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Research Article

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Successful Treatment Of COVID-19 With Convalescent Plasma Therapy, Actemra, Dexamethasone, Remdesivir and Oxygen Therapy and Other Medical, Surgical Diseases Treatment with The Help of Medical Sciences

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Abstract

Background and Objective: The Main theme of this Article is to discuss and prove the successful treatment of COVID-19 with Convalescent plasma therapy, Actemra, Dexamethasone, Remdesivir and Oxygen therapy and other Medical, surgical diseases treatment with the help of medical sciences.

Methods: The Author of this article has chosen literature review methodology of random research articles about successful treatment of COVID-19 patients with Convalescent plasma therapy, Actemra, Dexamethasone, Remdesivir and Oxygen therapy. 28 Articles were reviewed to prove the theme that COVID19 is controlled by getting benefit from Convalescent plasma therapy, Actemra, Dexamethasone, Remdesivir and Oxygen therapy. Medical sciences and scientists are doing great effort to save the lives of human beings in current Pandemic. Words such as plasma therapy, Actemra, Dexamethasone, Remdesivir and Oxygen therapy are used in PUBMED and Google to search for related articles.

Results: The two tables and three SPSS Diagrams clearly states the data collection and Analysis regarding the literature review. First table shows the articles discuss the methods of treatment of Covid19 infection and their numbers. Second tables discuss the 27 randomly selected articles to show the successful treatment of COVID-19 infection by using different drugs and methods. SPSS Diagrams shows the article numbers and their percentages in the favor/ Not in favor/ Neutral of the current study.

Conclusion: To sum up, Plasma therapy, Oxygen therapy, Actemra, Dexamethasone, Remdesivir and other antibiotics has proven to be effective against the covid19 infection. Oxygen therapy at very initial stage of infection reduces the hypoxia and damage to lungs to the patient by the virus. The effort by this article is to discuss the treatment of covid19 infection and current published articles discussing the use of Medicines and medical methods.

Keywords: COVID-19 Convalescent Plasma (CCP), Polymerase Chain Reaction Test (PCR), SARS-Cov-2, Convalescent plasma, Actemra, Remdesivir and Oxygen therapy, Passive Immunization (PI).

Introduction

The disease burden for COVID-19 depends on [1] multiple factors like the local infection rate, susceptible population, mortality rate, and so on. The COVID-19 pandemic is a rapidly evolving emergency and is a subject of regular debate and advanced

research. Preliminary reports have shown positive outcomes with Remdesivir and tocilizumab, but this needs further confirmation. Recently, the therapeutic application of Convalescent Plasma therapy in critically ill patients suffering from COVID-19 has gained



momentum [1] Figure 1. There is currently no effective treatment for COVID-19, [2] and preliminary trials for convalescent plasma suggest that there may be some benefits. However, research to date

is at high risk of bias, and randomized control trials are desperately needed to determine the efficacy and safety of this therapeutic option.

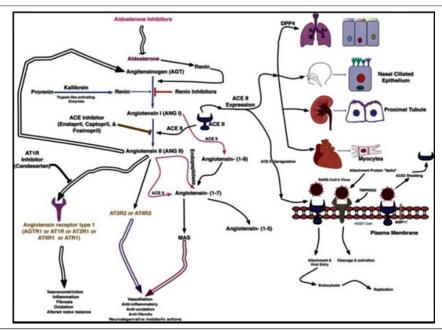


Figure 1: Major sites of ACE2 expression, Binding of SARS-CoV-2 to ACE2 receptor, and involvement of TMPRSS2, and DPP4 in SARS-CoV-2 entry. (Pravindra Kumar, Ashok Kumar Sah, Greesham Tripathi, Anjali Kashyap et al, 2021).

Convalescent plasma has been used to treat several infections during pandemics, including severe acute respiratory syndrome coronavirus (SARS-CoV), Middle Eastern respiratory syndrome coronavirus [2] (MERS-CoV) and now severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Convalescent plasma has emerged as a promising therapeutic agent for patients with coronavirus disease 2019 (COVID-19), [3] has received emergency

use authorization, and is being widely used during the COVID-19 pandemic. Passive antibody therapy via plasma or serum has been successfully used to treat infectious diseases for more than a century. Passive antibody administration is based on the presumption that convalescent plasma or serum contains therapeutic antibodies that can be passively transferred to the plasma recipient [3] (Figure 2).

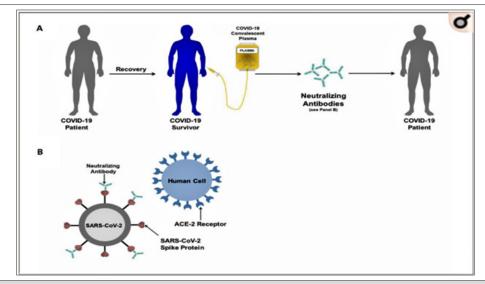


Figure 2: Schematic illustrating the use of convalescent plasma for COVID-19. An individual who was sick with COVID-19 and currently recovered (COVID-19 Survivor) has blood drawn and screened for virus neutralizing antibodies. Following identification of those with high levels of neutralizing antibody, plasma containing these virus neutralizing antibodies can be administered to individuals currently sick with COVID-19. (Juan G. Ripoll, Noud van Helmond, Jonathon W. Senefeld, Chad C. Wiggins et al, 2021).

Immune (i.e., "convalescent") plasma refers to plasma [4] that is collected from individuals following resolution of infection and development of antibodies. Passive antibody administration through transfusion of convalescent plasma may offer the only short-term strategy for conferring immediate immunity to susceptible individuals. There are numerous examples in which convalescent plasma has been used successfully as postexposure prophylaxis and/or treatment of infectious diseases, including

other outbreaks of coronaviruses (e.g., SARS-1, Middle East Respiratory Syndrome [MERS]). Globally, blood centers have robust infrastructure for undertaking collections and constructing inventories of convalescent plasma to meet the growing demand [4] (Figure 3). A cluster of pneumonia cases of unknown etiology [5] associated with pyrexia and acute respiratory distress was identified in Southern China.

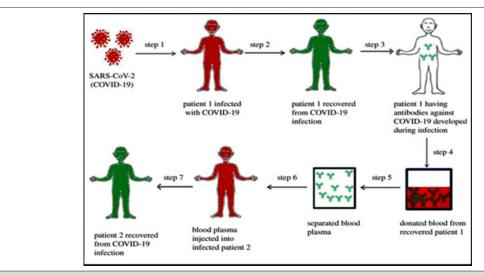


Figure 3: Schematic of plasma therapy. When the COVID-19-infected individuals recover, their blood plasma contains antibodies against the COVID-19 causing SARS-CoV-2 virus. The recovered individuals donate their blood, from which the plasma containing the required antibodies is extracted. This plasma is then administered to the infected individual(s) via transfusion. (Ravikant Piyush, Keshav Rajarshi, Rajni Khan, Shashikant Ray, 2020).

Links between the previous Severe Acute Respiratory Syndrome (SARS) cases and the region's seafood market were noted with the possibility of a new zoonosis and SARS-CoV-2 was identified as the responsible agent. Convalescent Plasma (CP) therapy is a classic adaptive immunotherapy which has been in use for more a century to prevent and treat infections including SARS, Middle East Respiratory Syndrome (MERS), and H1N1 pandemic [5]. The coronavirus disease 2019 (COVID-19) pandemic has [6] left the world in a state of desolation with overburdening public health systems in a short period. Finding possible preventative and therapeutic measures to counter severe respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, has been the priority.

Methods

The Author of this article has chosen literature review methodology of random research articles about successful treatment of COVID-19 patients with Convalescent plasma therapy, Actemra, Dexamethasone, Remdesivir and Oxygen therapy. 28 Articles were reviewed to prove the theme that COVID19 is controlled by getting benefit from Convalescent plasma therapy, Actemra, Dexamethasone, Remdesivir and Oxygen therapy. Medical sciences and scientists are doing great effort to save the lives of human beings in current Pandemic. Words such as plasma therapy, Actemra, Dexamethasone, Remdesivir and Oxygen therapy are used in PUBMED and Google to search for related articles (Table 1-2).

Table 1: Articles discusses the methods of treatment of Covid19 infection and their numbers.						
S. No	Treatment Methods	Number of Articles				
1	PLASMA THERAPY	10				
2	ACTERMA-TOCILIZUMAB	14				
3	DEXAMETHASONE	8				
4	REMDISIVIR	13				
5	OXYGEN THERAPY	18				
6	Azithromycin, Doxycycline, Clarithromycin, Ceftriaxone, Amoxicillin, Amoxicillin-clavulanic acid, Ampicillin, Gentamicin, Erythromycin,	15				
7	Benzylpenicillin, Piperacillin/tazobactam, Ciprofloxacin, Ceftazidime, Cefepime, Vancomycin, Meropenem, and Cefuroxime	19				

Table 2	Table 2: 27 Randomly selected Articles to show the successful treatment of COVID-19 infection by using different drugs and methods.						
S.NO	Complete Reference of The Articles Selected for The Study.	Study Favors the Significant Results of Drugs/ Methods -YES	Study Did Not Show the Significant Results of Drugs/ Methods - No	Percentages % Of Articles Agreed to The Treatment/ Methods.			
1	Kamal Sahu, Ajay Mishra, Manish Raturi and Amos Lal (2020) Current Perspectives of convalescent plasma therapy in COVID-19. Acta Biomed. 2020; 91(4): e2020175. Published online 2020 Nov 10.	YES		100%			
2	Pravindra Kumar, Ashok Kumar Sah, Greesham Tripathi, Anjali Kashyap et al (2021) Role of ACE2 receptor and the landscape of treatment options from convalescent plasma therapy to the drug repurposing in COVID-19. Mol Cell Biochem. 2021 Feb;476(2): 553-574.	YES		100%			
3	Denise J Wooding, Horacio Bach (2020) Treatment of COVID-19 with convalescent plasma: lessons from past coronavirus outbreaks. Clin Microbiol Infect. 2020 Oct;26(10): 1436-1446.	YES		70%			
4	Juan G. Ripoll, Noud van Helmond, Jonathon W. Senefeld, Chad C. Wiggins et al. (2021) Convalescent Plasma for Infectious Diseases: Historical Framework and Use in COVID-19. Clin Microbiol Newsl. 2021 Feb 15; 43(4): 23-32.	YES		100%			
5	Evan M Bloch, Shmuel Shoham, Arturo Casadevall, Bruce S Sachais. Et al. (2020) Deployment of convalescent plasma for the prevention and treatment of COVID-19. J Clin Invest. 2020 Jun 1;130(6): 2757-2765.	YES		100%			
6	Ravikant Piyush, Keshav Rajarshi, Rajni Khan, Shashikant Ray. (2020) Convalescent plasma therapy: a promising coronavirus disease 2019 treatment strategy. Open Biol. 2020 Sep;10(9): 200174.	YES		100%			
7	Daulat Khulood, Mir S Adil, Ruqiya Sultana, Nimra (2020) Convalescent plasma appears efficacious and safe in COVID-19. Ther Adv Infect Dis. 2020 Sep 28;7: 2049936120957931.	YES		100%			
8	Keegan C Long, Abida Sayed, Priyanka Karki, Yogesh Acharya (2020) Convalescent Blood Products in COVID-19: A Narrative Review. Ther Adv Infect Dis. 2020 Sep 22; 7: 2049936120960646.	YES		80%			
9	Hamidreza S, Monireh M, Shahram Ala, Shahnam S et al. (2020) Tocilizumab for treatment patients with COVID-19: Recommended medication for novel disease. Int Immunopharmacol. 2020 Dec; 89: 107018. Published online 2020 Sep 16.	YES		70%			
10	Xiao Bao Teng, Ya Shen, Ming-feng Han, Gang Yang et al. (2020) The value of high-flow nasal cannula oxygen therapy in treating novel coronavirus pneumonia. Eur J Clin Invest. 2020 Oct 31: e13435.	YES		100%			
11	Yue Nan Ni, Ting Wang, Binmiao Liang, and Zong An Liang (2021) The independent factors associated with oxygen therapy in COVID-19 patients under 65 years old. PLoS One. 2021; 16(1): e0245690. Published online 2021 Jan 22.	YES		80%			
12	Kelly Ansems, Felicitas Grundeis, Karolina Dahms, Agata Mikolajewska et al. (2021) Remdesivir for the treatment of COVID-19. Cochrane Database Syst Rev. 2021 Aug 5; 8(8):CD014962.	YES		100%			
13	Ahsan Ali Siddiqui (2020) The Role of Personal Protective Equipment (PPE) in Prevention of COVID-19 Novel Corona Virus and Fatalities occur due to Non-availability of the PPE. 2020-9(6). AJBSR. MS.ID.001458.	YES		80%			
14	Ahsan Siddiqui (2020) Is COVID-19 Pandemic is out of control as compared to other Medical and Surgical Diseases, where Proven treatment is available for ill Patients. Biomed J Sci & Tech Res 29(3)-2020. BJSTR. MS.ID.004816.	YES		100%			

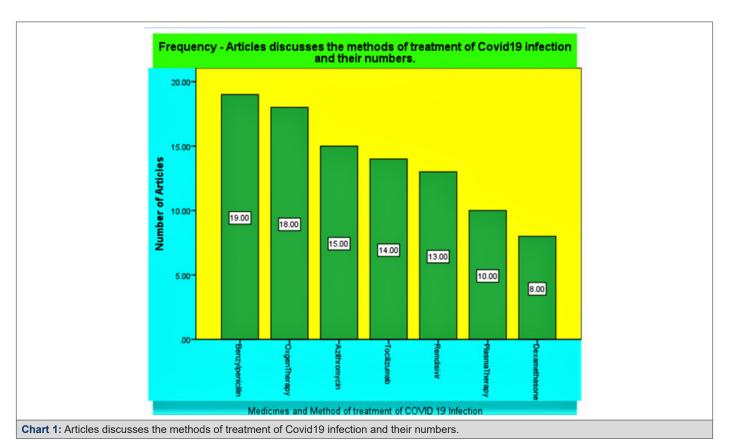
15	Ahsan Ali Siddiqui (2020) The Helpful Role of Medical Sciences and Technology for the Treatment of Medical/Surgical Diseases and the Epidemiology of COVID-19 Novel Corona Virus. 2020-2(4) OAJBS. ID.000200.	YES	 100%
16	Ahsan Ali Siddiqui (2020) Possible Treatment of COVID-19 in Current Pandemic and Successful Treatment of Other Medical and Surgical Diseases by Using Modern Medical Science and Technology. 2020-2(4) OAJBS.ID.000194.	YES	 100%
17	Ahsan Ali Siddiqui (2020) The Epidemiology of COVID-19 Novel Corona Virus in Incidence and the Distribution of the Disease across the World. 2020 - 9(4). AJBSR.MS.ID.001407.	YES	 80%
18	Ahsan Ali Siddiqui (2020) The Epidemiology of COVID-19 Novel Corona Virus in Incidence and the Distribution of the Disease across the World. 2020 - 9(4). AJBSR.MS.ID.001407.	YES	 100%
19	Ahsan Ali Siddiqui (2020) Covid-19 Proposed Treatment and other Medical Diseases Prevention and Treatment as Modern Medical Sciences is Beneficial for All of Us. Biomed J Sci & Tech Res 28(4)-2020. BJSTR. MS.ID.004696.	YES	 80%
20	Ahsan Ali Siddiqui (2020) Advancement in Medical Sciences to Treat Medical and Surgical Diseases including Prevention, Treatment and Vaccine Development of COVID-19 in Pandemic. Biomed J Sci & Tech Res 28(4)-2020. BJSTR. MS.ID.004695.	YES	 100%
21	Ahsan Ali Siddiqui (2020) The Use of Latest Medical Technology and Taking Benefits from Technology to Treat Various Medical Diseases Including Covid-19 in the Current Pandemic. 2020-2(3) OAJBS. ID.000185.	YES	 100%
22	Ahsan Ali Siddiqui, (2020) The Role of Medical Sciences to Save Lives of Mankind from Communicable and Non-Communicable Diseases Including Current COVID-19 Pandemic. 2020-2(3) OAJBS. ID.000184.	YES	 100%
23	Ahsan Ali Siddiqui. (2020) Covid-19 Novel Corona Virus Control and preventions In China and Discussing Their National Success to Back to Normal Life, While World Is Combatting the Deadly Viral Pandemic. Biomed J Sci & Tech Res 27(4)-2020. BJSTR. MS.ID.004544.	YES	 80%
24	Ahsan Ali Siddiqui (2020) The Recent Management and Treatment of COVID-19 Novel Corona Virus "Better use of Science, Better Treatment for COVID-19 Patients". 2020-2(3) OAJBS.ID.000181.	YES	 100%
25	Ahsan Ali Siddiqui. (2020) The Urgent Need of Reliable and Approved Vaccina-tion for COVID-19 Novel Corona Virus in Current Pandemic. Biomed J Sci & Tech Res 28(2)-2020. BJSTR. MS.ID.004623.	YES	 80%
26	Ahsan Ali Siddiqui. (2020) Role of Convalescent Plasma Therapy in Successful Prevention and Treatment of Covid-19 Novel Corona Virus Critical Patients, In 2020 Global Pandemic. Biomed J Sci & Tech Res 28(2)-2020.	YES	 100%
27	Ahsan Ali Siddiqui (2020) COVID-19 Pandemic and Public health Preventions to Reduce the Infection, Incidence and Distribution among the Community. 2020-2(2) OAJBS.ID.000178.	YES	 100%

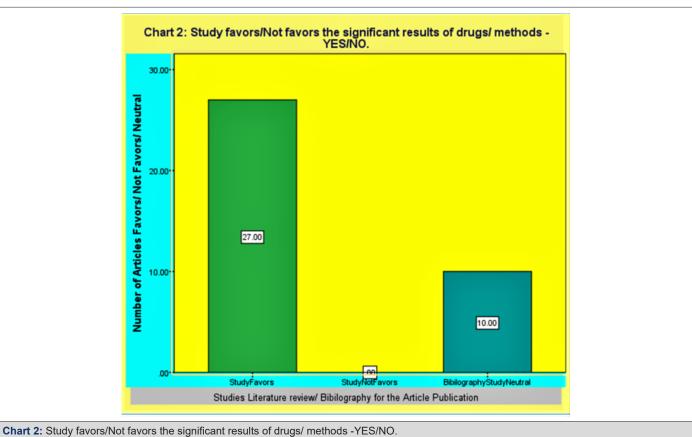
Measure and Statistical Analysis

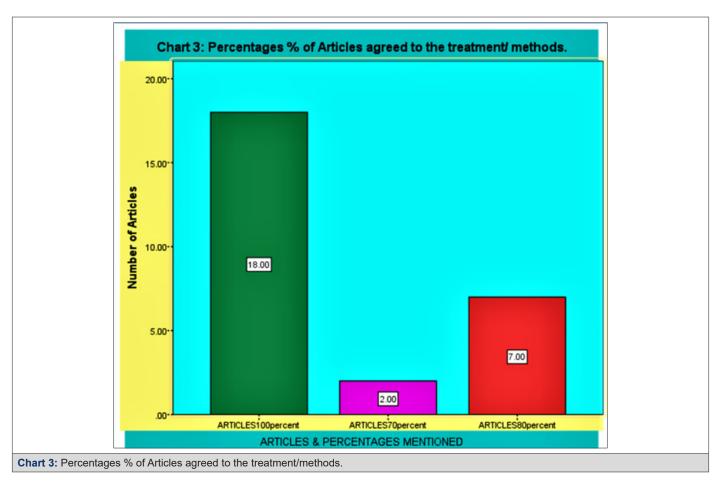
 $Chart\ 1: Articles\ discusses\ the\ methods\ of\ treatment\ of\ Covid\ 19$ infection and their numbers.

Chart 2: Study favors/Not favors the significant results of drugs/ methods -YES/NO.

Chart 3: Percentages % of Articles agreed to the treatment/ methods.







Results

The two tables and three SPSS Diagrams clearly states the data collection and Analysis regarding the literature review. First table shows the articles discuss the methods of treatment of Covid19 infection and their numbers. Second tables discuss the 27 randomly selected articles to show the successful treatment of COVID-19 infection by using different drugs and methods. SPSS Diagrams shows the article numbers and their percentages in the favor/ Not in favor/ Neutral of the current study. Recently Tocilizumab has been introduced to [7] treat patients with COVID-19 and researchers are investigating further the efficacy of this drug for different are patients. In Iran and China, some reports showed a positive effect of Tocilizumab on Saturation of Peripheral Oxygen (SPO₂) but results of CT scan in patients in different.

In some patients, CT scan showed reduced infiltration, however in other no change was observed [7] researchers hope this drug will make effective and promising treatment to improve lung tissue inflammation in patients with the fatal COVID-19 virus. The clinical data of 22 patients with severe COVID-19 were collected. [8] The Heart Rate (HR), Respiratory Rate (RR) and oxygenation index (PO_2/FiO_2) at 0, 6, 24 and 72 hours after treatment were compared between the HFNC oxygen therapy group and the Conventional Oxygen Therapy (COT) group. Current Pandemic of COVID-19 has taught all the [9] Global Health authorities such as WHO,

UN, UNESCO, UNICEF, UNHCR, EU Others and all Governments of 200 countries that we were not ready for COVID-19. Although Developed Countries such as USA, UK, France, and countries of EU spends Billions of US Dollars on their Health System but it did not stop the Deaths of COVID-19 Pandemic in their countries and they are affected the most in this world.

After seeing the Disaster resulting from [10] COVID-19 Pandemic in last five months all over the world, where almost 370,000 people died and approximately 6 million people are sick due to COVID-19. There is urgent need of VACCINE of COVID-19 Pandemic and there is news that may be Vaccine could be available in December 2020 or later. While there is no vaccine currently available for [11] COVID-19 patients the treatment with Convalescent Plasma with other western medicines saves lives of hundreds of thousands of patients in COVID-19 Pandemic. There is need of more advance research and action to find out the Treatment of COVID-19 Pandemic. Lessons should learn from COVID-19 Pandemic and it is not over yet as scientists predicts that COVID-19 is with us for next couple of years. The vaccine of [12] COVID-19 by medical sciences till now.

Discussion

Eight hundred thirty-three COVID-19 patients under 65 years old were included. [13] Oxygen therapy was required in 63.1%

of these patients, and the mortality was 2.9% among the oxygen therapy patients. Fever (odds ratio OR 2.072, 95% confidence interval CI 1.312-3.271, p=0.002), dyspnea (OR 2.522, 95% CI 1.213-5.243, p=0.013), chest distress (OR 2.278, 95% CI 1.160-4.473, p=0.017), elevated respiratory rate (OR 1.114, 95% CI 1.010-1.228, p=0.031), and decreased albumin (OR 0.932, 95% CI 0.880-0.987, p=0.016) and globulin levels (OR 0.929, 95% 0.881-0.980, p=0.007) were independent factors related to oxygen therapy. Oxygen therapy is highly required in COVID-19 patients under 65 years old who are admitted to the hospital, but the success rate is high [13] Based on the currently available evidence, [14]. We are moderately certain that remdesivir probably has little or no effect on all-cause mortality at up to day 28 in hospitalized adults with SARS-CoV-2 infection.

We are uncertain about the effects of remdesivir on clinical improvement and worsening. There were insufficient data available to validly examine the effect of remdesivir on mortality in subgroups depending on the extent of respiratory support at baseline. This could allow us to draw more reliable conclusions on the potential benefits and [14] harms of remdesivir in future updates of this review. Due to the living approach of this work, we will update the review periodically. Latest Inventions in Science and Medical Technology [15] are Blessing for all the Living being on this Planet Earth. From Human beings to Animals all are getting benefits to enjoy better health in twenty first century by modern treatment and surgical procedures for humans and Animals. Although the Advancement in Medical Technology and [15] Sciences still a lot of Research and hard work needed as still scientists could not find the appropriate and proven treatment and Vaccine of COVID-19.

This Article teaches us the lesson that [16] Technology in Medical Sciences and Inventions, Discovery of new Medicines and Surgical Instruments are Blessings for Mankind. Latest Technologies such as MRI Scans, CT scans, Chemotherapy, Radiotherapy, Nuclear Technology, X-rays/ Ultrasound, Latest Laparoscopic surgery, Endoscopy, Angioplasty others are treating more ill patients than ever before. But more medical research is needed to find the Treatment for COVID-19 Pandemic, Ebola, MERS, Avian Influenza, Swine Flu, and other Viral diseases. Urgent research institutes needed to [16] build up for the discovery of new Vaccines when needed in times of COVID-19 Pandemic. The main theme of this Article is to discuss the [17] Preventions, training, and control strategies against COVID-19 novel corona virus in China in initial first two months of Pandemic. When Chinese health authorities in Wuhan china found Novel Coronavirus Pneumonia (NCP) in patients in health facilities they first treated them with (TCM) Traditional Chinese medicines with western medicines. While the [17] Pandemic of COVID-19 is on the rise all around the world specially in the USA, Europe, and the UK.

Medical, Surgical Diseases Treatment with The Help of Medical Sciences

COVID-19 Pandemic has taught the [9] Global community a big lesson after losing Approximately 370,000 innocent lives and

approximately Half Million people being sick of COVID-19. The lesson is that in this high-tech 21st century where countries claim to be super Developed and Civilized countries don't have enough PPE for their health care workers and for local people. The Governments has not done their Homework to fight the Battle against COVID-19 Pandemic and people are still losing the [9] lives due to lack of PPE'S, not development of VACCINE, No confirmed TREATMENT available for COVID-19. Although the Incidence, Distribution, Illness, and mortality [18] due to COVID-19 Pandemic is reducing day by day as compared to peak in March 2020 in the EU, the UK, and the USA. But the Head of CDC USA warn the WHO and US Government that COVID-19 Pandemic has the tendency to become deadly as same as Spanish flu Pandemic in 1918 where approximately 60 to 100 million people died.

The governments of the 200 affected countries due to COVID-19 should understand the seriousness of the warnings and do the recommended preventions such as wearing Masks, washing hands with soap or sanitize it with Alcohol, social distancing and staying home as much as possible [18]. As we could compare Previous century [19] with current modern era of Medical Sciences and latest inventions. Sick patients are getting more better medicines and latest treatment/ surgical procedures and they are living longer than ever before. The availability of health services and latest medicines has made our life easier and solving the small health problems easier than ever before. Getting free prescriptions from pharmacies in some [19] countries with easily buying medicines is making good effect in the community. Modern Medical science inventions and latest treatment [20] has helped the people to live longer and enjoy healthy life as compared to past decades. Although still there is no Vaccination or treatment available for COVID-19 Pandemic but due to medical science and technology still supportive treatment is available. Currently Dexamethasone, Remdisivir, Favipiravir, Azithromycin and Plasma therapy has shown some promising results against COVID-19 Novel Cov. Preventions such as Hand washing for 40 seconds, Isolation, [20] wearing mask N95 others in crowded places also help to reduce the numbers of COVID-19 Cases. Current Pandemic of COVID-19 novel corona virus [21] has taught us a lesson that Global Health Agencies and Governments of the countries are not prepare for such Pandemic. The Governments has acted slowly or irresponsibly for the fight against COVID-19 Pandemic. Due to slow action to implement Preventive actions against COVID-19 approximately 300,000 people have lost their lives and more than four million people are Infected across the world.

[21] Better preparations are needed in the future to fight against such a cruel Pandemic disease. Current Pandemic of COVID-19 novel corona virus [22] has taught us a lesson that Global Health Agencies and Governments of the countries are not prepare for such Pandemic. The Governments has acted slowly or irresponsibly for the fight against COVID-19 Pandemic. Due to slow action to implement Preventive actions against COVID-19 approximately 300,000 people have lost their lives and more than four million people are Infected across the world. Better [22]

preparations are needed in the future to fight against such a cruel Pandemic disease. In the current 21st century [23] still people are dying with diseases without the treatment available as still we lack knowledge and research facilities to tackle the diseases. International health organizations for example WHO, UNICEF and UN should invest more on medical research and pharmaceuticals to find the upcoming Epidemics or Pandemics and prepare their available Vaccines and Treatment.

[23] Without taking serious steps and proper design and management the Task for Medical research for disease Preventions could not be complete. Due to the Advancement in Medical Sciences and Medical Treatment, [24] Invention's people are living longer and healthier than ever before. Nuclear Radiotherapy, Nuclear radiology, MRI Scan, CT scan, X Rays, Ultrasound, Angioplasty and Angiography others made the diagnosing and treatment easier for the patients. Current COVID-19 Pandemic, MERS, SARS, EBOLA, and other epidemics teaches us the lesson than as the world population grows, we need more research and technology to handle Pandemic such as COVID-19. [24] More resources and advance technology are needed to battle diseases and training for medical staff is needed [25-27].

Conclusion

To sum up, Plasma therapy, Oxygen therapy, Actemra, Dexamethasone, Remdesivir and other antibiotics has proven to be effective against the covid19 infection. Oxygen therapy at very initial stage of infection reduces the hypoxia and damage to lungs to the patient by the virus. The effort by this article is to discuss the treatment of covid19 infection and current published articles discussing the use of Medicines and medical methods.

Conflict of Interest

No conflict of interest

Acknowledgement

None

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