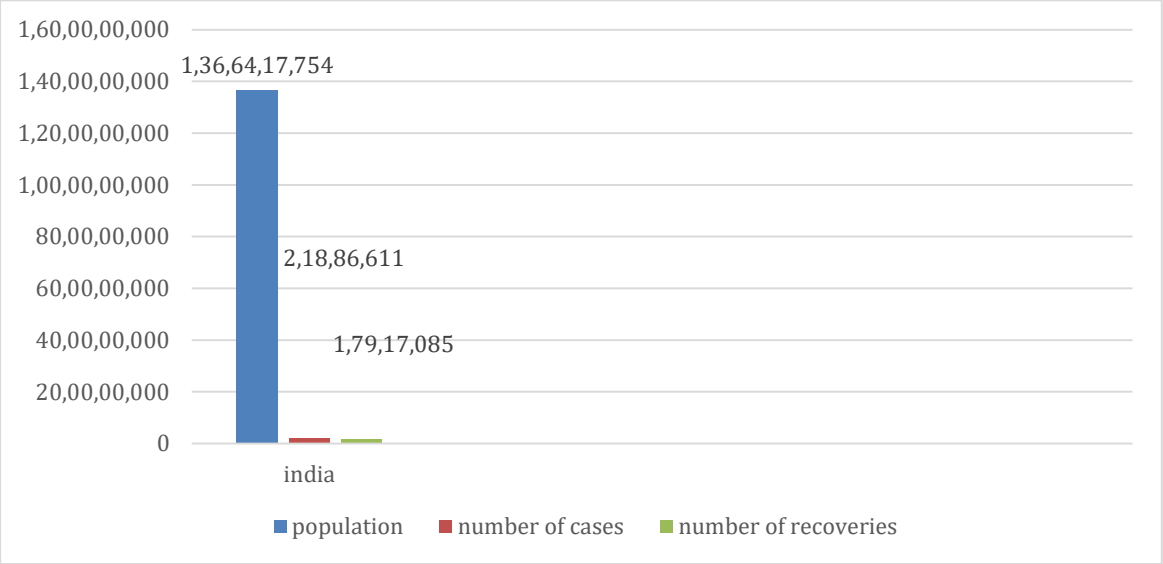
Articles discussing treatment strategies of COVID-19 patients in countries with 5 million or more reported COVID-19 cases and 4 million or more total recoveries and articles discussing solidarity trials of COVID-19 by WHO are included in this research.

NAME OF COUNTRY	TOTAL POPULATION	TOTAL NUMBER OF CASES (AS OF MAY 07, 2021)	TOTAL NUMBER OF RECOVERIES (AS OF MAY, 07,2021)
U.S.A	329,064,917	33,418,826	26,324,757
FRANCE	65,129,728	5,747,214	4,817,288
INDIA	1,366,417,754	21,886,611	17,917,085
BRAZIL	214,013,244	15,087,360	13,640,478

Table 1: Countries under inclusion criteria.



GRAPH 1: Comparison of population, total number of cases, total number of recoveries in USA, France and Brazil.



GRAPH 2: Comparison between population, number of cases, number of recoveries in USA, France and Brazil.

Exclusion Criteria

Articles discussing diagnosis, addressing the cause of COVID-19, the effect of comorbidities in COVID-19 treatment, and prevention and control strategies were excluded from the study.

Risk of Bias

Possible bias in this systematic review is evidence selection bias and publication bias. Since the data were collected from publicly accessible data sources and some of the sites were government regulated and inaccessible, it is not possible to identify all available data on this topic.

6. Results

We identified 256 articles and 11 articles were included in the study. From the initial search, a total of 256 articles were identified from PubMed and other databases. 115 duplicate articles were removed from the initial articles. 130 articles were excluded based on inclusion and exclusion criteria. We finally selected 11 articles for the systematic review, which included treatment strategies of COVID-19 in the selected countries with 5 million or more reported COVID-19 cases and 4 million or more total recoveries as of May 7,2021 and solidarity trial by WHO. The data was analyzed by the statistician and presented in the form of Graph/Pie Chart/ Pyramid.

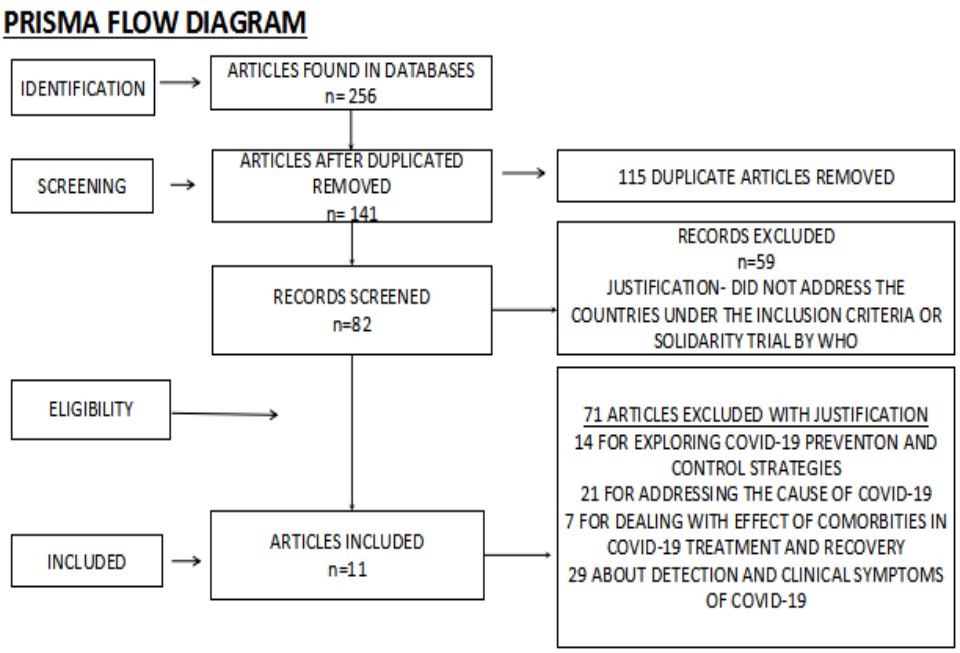


Figure 1. Prisma flow diagram for comparison of COVID-19 treatment strategies: systematic review

ARTICLE (Title, Author, Year, Country of Origin)	PHARMACOLOGIC TREATMENT	NON-PHARMACOLOGIC TREATMENT
1. Current treatment protocol for COVID-19 in India, Surbhi Sharma et.al. 2020, India.	Anti-malarial drug HCQ is recommended for prophylactic use by the asymptomatic cases. However, reports have advocated that a cure with HCQ or its combination with a macrolide might result in the cardiovascular adverse outcome of the extension of the QT interval. No evidence is exactly given yet to prove the benefit of this drug (alone or in combination with azithromycin).	India has commenced controlled trials of convalescent plasma therapy on severely-ill patients; those having respiratory rate > 30 breaths per min, oxygen saturation of < 90%, or else have infiltrated in the lungs.
2. Clinical management of COVID-19,George M. Varghese et.al, 2020, India	According to this article, the following drugs have shown some promise for the management of COVID-19: hydroxychloroquine and chloroquine, lopinavir/ritonavir, oseltamivir, remdesivir, favipiravir, interleukin-6 inhibitors, corticosteroids.	Lung protective ventilation strategies, careful fluid monitoring, prone ventilation, and when clinically indicated extracorporeal membrane oxygenation have been recommended in the management of the critically ill. Humidified oxygen via nasal cannula for non-severe pneumonia is a useful strategy as in any hypoxemia. Dry venturi masks without humidification should be used to avoid aerosolization risk.

3. Comparative Analytical Study of Two Different Drug Regimens in Treatment of Covid 19 Positive Patients in Index Medical College Hospital and Research Center, Indore, Mourya, S., Thakur, A. S., Hada, D. S., Kulshreshtha, V. S., & Sharma, Y., 2021,India	Comparative Analytical Study of Two Different Drug Regimens in Treatment of Covid 19 Positive Patients in Index Medical College Hospital and Research Center, Professor and Head, Department of Internal Medicine, Index Medical College Hospital and Research Center, Indore, Madhya Pradesh, India. Associate Professor, Department of Orthopedics, Index Medical College Hospital and Research Center, Indore, Madhya Pradesh, India Under Pharmacology: According to this study, the treatment with HCQ, azithromycin, and ivermectin had a better success rate compared to HCQ and azithromycin. Based on the results, ivermectin could be the potential therapeutic agent for the COVID-19 disease.	Non-pharmacological treatment is not included in this article.
4. Treatment of Coronavirus Disease 2019 (COVID-19) Patients with Convalescent Plasma, Eric Salazar, et.al. 2020, United States of America.	Hydroxychloroquine and azithromycin were reported to have beneficial effects early in the pandemic. Subsequent larger and more controlled studies determined that this combination has no benefits to patients and could be harmful. Many patients were also administered oral ribavirin. Patients who received remdesivir were shown to modestly reduce recovery time.	Convalescent plasma therapy has been administered on the frontlines during emergencies, and the need for controlled clinical trials to determine its therapeutic efficacy has been recognized

	Anti-inflammatory compounds, such as the IL-6 inhibitor tocilizumab and methylprednisolone, were administered per institutional protocols. Tocilizumab was recently shown to reduce mortality in a retrospective analysis of 20 severe COVID-19 patients.	
5. COVID-19 Treatment Guidance, Massachusetts General Hospital (MGH),2020, United States of America.	Remdesivir is FDA-approved for hospitalized adults and children (≥12 years and ≥40 Kg). Dexamethasone is recommended for hospitalized patients with severe COVID-19 who require supplementary oxygen. Tocilizumab 8 mg/kg may be considered on a case-by-case basis for patients with COVID-19 progressing on dexamethasone, oxygen <=92% RA and/or on escalating oxygen requirements and CRP ≥ 75 mg/L.	Supplemental oxygen or mechanical ventilation are suggested for critically ill patients.

6. Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19), James M. Sanders et.al., 2020, U.S.A.	A new briefing from China reported chloroquine was successfully used to treat a series of more than 100 COVID-19 cases resulting in improved radiologic findings, enhanced viral clearance, and reduced disease progression. Lopinavir/ritonavir, demonstrated in vitro activity against other novel coronaviruses but no published SARS-CoV-2 in vitro data exist for lopinavir/ritonavir Umifenovir (also known as Arbidol) is currently approved in Russia and China for the treatment and prophylaxis of influenza and is of increasing interest for treating COVID-19 based on in vitro data suggesting activity against SARS. Nitazoxanide has demonstrated in vitro antiviral activity against MERS and SARS-CoV-2. Currently, remdesivir is a promising potential therapy for COVID-19 due to its broad-spectrum, potent in vitro activity against several nCoVs, including SARS-CoV-2.	Non-pharmacological treatment is not included in this article.

7. Hydroxychloroquine and azithromycin as a treatment of COVID-19results of an open-label non-randomized clinical trial, Philippe Gautret, et.al., 2020,France	Survey conducted for this article shows that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.	Non-pharmacological treatment is not included in this article.
8. Non-pharmacological treatments for COVID-19: current status and consensus, Adriano Alves Pereira et.al., 2021, France	Pharmacological treatments were not included in the article.	Supportive treatments are the same as those applied to people with acute respiratory distress syndrome (ARDS) in the absence of specific treatment for COVID-19. In the examined data sources, six supporting treatments were found (oxygen therapy, prone position, inhaled nitric oxide, intravenous infusion, passive immunotherapy, mesenchymal stem cells (MSC))
9) Effect of Hydroxychloroquine on Clinical Status at 14 Days in Hospitalized Patients With COVID-19, Wesley H. Self, MD, MPH[1]; Matthew W. Semler, MD[2]; Linds a M. Leither, DO[3,4]; et al 2020, Brazil.	Among The adults hospitalized with covid-19, are treated with hydroxychloroquine, compared with placebo did not significantly improve the status at day 14 these findings do not support the use of hydroxychloroquine for treatment of covid-19 among the hospitalized.	Non-pharmacological treatment is not included in this article.

10.Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19: The CoDEX Randomized Clinical Trial, Bruno M Tomazini et.al., 2020, Brazil	The patients with moderate to severe covid-19 and ARDS, use of IV dexamethasone plus standard care resulted in a statistically significant increase in the number of ventilator free days compared with standard care alone.	Mechanical ventilation was given for critically ill patients.

Table 2. Data taken from articles discussing treatment strategies of COVID-19 in the selected countries.

7. Summary

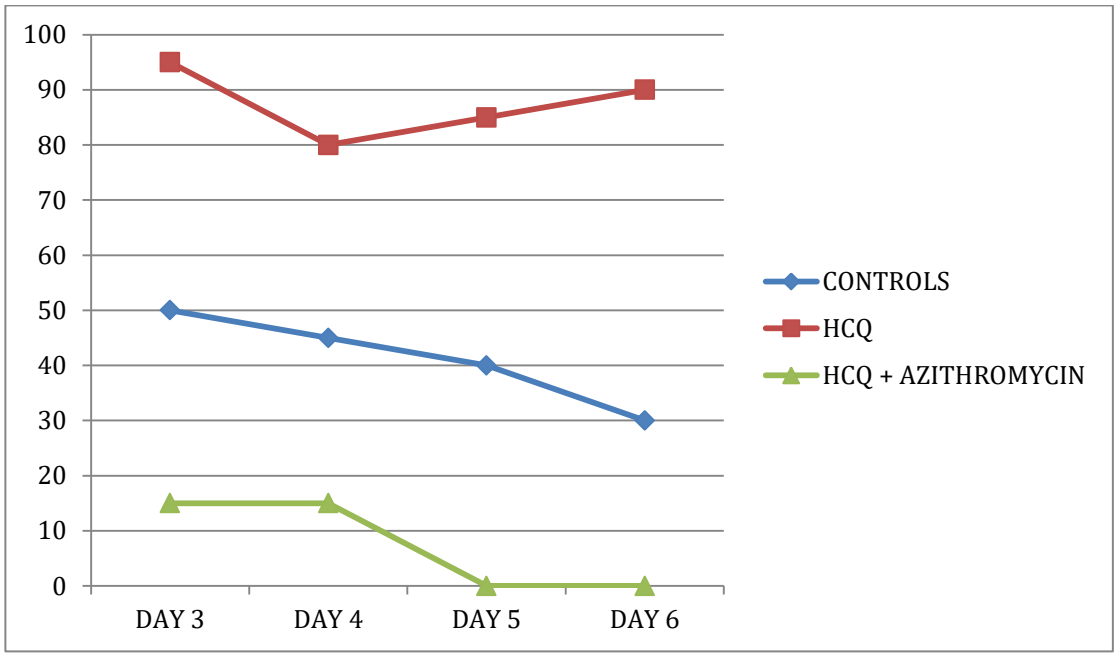
This table (table 1) lists 10 articles, each of which discusses COVID-19 treatment strategies of any of the selected countries (U.S.A, France, India, and Brazil). articles 1 and 2 discuss both pharmacological and non-pharmacological treatment of COVID-19 in India. Article 3 discusses the pharmacological treatment of COVID-19 in India. Articles 4 and 5 discuss both pharmacological and non-pharmacological treatment of COVID in the U.S.A, whereas, article 6 discusses pharmacological treatment only in the U.S.A. article 7 discusses pharmacological treatment and article 8 discusses non - pharmacological treatment of COVID-19 in France. Article 9 discusses pharmacological treatment and article 10 discusses both pharmacological and non-pharmacological treatment of COVID - 19 in Brazil.

Statistical Analysis

● France

Drugs studied - Hydroxychloroquine (HCQ) and azithromycin
Oral HCQ was given 200 mg thrice daily for 10 days.

NUMBER OF PATIENTS RECEIVED HCQ IN THE BEGINNING= 26 **CONTROL PATIENT = 16**	6 patients - early caseation of treatment- ● 3 patients transferred to ICU. ● 1 patient died on day 3. ● 1 patient decided to leave on day 3. ● 1 patient stopped treatment.
TOTAL POPULATION = 36	● 20 on treatment- out of this 6 patients received azithromycin 500 mg on day 1 and 250 mg per day for next 4 days ● 16 control group



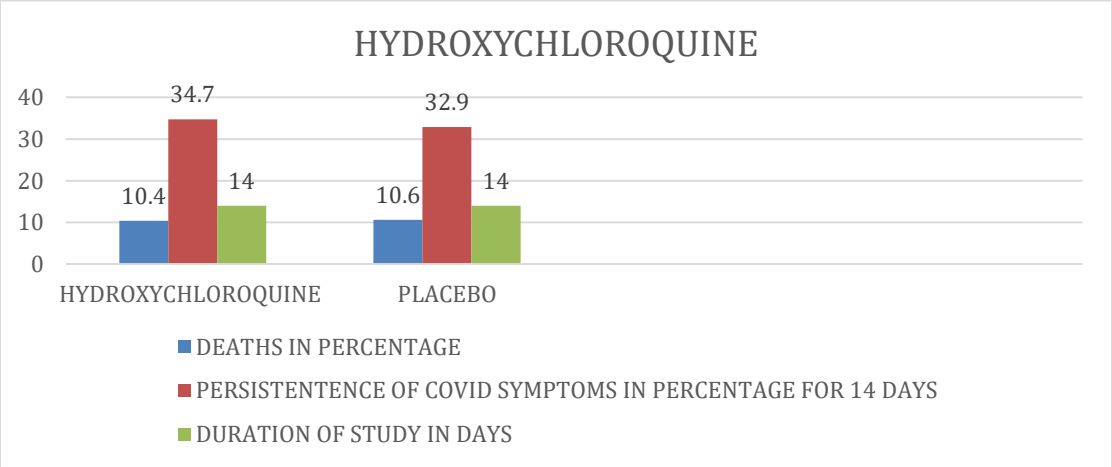
GRAPH 3: graph comparing efficiency of different drugs used in covid 19 treatment.

Statistics showed that HCQ is efficient in clearing viral load in COVID-19 in 3-6 days in most patients. Also, the study shows that 70% of HCQ treated patients were virologically cured,1 patient still PCR positive at day 6 , received azithromycin+HCQ at day 8 and was cured at day 9.

- **Brazil**

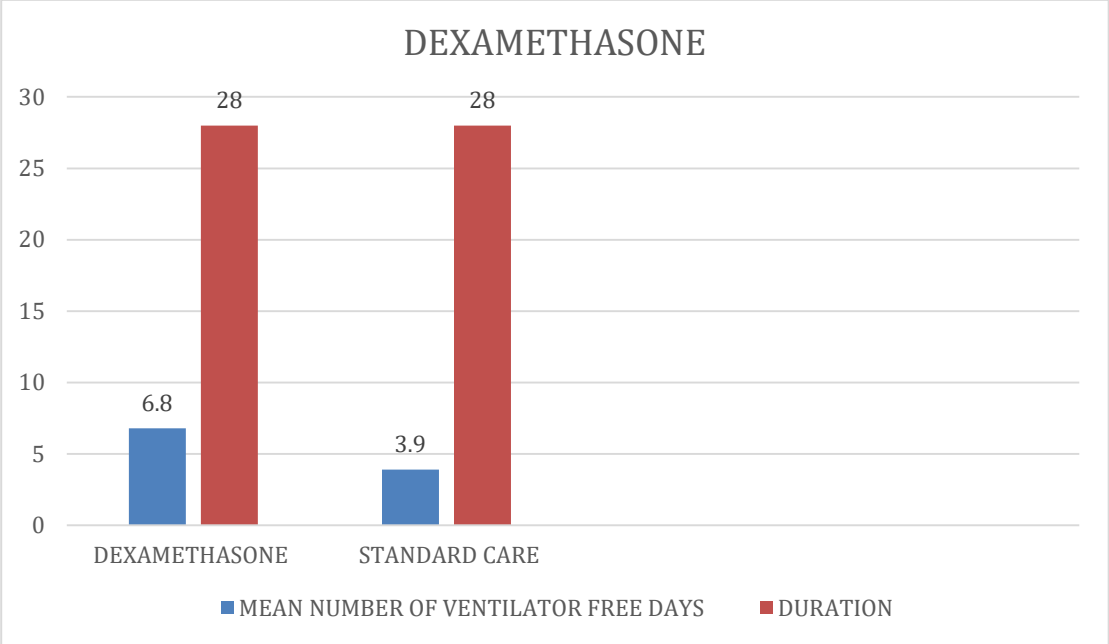
Drugs studied - hydroxychloroquine and dexamethasone.

DRUG	Hydroxychloroquine	Dexamethasone
DURATION	April 2 - June 19	April 17- June 21
MORTALITY RATE	10.4%	No significant difference
OUTCOME	There was no significant difference in the covid outcomes scaled score between the hydroxychloroquine group and placebo group.	Patients randomized to the dexamethasone group had a mean of 6.6 ventilator free days vs 4.0 ventilator free days in the standard care group.



GRAPH 4: Comparing death percentage, persistence of covid symptoms in present for 14 days, duration of study in days of hydroxychloroquine.

From the above graph we can depict that there was no significant difference in the covid outcomes between the hydroxychloroquine and placebo group i.e. the persistence of covid symptoms for 14 days and also similar mortality to that of placebo group (34.7 vs. 32.9).



GRAPH 5: Comparing mean number of ventilator free days, duration of dexamethasone.

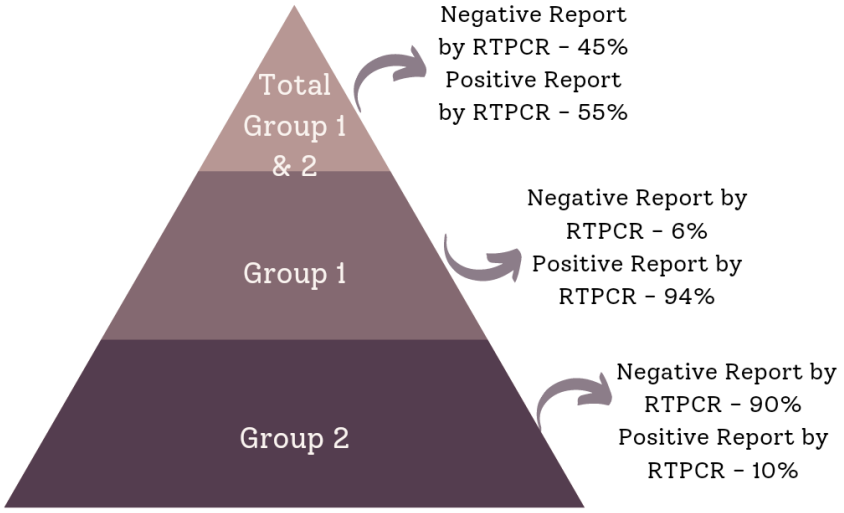
From the above graph we can depict that the use of dexamethasone with
standard care has more mean ventilation free days compared with standard care
alone i.e. (6.8 vs. 3.9).

- **India**

Drugs Studied - Hydroxychloroquine, Azithromycin, and Ivermectin
Hydroxychloroquine (HCQ)400 MG BID
Azithromycin 400 MG Once a Day
Ivermectin 12 MG once a day

	Drug combination	Negative Report by RTPCR	Positive Report by RTPCR
Group 1	HCQ+ Azithromycin	6%	94%
Group 2	HCQ + Azithromycin + Ivermectin	90%	10%
Total	Group 1 and Group 2	45%	55%

Pyramid Chart



Hydroxychloroquine (HCQ) 400MG BID
Azithromycin 400 MG Once a Day
Ivermectin 12 MG once a day

Fig shows: 2 groups in which grp one has negative report by RTPCR-6%
And positive report by RTPCR-94%
Group 2 shows negative report 90% positive 10% by RTPCR.
In total , both groups' positive reports are higher than negative.

• U.S.A

Main Agents Studied - Lopinavir, Hydroxychloroquine, Ribavirin, and Convalescent Plasma Therapy

DRUG	DURATION	RECOVERY RATE	DEATH RATE
Lopinavir	14 days	74%	19.2%
Hydroxychloroquine	5 days	62.9%	19.7%
Ribavirin	14 days	87%	17.1%
Convalescent Plasma Therapy	March 28, 2020, to April 14, 2020	76%	4%

Other Drugs Studied

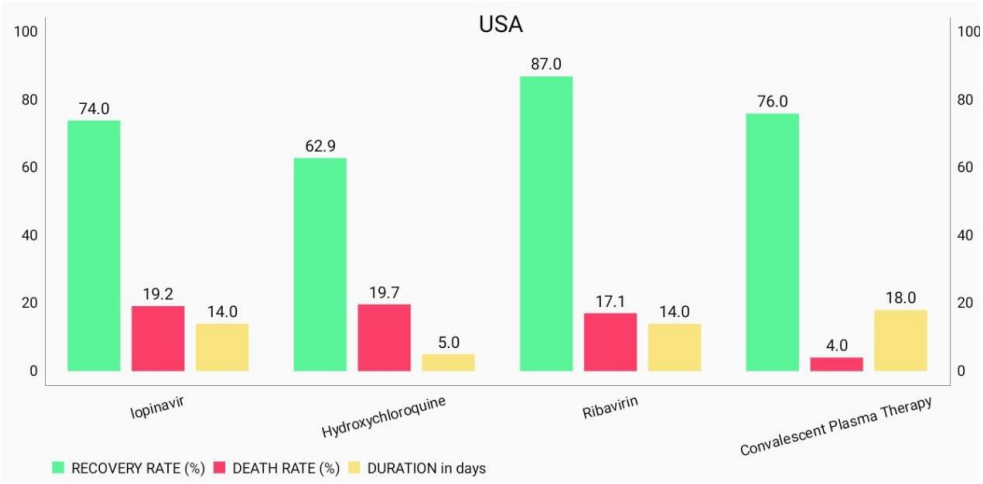
• Ivermectin: FDA approved (No data for death and recovery).

• Interferon-α and -β have been studied for nCoVs, with interferon-β demonstrating activity against MERS.37,38 Most published studies reported results of therapy combined with ribavirin and/or lopinavir/ ritonavir. Similar to other agents, delayed treatment may limit effectiveness of these agents. Given conflicting invitro and animal data and the absence of clinical trials, the use of interferons to treat SARSCoV-2 cannot currently be recommended.

• Corticosteroids: The rationale for the use of corticosteroids is to decrease the host inflammatory responses in the lungs, which may lead to acute lung injury acute respiratory distress syndrome (ARDS).However, this benefit may be outweighed by adverse effects, including delayed viral clearance and increased risk of secondary infection.

• Immunoglobulin Therapy: A potential adjunctive therapy for COVID-19 is the use of convalescent plasma or hyperimmune immunoglobulin. The rationale for this treatment is that antibodies from recovered patients may help with both free virus and infected cell immune clearance. Anecdotal reports or protocols for convalescent plasma have been reported as salvage therapy in SARS and MERS.

• Tocilizumab: 8 mg/kg (maximum dose 800 mg) may be considered on a case-by-case basis for patients with COVID-19 progressing on dexamethasone, oxygen <=92% RA and/or on escalating oxygen requirements and CRP ≥ 75 mg/L.(No data for death and recovery)



GRAPH 6: comparing recovery rate, death rate and duration in days of the USA.

According to this graph, there is no evidence from randomized clinical controls that any potential therapy improves outcomes in patients with either suspected or confirmed COVID-19. This provides a summary of current clinical experience and treatment guidance for this novel epidemic coronavirus. Hydroxychloroquine, Lopinavir, Favipiravir and Ribavirin are the drugs that were studied and among the four of them, ribavirin showed lowest mortality rate (17.1%) and highest recovery rate (87%), relatively.

Solidarity Trial by WHO

ARTICLE (Title, Author, Year, Country of Origin)	PHARMACOLOGIC TREATMENT	NONPHARMACOLOGIC TREATMENT
Repurposed antiviral drugs for COVID-19 – interim WHO SOLIDARITY trial results, , Hongchao Pan, Richard Peto, Quarraisha Abdool Karim, Marissa Alejandria, AnaMaria He naoRestrepo, César Hernández García, Marie Paule Kieny, Reza Malek zadeh, Srinivas Murthy, MariePierre Preziosi, Srin ath Reddy, MirtaRoses P eriago, Vasee Sathiyamo orthy, John	4 treatments evaluated by the trial; remdesivir, hydroxychloroquine, lopinavir/ritonavir, and interferon had little or no effect on overall mortality, initiation of ventilation, and duration of hospital stay in patients. Trial results showed that HCQ and lopinavir/ritonavir produce little or no reduction in mortality of hospitalized COVID-19	Non-pharmacological treatment of COVID-19 is not yet included in the solidarity trial.

Arne Røttingen, Soumya Swaminathan,2020.	patients when compared to standard care. So far, only corticosteroids have been proven effective against severe and critical COVID-19.	

TABLE 3. Data taken from an article discussing the solidarity trial by WHO.

7.1 Summary

This table (table 3) discusses the solidarity trial of COVID-19 treatment by WHO. In this solidarity trial, only pharmacological treatment of COVID-19 was discussed.

Statistical Analysis

Drugs Studied - Remdesivir, Hydroxychloroquine, Lopinavir/Ritonavir and Interferon- Beta 1a

TOTAL PARTICIPANTS	REMDESIVIR	HCQ	LOPINAVIR/RITONAVIR	LOPINAVIR + INTERFERON	INTERFERON ALONE	NO STUDY DRUG
11,266	2,750	954	1,411	651	1,412	4088

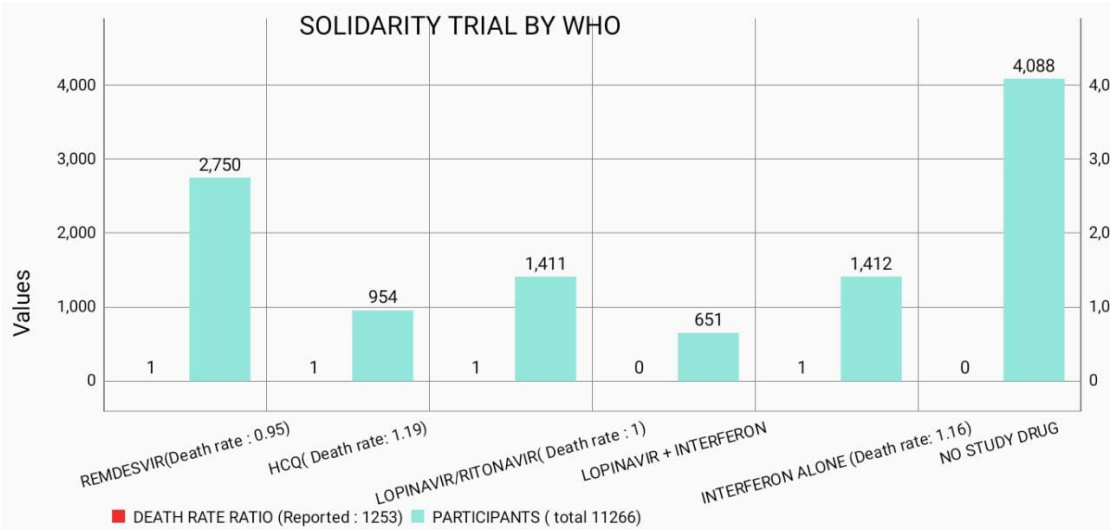
REPORTED DEATHS - 1,253
DEATH RATE RATIO

REMDESIVIR	HCQ	LOPINAVIR/RITONAVIR	INTERFERON
0.95	1.19	1.00	1.16

HYDROXYCHLOROQUINE - discontinued on June 1, 2020
LOPINAVIR/RITONAVIR - discontinued on July 4, 2020
INTERFERON - discontinued on Oct 16, 2020

DRUG DOSE, ROUTE OF ADMINISTRATION, AND NUMBER OF DEATHS DURING 14-DAY PERIOD.

DRUG	REMDESIVIR	HCQ	LOPINAVIR/RITONAVIR	INTERFERON
DOSE	Day 0 -200mg Day 1-9 - 100mg	200 mg	200mg/50mg	44 microgram
ROA	Intravenous	Oral	oral	Subcutaneous
DEATHS	7v8	4v2	6v3	6v8



GRAPH 7: comparing death rate ratio and participants of solidarity trials.

Above graph shows that among the drugs that were studied by WHO for solidarity trials, remdesivir showed the lowest death rate with the highest study population.

8. Discussion

In the U.S.A, the only approved drug by FDA is remdesivir to treat COVID-19. Patients receiving remdesivir showed a modest reduction in recovery time. dexamethasone is recommended for hospitalized, severely ill patients who require supplementary oxygen. Hydroxychloroquine and azithromycin were earlier reported to be beneficial but later were found to be harmful. Other drugs under consideration included anti-inflammatory compounds such as tocilizumab, and methylprednisolone, lopinavir/ritonavir, umifenovir, and nitazoxanide. Convalescent plasma therapy has been used during emergencies.from interpreting the graph, there is no evidence from randomized clinical controls that any potential therapy improves outcomes in patients with either suspected or confirmed COVID-19. Among the 4 drugs studied, ribavirin showed the lowest mortality rate (17.1%) and highest recovery rate (87%), relatively. The non-pharmacological intervention included supplemental oxygen or mechanical ventilation for critically ill patients.

In France, a survey conducted in article 7 concluded that hydroxychloroquine showed a significant reduction in viral load, and its effect was reinforced by azithromycin. Statistical study showed that HCQ is efficient in clearing viral load in COVID-19 in 3-6 days in most patients. Also, the study shows that 70% of HCQ treated patients were virologically cured,1 patient still PCR positive at day 6 , received azithromycin+HCQ at day 8 and was cured at day 9. The non-pharmacological regimen included oxygen therapy, prone position, inhaled nitric oxide, intravenous infusion, passive immunotherapy, and mesenchymal stem cells.

In India, remdesivir is showing great promise in COVID-19 management.

Hydroxychloroquine and azithromycin were earlier used for treating COVID-19 patients, but no exact evidence is given yet for its efficacy. Other drugs that were promising for COVID-19 management included lopinavir/ritonavir, oseltamivir, favipiravir, interleukin- 6 inhibitors, and corticosteroids. Trials are going on for the use of convalescent plasma therapy on critically ill patients. Graphical study showed that 2 groups in which grp one has a negative report by RTPCR-6% and positive report by RTPCR-94%, Group 2 shows negative report 90% positive 10% by RTPCR. In total, both groups' positive report is higher than negative. The non-pharmacological intervention included lung-protective ventilation, prone ventilation, extracorporeal membrane oxygenation, and humidified oxygen via nasal cannula for critically ill patients.

In Brazil, among the 11 recommendations mentioned in article 9, hydroxychloroquine, chloroquine, azithromycin, lopinavir/ritonavir, corticosteroids, or tocilizumab is not recommended anymore for the treatment of COVID-19. From the statistical study, we came to the conclusion that there was no significant difference in the COVID-19 outcomes between the hydroxychloroquine and placebo group i.e. the persistence of COVID-19 symptoms for 14 days and also similar mortality to that of placebo group and the use of dexamethasone with standard care has more mean ventilation free days compared with standard care alone. The non-pharmacological intervention included mechanical ventilation for critically ill patients.

Solidarity trial by WHO evaluated 4 pharmacological treatment regimens for COVID-19 which included Remdesivir, Hydroxychloroquine, Lopinavir/Ritonavir, and Interferon. But, these drugs showed no beneficial effects in treating COVID-19 patients. According to the WHO solidarity trial, so far, only corticosteroids have been proven effective in severe or critically ill COVID-19 patients. From graphical study of death rate ratio and population, we interpreted that among the drugs that were studied by WHO for solidarity trials, remdesivir showed the lowest death rate with highest study population.

9. Conclusion

Containment strategies for COVID-19 such as lockdown, social distancing, and wearing masks cannot continue in the long term. Therefore, it is necessary to formulate a foolproof universal strategy in treating the disease and to curtail the death rates. By comparing the pharmacological and non-pharmacological treatment strategies of selected developed and developing countries and solidarity trials of treatment of COVID-19 by WHO and statistically analyzing it from graphs , we concluded that it is still not possible to come up with universal guidelines for the treatment of COVID-19.

Though hydroxychloroquine is used by all the four selected countries and also included in the WHO solidarity trial, it showed little or no reduction in overall mortality rate and duration of hospital stay of COVID-19 patients. Hydroxychloroquine and azithromycin showed harmful effects rather than beneficial effects in COVID-19 patients.

Corticosteroids are, so far, the only drug that has been proven effective against severe and critical COVID-19, according to WHO. Articles 5 and 10 discussing COVID-19 treatment in the U.S.A and France respectively also showed the efficacy of corticosteroids in treating COVID-19 patients.

According to articles 3, 4, and 5, remdesivir is a great promise in treating patients with COVID-19.

Other drugs included in the articles which included lopinavir/ritonavir, oseltamivir, favipiravir, tocilizumab, methylprednisolone, umifenovir, and nitazoxanide and interferon have no proven efficacy in the treatment of COVID-19 yet.

Non-pharmacological management of severely or critically ill patients included oxygen therapy, invasive and non-invasive mechanical ventilation, extracorporeal membrane oxygenation

were used by the selected countries. This can be followed universally. Since low oxygen saturation is the main cause of death in COVID-19 patients, these are few of the best possible supportive management for severely or critically ill COVID-19 patients [1-11].

Recommendation

While mutations of SARS COV-2 are expected, new variants are formed which are associated with increase in transmissibility and making it difficult to control. We are still trying to understand how this new variant amplifies the severity of the virus.

1. IISc study reveals new mutations, proteins of novel coronavirus.
2. Mutated COVID-19 may foretell a great risk for mankind in the future.

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