

A Systematic Review on Comparative Analysis among the Treatment Modalities of Covid-19 Infection

Dr. Mukundan P.E ¹, Dr. Satish Vasanth ², Dr. Ranjith Kannan ³, Dr. Vasudevi R ⁴,
Dr. Lubna Fathima ^{5*}, Dr. Aravinth V ⁶

^{1,5} *Master of Dental Surgery, Senior lecturer, Madha Dental College and Hospital, Chennai, India.*

² *Master of Dental Surgery, Lecturer, Aimst Unoversity, Kedah, Malaysia.*

³ *Master of Dental Surgery, Reader, Chettinad Dental College and Research Institute, Chennai, India.*

⁴ *Master of Dental Surgery, Government Medical College, Krishnagiri, India.*

⁶ *Master of Dental Surgery, Reader, Madha Dental College and Hospital, Kundrathur, Chennai, India.*

Email: ^{5} dr.lubnafathima@gmail.com*

Abstract

Background: Outbreak of corona virus is an emerging issue in the field of medical science and finding treatment modality to cure the corona virus has become a challenging task to the medical professionals. **Aim:** To compare the clinical features of corona virus among the articles published in different sources or database. **Study Design:** A systematic review of articles published with full text which contains the clinical features of corona virus. **Materials and method:** The literature search yielded 44 articles, of which 35 were screened and were independently assessed. Among these potentially eligible articles included for systematic review. **Results:** Three studies were included in our systematic reviews which has relevant information about the clinical features of corona virus. We were not able to conduct Meta-analysis due to clinical heterogeneity among the study design and difference occurred in reporting of data. **Conclusion:** Corona virus has developed as alarming threat to the society. This article might create public health awareness among the medical professionals and the entire research scholar to gather information about the clinical features of corona virus.

Keywords: Corona virus, clinical features, treatment and systematic review.

I. INTRODUCTION

Corona virus is a dreadful virus which belongs to family coronaviridae and nidovirale order which has the potential to transmit as viral particle by entering into lungs via droplets. The biology of coronavirus is that the viral S spike binds to the ACE2 receptor on type 2 pneumocyte. The incubation period of coronavirus many range from 4-14 days may extend upto 24 days also. The symptoms during incubation period might remain either symptomatic or Asymptomatic also. It is a known to spread through humans and other

mammals¹. The structure of corona virus is a non segmented, enveloped RNA virus. They is a history that from past two decades the coronavirus is subjected to cause severe acute respiratory syndrome and thereby causing shortness of breathing and thereby leading to death². The first case was notified by WHO on 31st December 2019 in wuhan, china. The first case in US was notified by WHO in seattle on 15TH January 2020. The first case in India was reported on 30th January 2020 in kerala. This coronavirus was declared as pandemic by WHO on 11th march 2020. The national emergency alert by WHO was given to overall the world on

12th march 2020. The purpose of this virus came into notice went several cases of pneumonia was reported and lower respiratory tract samples were send to laboratory and found that a viral infection is persistent which lead to detection of corona virus^{3,4}. Due to this virus million of people around the world were affected even a large number of health care professionals were also affected⁵. The symptoms seen among the coronavirus affected patients are fever, cough followed by shortness of breath, soreness of throat along with diarrhoea^{6,7,8}. Since covid-19 has been declared by World health organisation as pandemic the demand to find the solution and cure is increasing hence this paper highlights on all the treatment modalities available to treat positive coronavirus infected person. Now since the virus cluster has spread to Kerala and the recent report released by Kerala found that 3 person were found to have positive result for corona virus which is caused by the betacoronavirus novel. The symptoms include coughing; running nose, sore throat, sneezing and sometimes fever is also reported⁵. World health organisation⁶ has updated a guideline to reduce the spread of corona virus infection which involves washing hands with soap and water. The preferred element is alcohol based hand rub, cover the nose while sneezing to avoid the spread of infection, avoid close contact with person having cold or flu like syndrome, they should be a protected contact with wild or farm animals. The incubation of corona virus is 5 days and approximately 2-14 days. Since corona virus starts with mild symptoms they are several cases reported among children in Shenzhen, china that they do not have symptoms but developed corona virus⁶.

II. OBJECTIVES

To assess the various treatment modalities of corona virus among the articles published in different sources or database.

III. MATERIALS AND METHOD:

Study Design

All the studies which contain the data related to treatment modalities of corona virus were taken into account.

IV. ELIGIBILITY CRITERIA

Inclusion criteria

1. All the articles which described the treatment modalities of corona virus were included.
2. Full text articles available in the search engine mentioned in search strategy in English were included.
3. Case reports were included in the analysis.
4. Case series were included.
5. All the clinical trial were included.

Exclusion Criteria

1. Articles published other language than in English were excluded.

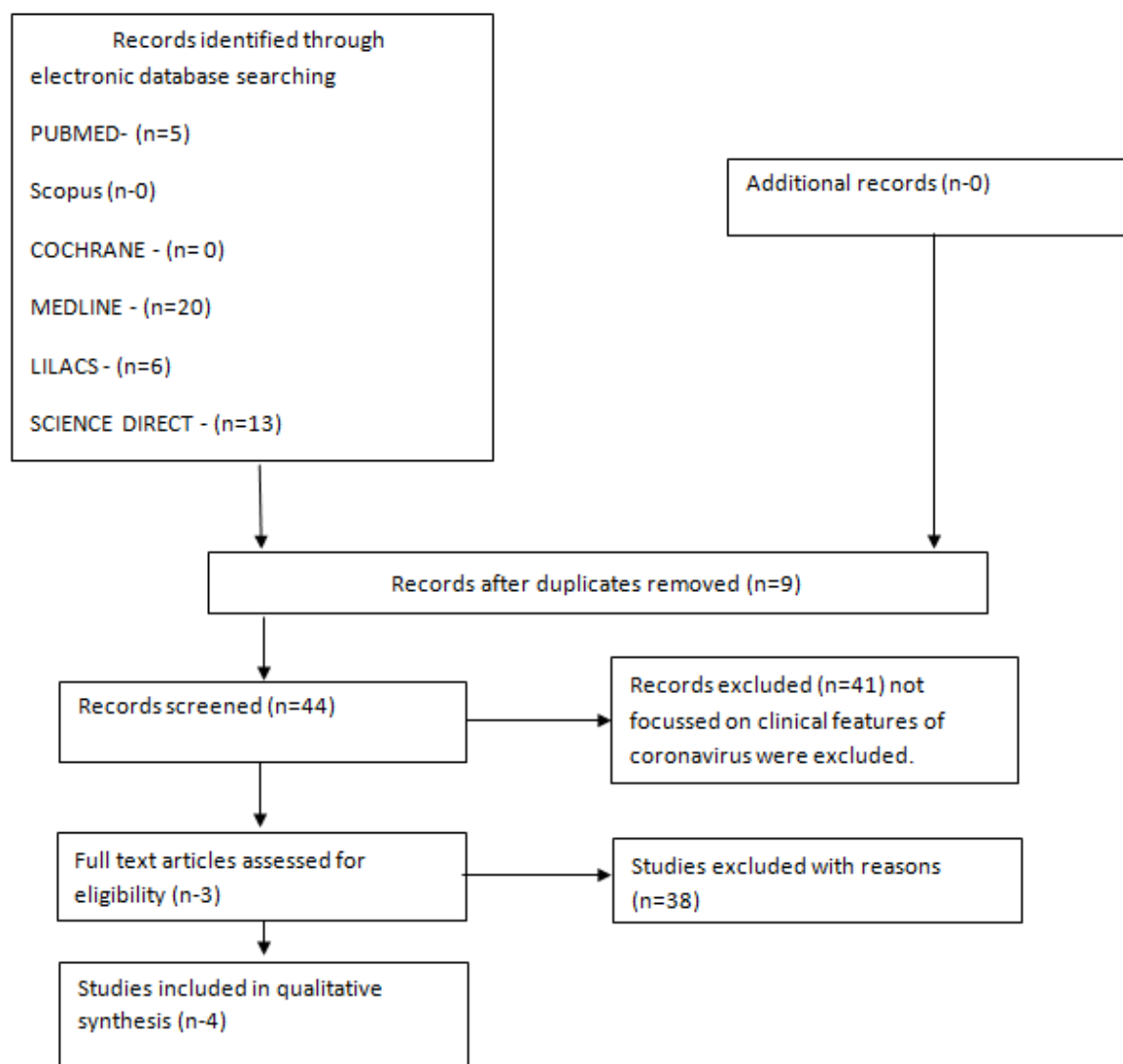
Search Strategy

Published literature were assessed and focussed on the treatment modalities of corona virus which includes original articles and research papers in databases such as Pub Med Central, Science direct, Cochrane Central Register of Controlled Trials (CENTRAL), grey literature, scopus, lilacs were taken into study for review from dec 2019- till date. A literature search to collect relevant article was performed using the keywords “corona virus” AND “treatment modalities” AND “covid 19”. According to the PRISMA guidelines the keywords were altered in each search engine when the results produced were many or too few.

Search Engine

1. Pub Med
2. Scopus
3. Cochrane central register of controlled trials (CENTRAL)
4. Medline
5. Lilacs
6. Science direct
7. Grey literature

Figure 1: Flow diagram showing the number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review



V. RESULTS:

The search yielded 44 articles, of which 35 were screened and were independently assessed. Among these potentially eligible articles included, figure 1 shows the flow diagram of the reports that were identified, screened, assessed for eligibility, excluded and included in the review. Table 1 shows the clinical features of the included studies which shows the overall percentage of the people affected by the symptoms of coronavirus which includes fever, cough, dyspnoea, diarrhoea, muscle pain, sore throat, confusion, chest pain, headache, nausea and haemoptysis which shows that several symptoms were not recorded in

several studies. Figure 1 illustrates the clinical feature of coronavirus various studies included in the systematic review. Table 2 shows the associated medical illness along the symptoms of the coronavirus which includes diabetes, hypertension, cardiovascular disease, chronic pulmonary disease, malignancy, chronic liver disease, digestive system and nervous system and found that the associated medical illness was not recorded in one of the study taken into analysis. Table 3 shows the laboratory findings of the included studies in which chest x-ray and CT were found to be the diagnostic method to rule out coronavirus infection.

Table 1: Characteristics of the clinical features of coronavirus in the included studies

S.no	Author name	Date, year	Treatment modalities discussed
1.	Changcheng Zheng et al	March 27, 2020	<ol style="list-style-type: none"> 1. Low level oxygen with intermitted Flow at the rate of ≤ 3 L/min. 2. Antiviral drug such as arbutol tablet 200 mg given three times daily. 3. Middle level oxygen was given with continuous flow at the rate of $3 \sim 5$ L/min. 4. Triple antiviral therapy is given along with ribavirin-500 mg twice daily, recombinant interferon-$\alpha 2b$ (5 million units twice daily, aerosol) are given. 5. High level oxygen flow with > 5 L/min. 6. Corticosteroid which include methylprednisolone-0.5mg for 5 days was given.
2.	Nicole wetsman et al	February 26, 2020	Remdesivir an antiretroviral drug was given to the patients
3.	Nitesh Gupta et al	2020	<ol style="list-style-type: none"> 1. Remdesivir was given invitro method. 2. Chloroquine was given in invivo method to the humans as 500 mg twice daily for 10 days. Although the treatment varied from 5-20 days according to the severity.
4.	Bin cao et al	March 18 th , 2020	Ritonavir and lopinavir are the antiretroviral drug used in combination approved its effectiveness.

Table 2: The characteristics of study location of the included article

s.no	Author name	Date, year	Study location
1.	Changcheng Zheng et al	March 27,2020	Cancer center of Wuhan Union Hospital, china
2.	Nicole wetsman et al	Febuary 26, 2020	University of Nebraska Medical Center, united kingdom
3.	Nitesh Gupta et al	2020	Mahavir Medical College and Safdarjung Hospital, New Delhi, India
4.	Bin cao et al	March 18 th , 2020	Jin Yin-Tan Hospital, Wuhan, Hubei Province, China.

Table 3: mechanism of action of the drugs included in various article to treat covid-19 infection

s.no	Drug name	Mechanism of action
1.	Ribavirin	It is a nucleoside inhibitor which interferes with RNA metabolism and stops the viral RNA synthesis. Is is found to be a guanosine analaog which helps for viral replication.
2.	Recombinant interferon	It is found to cause inhibition of protein synthesis along with the degradation of viral messenger RNA. This drug is available in the form of endogenous interferon.

3.	Remdesivir	It blocks the dependant RNA polymerase enzyme and thereby inhibits the viral replication of the virus responsible to cause the infection.
4.	Chloroquine	The main action of chloroquine is to helps the inhibition of hemozoin formed in the body. It enters the red blood cell and inhibits the parasitic cell. It also produces an antiviral effect which increases the PH of lysosomal and endosomal cells therefore inhibiting the viral RNA dependant RNA polymerase.
5.	Ritonavir	It inhibits the protease inhibitor and cytochrome P450 thereby inhibits the viral replication that takes place in the body.
6.	Lopinavir	The main action is to inhibit the protease enzyme by preventing the cleavage of polyprotien thereby inhinting the complex enzyme which helps the viral replication.

VI. DISCUSSION

The covid-19 virus started to be epidemic which began from wuhan and now it spreaded to various countries around the globe and became an life threatening and emerging pandemic disease. In our day to day world, we in the field of medical science, revolution of new disease is always an emerging trend and to treat it with proper treatment is essential for the patient to live a healthy life. Here occurrence of coronavirus is emerging in the field of medical science and has become a challenging task for the medical professionals to treat the coronavirus symptoms and cure the patient from death. The treatment modalities for coronavirus so far used were medicines used to treat HIV infection namely the lopinavir and ritonavir and anti-flu drugs were also used namely the oseltamivir. Recently, nineteen cases were repoted as positive in Thailand and they followed they were treated with the drugs mentioned above in which three patients started the drug regimen and one patient discontinued due to development of rash and out of two patients who continued the treatment one patient diagnosed with coronavirus as negative.

Chen wang et al⁷ reported that 98% of people were suffering from fever which was found maximum among the patients included in the data and sore throat was reported by none of the patients ncluded in this study. Associated medical illness was not recorded in the study and chest X-ray and computed tomography scan was used as a diagnostic method to rule out the

presence of coronavirus. Chaol in haung et al⁸ reported that 76% of patients included in this study had fever was the maximum symptoms among the individuals recorded and only 3 % of patients were reported with diarrhoea, associated medical illness was also reported and found that 20% of patients reported with diabetes and least was found in chronic pulmonary disease, malignancy and chronic liver disease with 2% occurrence data. Here to rule out the disease RNA of the affected individual was extracted and the presence were ruled out using direct zol RNA mini prep kit.

Nanshan chen et al⁹ repoted in this study that maximum number of people included in their study was reported with fever comprised of 83% and least was found to be 1% of nausea and vomiting symptoms reported. Associated medical illness was found to be maximum in cardiovascular disease consists of 51% and least was found in chronic pulmonary disease, malignancy and nervous system disorder and to rule out the coronavirus infection, chest x-ray and computed tomography was used as diagnostic method. According to recent literature of review, nearly 37,000 people have found to be infected with coronavirus in china and found that the economic growth has gone down due to the occurrence of coronavirus^{10,11,12}. Measures by the government should be taken immediately to stop the occurrence of coronavirus^{13,14}.

VII. CONCLUSION

Worldwide, coronavirus has become an alarming threat to the society. It is the duty of all medical professionals to spread awareness and knowledge among the people or population about the coronavirus infection. Fever was the common symptoms which was seen in all three studies to maximum number of patients and in associated medical illness, cardiovascular disease and diabetes were common in maximum number of patients. This attempt might help the people in the society to be aware about the clinical features of coronavirus infection.

REFERENCES

- Nasir MS, Ahsan MQ. Coronavirus pandemic and its impacts on the world's economy. *Journal of Sustainable Tourism and Entrepreneurship*. 2020;1(4):321-31.
- Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, Ahuja A, Yung MY, Leung CB, To KF, Lui SF. A major outbreak of severe acute respiratory syndrome in Hong Kong. *New England Journal of Medicine*. 2003;348(20):1986-94.
- Perlman S, Netland J. Coronaviruses post-SARS: update on replication and pathogenesis. *Nature reviews microbiology*. 2009;7(6):439-50.
- Yu N, Li W, Kang Q, Xiong Z, Wang S, Lin X, Liu Y, Xiao J, Liu H, Deng D, Chen S. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *The Lancet Infectious Diseases*. 2020;20(5):559-64.
- Assiri A, Al-Tawfiq JA, Al-Rabeeh AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, Flemban H, Al-Nassir WN, Balkhy HH, Al-Hakeem RF, Makhdoom HQ. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study. *The Lancet infectious diseases*. 2013;13(9):752-61.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*. 2020;395(10223):497-506.
- Arabi YM, Arifi AA, Balkhy HH, Najm H, Aldawood AS, Ghabashi A, Hawa H, Althman A, Khaldi A, Al Raiy B. Clinical course and outcomes of critically ill patients with Middle East respiratory syndrome coronavirus infection. *Annals of internal medicine*. 2014;160(6):389-97.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*. 2020;395(10223):497-506.
- Memish ZA, Assiri A, Alhakeem R, Yezli S, Almasri M, Zumla A, Al-Tawfiq JA, Drosten C, Albarrak A, Petersen E. Middle East respiratory syndrome coronavirus, MERS-CoV. conclusions from the 2nd scientific advisory board meeting of the WHO collaborating center for mass gathering medicine, Riyadh. *International Journal of Infectious Diseases*. 2014;24(7):51-3.
- Singhal T. A review of coronavirus disease-2019 (COVID-19). *The indian journal of pediatrics*. 2020;87(4):281-6.
- Al-Dorzi HM, Alsolamy S, Arabi YM. Critically ill patients with Middle East respiratory syndrome coronavirus infection. *Critical Care*. 2016;20(1):1-6.
- Zhou G, Chen S, Chen Z. Back to the spring of 2020: facts and hope of COVID-19 outbreak. *Frontiers of Medicine*. 2020;14(2):113-6.
- Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *International urology and nephrology*. 2020;52(6):1193-4.

14. DeBiasi RL, Song X, Delaney M, Bell M, Smith K, Pershad J, Ansusinha E, Hahn A, Hamdy R, Harik N, Hanisch B. Severe coronavirus disease-2019 in children and young adults in the Washington, DC, metropolitan region. *The Journal of pediatrics*. 2020;223(8):199-203.