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COVID-19 (An International Trauma): A Brief Analysis on Research Trends, Impacts and Solutions

Dr. Mahima Sharma
Asst. Prof., Department of Zoology, S.S. Jain Subodh Girls College, Jaipur, Rajasthan, INDIA

Corresponding Author: mahima.sharma06@gmail.com

ABSTRACT

Corona virus disease (COVID-19); have been established as an epidemic of the century. COVID-19, a pandemic is spreading its web throughout the world affecting everyone resulting into mass destruction of populations causing human suffering, creating panic, disturbing everyone economically and stressing all kind of development of entire mankind. COVID-19 is a deadly disease that is supposed to be fatal in 4% of cases. In Severe cases this disease produces enormous respiratory harm like pneumonia, gastrointestinal disorders, weakened immune systems, kidney failure or even death. The pathology of COVID-19 is just similar to SARS and Middle Eastern respiratory syndrome (MERS) corona virus infection. There are no drugs or vaccines for corona viruses yet, including COVID-19. According to WHO Corona virus disease (COVID-19) outbreak situation is persisting with 421,792 confirmed cases and 18,883 confirmed deaths till 23 March 2020. Till now, there are no specific vaccines or treatments for COVID-19. Though, there are multiple of clinical trials, evaluations that may result into potential treatments are ongoing.

***Keywords*--** COVID-19, Corona Virus, Pneumonia, Immune System, Fatal, Epidemic

I. INTRODUCTION

COVID-19 is an emerging, rapidly evolving situation, continuously affecting the populations worldwide. COVID-19 is an acute disease which In Severe cases produces enormous alveolar damage and progressive respiratory harm and then to death [(1)]. COVID-19, a kind of pneumonia due to a kind of virus known as Corona virus was first diagnosed in Wuhan, China on 31 December 2019 [(2)]. On 30 January 2020 this disease was declared as a Public Health Emergency of International Concern. WHO named new corona virus disease as COVID-19 on 11 February 2020? WHO also characterized this disease as a pandemic on 11 March 2020, the first pandemic of corona virus [(3)]. COVID-19 is disease originated by a typical type of virus, causes disease in mammals as well as in birds. There is no specific treatment or vaccine for COVID-19 and Treatments include only, the management of diagnosed symptoms, strict isolation, supportive care and further experimental treatments [(4)]. Common symptoms include fever, sore throat, fatigue, coughing and shortness of breath. Most COVID-19 infected people face mild to moderate respiratory problems and can recover without requiring special treatment but older people and persons with pre-existing medical issues such as heart problems, diabetes, asthma and cancer may develop serious complications [(5)]. An individual is measured at risk if they have travelled to an area with group of people having transmission or had close contact with an infected person within the 14 days. (58).

II. EPIDEMIOLOGICAL METHODOLOGY

The best way to prevent and slow down transmission is be well informed about the COVID-19 virus by which the disease spreads. One can protect himself from infection by quarantines, staying self isolated at home, avoiding crowded places by washing your hands at least 20 seconds or using an alcohol based rub frequently and not touching eyes, nose, or mouth and face with unwashed hands. The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that everyone must be used to for respiratory etiquette [(23)]. On February 28, 2020, the WHO raised the threat of COVID-19 epidemic to grow as a pandemic worldwide at a "very high" level and result in to a serious public health risk. And now Probably, COVID-19 has emerged as a rapidly spreading situation. Situation was seen in China, on March 11, where COVID-19 cases has increased 13 times and in other countries cases tripled with 118,000 cases in 114 countries with 4,000 deaths (62). The corona viruses are continuously circulating in the human population and causing serious respiratory infections in adults and children world-wide [(8)].

Table 1: indicating the number of patients in different countries: source- Wikipedia (5th april 2020) corona virus pandemic

S. No	Epidemiological Rank	Country	Patients	Deaths	Persons Recovered	Ref. No.
1.	1.	United States	311,616	8489	14,943	36
2.	2.	Spain	126198	11,947	34,219	38
3.	3.	Italy	124,632	15,362	20,996	37
4.	4.	Germany	96,108	1446	23,192	40
5.	5.	France	89,953	7,560	14,008	41
6.	6.	China	81669	3,329	76,964	39
7.	7.	Iran	55,743	3,452	17,935	42
8.	8.	United Kingdom	41,903	4,313	-	43
9.	9.	Turkey	23,934	501	786	77
10.	10.	Switzerland	20,505	666	6,415	44
11	31.	India	3,374	77	267	45
12.	Total numbers	World	1203459	64,772	274,294	78

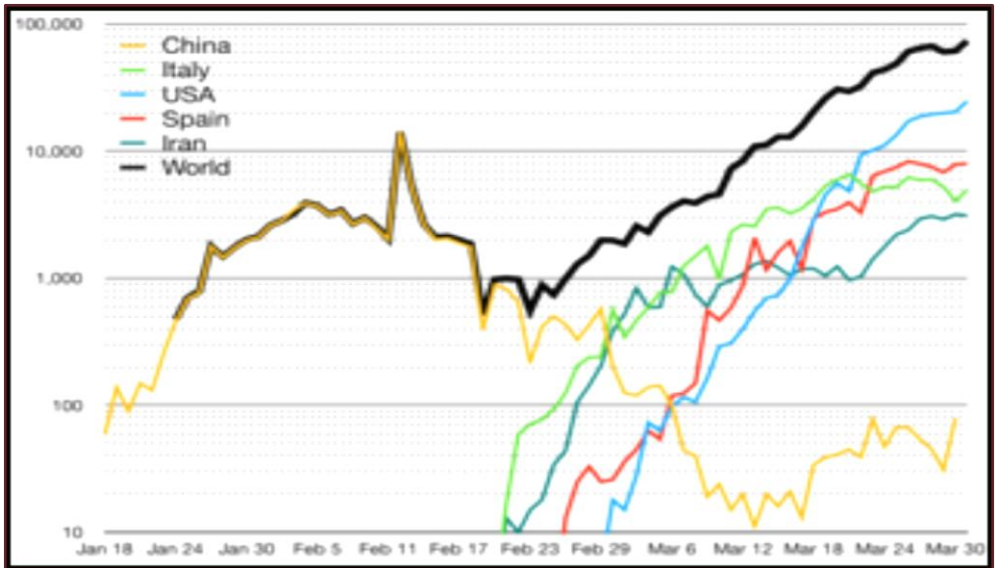

Figure 1: Semi-log plot of daily deaths due to COVID-19 in the world and top 5 countries (averaged with cases)(46)

WHO and other health organisations On March 2020, replaced the term of "social distancing" with "physical distancing", that explains the purpose to reduce physical contact and distance from social circles (56). The governments of many countries have or recommended self-quarantine for entire populations who were living in affected regions. Travel restrictions bans for citizens or visitors were implemented in many countries of the most affected areas of the pandemic.[47]. WHO general recommends to Avoid close contact with from acute respiratory infection people and to keep proper hygienic environment. They have suggested to avoid public exposure and gatherings by Immunocompromised individuals. Countries around the world begun mass quarantines and lockdown to prevent spread of the epidemic (80). India and many other countries launched complete nation-wide lockdown in the areas affected by novel Corona virus or Covid-19 to save millions of lives (81). In many countries of world after reviewing the status of corona virus cases decided, to discontinue travelling by different manner to prevent the spread of the infection.

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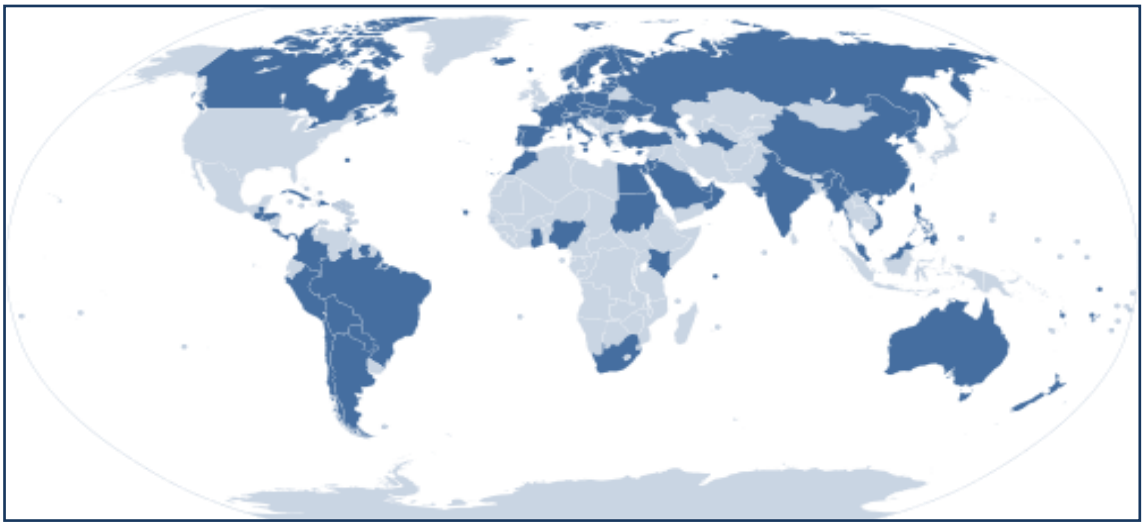

Figure 2: Countries with traveling ban due to COVID-19 pandemic (dark blue)(47)

COVID-19 virus or Corona viruses possess positive sensed single-stranded RNA (ssRNA) genome and a capsid of helical symmetry with the genome size of approximately 27 to 34 kilobases belonging to the Coronaviridae, supposed to be the largest among known RNA viruses [(6)]. The virus RNA contains 29,891 nucleotides, encode for 9,860 amino acids (63). The virus contains RNA-dependent RNA polymerase and exoribonuclease as a main replication and transcription machinery by which it divides continuously and reproduces [(7)] (57). The main replicase-transcriptase protein is the RNA-dependent RNA polymerase (RdRp). It is directly involved in the replication and transcription of RNA from an RNA strand. The other nonstructural proteins in the complex assist in the replication and transcription process. The exoribonuclease non-structural protein, for instance, provides extra fidelity to replication by providing a proofreading function which the RNA-dependent RNA polymerase (RdRp) doesn't have (7). RdRp directly participate in the synthesis of negative-sense RNA from the positive-sense RNA. Later on the replication of positive-sense RNA is formed from the negative-sense genomic RNA. (64). CoVs have RNA with a 5′-cap and 3′-poly-A tail and polyprotein 1a/1ab (pp1a/pp1ab). The transcription occurs through replication-transcription complex (RCT) enveloped in double-membrane vesicles. Transcription termination occurs at transcription regulatory sequences, present between six open reading frames (ORFs). Amongst them, a frameshift found between ORF1a and ORF1b produce of both polypeptides pp1a and pp1ab. Processing is done by chymotrypsin like protease or main protease present in virus. One or two papain-like proteases produce 16 non-structural proteins. Other ORFs encode for structural proteins, including membrane, envelope, spikes, and nucleocapsid proteins. (65). These non-structural proteins (nsp) show virulence mechanism and block the host innate immune response. [7]. Structural proteins, the envelope has a essential role in pathogenicity as it support viral assembly and release (66). The spike composed of glycoproteins made up of two subunits (S1 and S2). These S proteins make Homotrimers support to link with host receptors. (67) The comparision between the Sars-Cov-2 and Sars-CoV gene sequence analyzed the structure of transmembrane helical segments in the ORF1ab that encode for nsp2 and nsp3 and the presence of serine at position 723 instead of glycine residue, though the position 1010 is taken by proline at the place of isoleucine.(68).

Human coronaviruses were first of all discovered in 1960s [(5).] Corona viruses present in humans are of seven strains out of which four exhibit mild indications of the common cold. They are Human coronavirus OC43 (HCoV-OC43), Human coronavirus HKU1, Human coronavirus NL63 (HCoV-NL63, New Haven coronavirus) and Human coronavirus 229E (HCoV-229E) [(8)].

Other three exhibit symptoms which are much rigorous including Middle East respiratory syndrome-related corona virus (MERS-CoV) (novel coronavirus 2012), Severe acute respiratory syndrome corona virus (SARS-CoV or SARS-classic) and Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) also known as 2019-nCoV or "novel corona virus 2019 [(8)].

A critical type of corona virus SARS-CoV, Severe acute respiratory syndrome or SARS-classic out broke in 2003 and More than 8,000 people were infected out of which ten percent of them were announced dead [(9)]. An another new type of corona virus (MERS-CoV), Middle East respiratory syndrome (novel coronavirus 2012), outbroke in September 2012, caused the mortality of approximately 252 persons [(10)].

And now in December, 2019, an outbreak of another corona virus, Novel corona virus (COVID-19; previously known as 2019-nCoV) was reported in Wuhan, China [(11)] which has subsequently affected

multiple of countries globally. Corona virus disease 2019 (COVID-19) is a pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The Wuhan strain has been identified as a new strain of Betacoronavirus from group 2B and keeps genetic similarity approximately 70% to the SARS-CoV [12]. The virus was initially referred to as the 2019 novel corona virus or 2019-nCoV and now Covid-19 virus on 13 March 2020 [14]. The virus is 96% similar to a bat corona virus, thus it is suspecting to be originated from bats [13]. The genome of COVID-19 (HCoV), collected from Wuhan patients with atypical pneumonia possess 89% nucleotide features of bat SARS like CoVZXC21 and 82% with that of human SARS-CoV these analysis gives indication that evolving probability of SARS-CoV-2 can be from a strain found in bats. Though, its origin is completely unidentified. (63).

III. DISCUSSION

Research is needed to identify the exact characteristics of COVID-19 and its pathogenic mechanism. The data related to pathogenic mechanism confirm the pneumonia and inhibition in immune response. It is mainly spread among people through respiratory droplets from coughing and sneezing. The viability of virus varies depending on the surface attached such as for three hours in aerosols and up to three days on plastic and stainless steel [16]. Though the persons infected with the virus may exhibit asymptomatic features, and many of them developed flu-like symptoms including cough, fever and shortness of breathe [17]. Emergency signs include difficulty in breathing, constant chest pain or tightness, dizziness and bluish face or lips. These symptoms require instantaneous medical attention [18]. Less commonly, upper respiratory symptoms such as sneezing, runny nose, sore throat may be seen. Symptoms such as nausea, vomiting, and diarrhoea have been seen among patients in several studies, with percentages varying from 3% to 31% of cases depending on the study [19] [20]. The pandemic has resulted in travel restrictions and nationwide lockdowns in several countries. As of 5 April 2020, there have been at least 64,700 deaths confirmed deaths and more than 1.2 million confirmed cases in the corona virus pneumonia pandemic and more than people with 247,000 got recovery from the disease [15]. In some, the disease may progress to exhaustive pneumonia [21] and many Critical diseases such as respiratory failure, septic shock, and/or multiple organ dysfunction (MOD) or failure (MOF) which occurred in 5% of cases [73]. As it is common in this infection, that there is delay of developing symptoms, from the time when a person was infected with the virus, known as the incubation period. The incubation period for COVID-19 is typically five to six days but may range from two to fourteen days [21]. Histopathological data suggested that the lungs of patients who undergone for lung lobectomies due to adenocarcinoma got infection at the time of surgery. Vascular congestion and inflammatory fibrinoid and hyperplasia of pneumocytes were also seen in other patients (69). According to the International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), gives a life-threatening organ dysfunctioning (74). The COVID-19 patients with sepsis show serious symptoms of multi organ failure including respiratory problems such as severe dyspnea and hypoxemia, renal disorders, tachycardia, hyperbilirubinemia, acidosis, coagulopathy, and thrombocytopenia. The Sequential Organ Failure Assessment (SOFA) score calculated ICU mortality due to multi organ failure by assaying the given clinical data. (75). These datas are also give validation in childeren. (76). WHO guidelines Released on January 28, 2020 suggest the measures to recognize COVID-19 patients with severe acute respiratory disease (ARDS) and to make strategies for prevention, to provide supportive therapy, monitoring and management of respiratory collapse and septic shock due to ARDS. There is a sudden rapidly worsening of clinical conditions were seen in a percentage of cases after a week including respiratory failure and MOD/MOF. As a reference, the criteria of the severity of respiratory insufficiency and the diagnostic criteria of sepsis and septic shock can be used. [13]

Diagnostic procedure includes respiratory or blood samples. Reports are usually available within a few hours to days (59) (60). At this time, there are no specific treatments that are both safe and effective in humans for COVID-19 [26]. However, there are many ongoing clinical trials evaluating potential treatments. WHO is continuously providing updated information and clinical findings concluding that only to slow down the sociability rate will decrease the risk of infection? There are multiple of attempts are in progress to develop a vaccine for COVID-19 effective in humans. WHO In February 2020 said that not to expect for availability of vaccine in less than 18 months for SARS-CoV-2 [25]. Previously, vaccines were tried to develop for the family of corona virus effective to treat, humans (SARS) and (MERS). Till date Vaccines against SARS and MERS have been tested in animals only. Till 2020, there is no cure or vaccine for SARS that is seen effective in humans [26]. Several investigational drugs are being tested in hundreds of clinical trials including two of the approved drugs (chloroquine and hydroxychloroquine) and one of the investigational agents Remdesivir is currently used in the United States [30]. Chloroquine is an orally administered drug that is well known for the treatment of malaria and certain inflammatory conditions. Hydroxychloroquine is used for treatment of rheumatoid arthritis and systemic lupus erythematosus. Both drugs show in-vitro activity against SARS-CoV, SARS-CoV-2 and other Corona viruses [32]. Clinical trials reported that hydroxychloroquine alone or in the combination of azithromycin reduces findings of SARS-CoV-2 RNA in upper respiratory tract [33]. Remdesivir is an intravenous drug with wide spectrum of antiviral activity that inhibits RNA replication by premature termination of RNA

transcription and show in-vitro activity against SARS-CoV-2 and in-vitro as well as in-vivo activity against betacoronaviruses [31]. Studies suggested remdesivir (GS5734) an antiviral drug which was positively tested in a rhesus macaque for MERS-CoV infection (71) act as an inhibitor of RNA polymerase against multiple of RNA viruses, could be effective for prophylaxis and therapy of HCoVs infections. (70) Lopinavir-Ritonavir are the drugs still under clinical trials in China (34). Both of these drugs Lopinavir and Saquinavir were the most and the least powerful inhibitors of cronovirus proteinase, respectively. (35) A combination of anti-HIV drugs Lopinavir and Ritonavir administered to treat patients with the Corona virus infection. The Indian Council of Medical Research (ICMR) had approved the use of this drug combination even in patients of old ages [18].

The known human CoV (HCoV) includes HCoV-229E, -OC43, -NL63, -HKU1, and the more widely known severe acute respiratory syndrome coronavirus (SARS-CoV) which caused a global threat with high mortality in 2003. [12]. In 2012, the World Health Organization (WHO) designated a sixth type of HCoV infection identified as the Middle East respiratory syndrome coronavirus (MERS-CoV) which is associated with high fatality.[13]. World Corona virus Infection can be diagnosed and confirmed by reverse transcription polymerase chain reaction (rRT-PCR) of infected secretions or CT imaging(48)(49). The WHO [27], US-FDA Food and Drug Administration [28], and the Chinese government and drug administration [29] are coordinating with academic and industry researchers to speed development of vaccines, antiviral medicines and antibodies therapies. The Chinese medicinal plants Bupleurum spp, Heteromorpha species, and Scrophularia scorodonia, possess triterpene glycosides such as saikosaponins (A, B_2, C, and D), that act against HCoV-22E9 (50). Extracts from Lycoris radiata, Artemisia annua, Pyrrosia lingua, and Lindera aggregata also showed anti–SARS-CoV effect from a screening analysis using hundreds of people (51). Isatis indigotica and Torreya nucifera also show antiviral activity against SARS-CoV enzymes, due to the presence of nsP13 helicase and 3CL protease, myricetin, scutellarein, and phenolic compounds (52) (53) (54). Other anti-CoV natural medicines include the water extract from Houttuynia cordata , which has been observed to exhibit several antiviral mechanisms against SARS-CoV, such as inhibiting the viral 3CL protease and blocking the viral RNA-dependent RNA polymerase activity(55). The death-to-case ratio Based on Johns Hopkins University statistics is measured 5.0% (47,256/937,567) as on 2 April 2020 (61).

IV. CONCLUSION

There are no specific treatments for CoV infection and preventive vaccines are still being explored. Thus, the situation reflects the need to develop effective antivirals for prophylaxis and treatment of CoV infection. The public of whole world should be provided with appropriate health advices, suggestions and formal Temporary Recommendations. An emergency committee set up by WHO overviews the situation, for countries of entire world about the investigations, the extent of human-to-human transmission, the medical spectrum of the disease, healthcare facilities for prevention and controls its severity in the community. A continuous emphasis on the research of Corona virus genomic sequencing, way of transmission, diagnostics, quick formation of potential vaccines medicines and other therapeutics that would be feasible for low and middle income countries also. The COVID-19 pandemic outbreak has impacted everyone all across the world socially, mentally, physically, psychologically and economically. There is still necessary to increase the support to health workers, manufacturing capability and strengthening critical medical supplies. Regular communication and providing advice through trusted experts to the public should be prioritize for positive outcomes.

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