

COVID-19: An overview of current scenario

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ABSTRACT

Over a span of few decades, the world has seen the emergence of new viruses that have posed serious problems to global health. COVID-19 is a major pathogenic threat to the modern world that primarily shoots the respiratory system of human beings. Wuhan which is the capital city of Hubei, China was the first place in the world where first cases of COVID-19 emerged and the scores of cases significantly increased at an immense rate leading to city isolation and establishment of new specially designed hospitals. SARS-CoV had emerged from bats in china (2002) and MERS-CoV from camels transmitted via bats in Middle East (2012) where the previous versions of COVID-19 took place. Infections with SARS-CoV-2 are now widespread, like Nuclear Chain Reaction (NRC). In this review we will discuss the COVID-19 origin, transmission, incubation, diagnosis and therapies available at the present scenario.

Keywords COVID-19, SARS-CoV-2, therapies, diagnosis

INTRODUCTION

COVID-19 is a major pathogenic threat to the modern world that primarily shoots the respiratory system of human beings. Wuhan which is the capital city of Hubei, China was the first place in the world where first cases of COVID-19 emerged and the scores of cases significantly increased at an immense rate leading to city isolation and establishment of new specially designed hospitals. After china the COVID-19 reached almost every corner of the world in which some of the countries were badly hit in the early time like South Korea, Iran, and in the later United States of America, Spain, Italy, Germany, Turkey, Russia, United Kingdom, France. SARS-CoV had emerged from bats in china in 2002 (Li et al., 2005) and MERS-CoV from camels transmitted via bats in Middle East (2012) where the previous versions of COVID-19 took place (Corman et al., 2014; Rothan et al., 2020b). The causative pathogen responsible for the emergence of COVID-19 was found to be a novel corona-virus declared on eight January, 2020 by CCDCP (Li et al., 2020b). WHO on 30 January, 2020 declared that COVID-19 emergence worldwide is a public health emergency and announced measures for its management (Mahase, 2020). Phylogenetically after viral genetic makeup analysis it has been demonstrated that COVID-19 is very close to SARS-CoV (Lu et al., 2020). Corona-viridae is the family of viruses of ssRNA to which COVID-19 belongs. There are about eight to ten ORF in maximum number of coronaviruses. COVID-19 produces about six to nine sub-genomic RNAs during the process of replication resulting protein bio-synthesis of associated & structural protein molecules from downstream open reading frames (Sola et al., 2015). To accomplish the viral replication

cycle proteins like nucleocapsid-protein, membrane-protein, spike-protein and envelope-proteins are mandatory which are bio-synthesized from sub-genomic mRNA (Fehr et al., 2015). About fifteen to thirty percent of CCs are caused by human COVID-19 (Fung et al., 2019). In human blood circulation about 4 COVID-19 viruses like 229E, OC43, HKU1 and NL63 which are responsible for mild respiratory problems (Singhal, 2020). As of 5th of May 2020 3,365,052 cases of COVID-19 globally were reported in which 237,720 died and 1,069,801 subjects recovered (<https://www.worldometers.info/coronavirus/>).

Origin and transmission

The origin & transmission are very crucial to be elucidated in order to combat the deadly virus by taking effective management plans. Results from various genetic & epidemiologic findings, proposed that Corona virus emerged from an animal to human transmission then it lead to human-human communication (Chan et al., 2020; Rothe et al., 2020). One of the most important point is that subjects in recovering stage are dormant source of emanation (Rothe et al., 2020). Scientists in the early stages of SARS-CoV pointed on raccoon dogs & palm civets as main reservoir of source. In addition the samples of civets at food market were only diagnosed positive for viral infection which proposed civet palm may be the secondary hosts (Kan et al., 2005). Samples taken from healthy subjects in Hong Kong during the year 2001 demonstrated 2.5% increase in antibodies against SARS-CoV, showing SARS-CoV was already present in blood just before the outburst in 2003 (Zheng et al., 2004). The anti-SARS-CoV antibodies were also found in rhinolophus bats showing another evidence of viral multiplication source (Shi et al., 2008). Now considering bats as the main source of corona virus was supported by a study via research that MERS-CoV was found to be in *Perimyotis* & *Pipistrellus* bats (Annan et al., 2013; Huynh et al., 2012; Lau et al., 2013). Some scientists proposed snakes may be the host but the genetic makeup similarities between COVID-19 and SARS-CoV in bats rejected the statement and bats were declared as main key reservoirs based on the evidence (Chan et al., 2020; Lu et al., 2020).

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Incubation period

It has not been finalized the actual incubation time of COVID-19 however it has been proposed based on findings to be five to six days on an average basis, in addition there is evidence that the incubation time may be up to fourteen days and is required to be upper limit to keep the suspected subjects under medical attention & quarantine (Backer et al., 2020b; Li et al., 2020a). The eighty eight subjects confirmed in Wuhan, China in the initial days of pandemic were focused to analyze the data on travel to & from Wuhan to find out the vulnerability of exposure time designating interval of 6.4 days ranging from 2.1 to 11.1 days (Backer et al., 2020a). The one fifty eight cases which were outside the Wuhan city proposed a median incubation time of five days ranging from two to fourteen days (Linton et al., 2020). Evidence revealed by analyzing more ten cases in China indicate the incubation time of 5.2 days (Bai et al., 2020). The SARS-CoV is having a mean of 5 days incubation period ranging from two to fourteen days which is in the line of human COVID-19 and the non-SARS is having three days ranging from two to five days (Lessler et al., 2009; Varia et al., 2003).

Mortality rate

As of 2nd May, 2020 out total 3,443,306 number of COVID-19 cases death of 242,244 subjects happened worldwide which is comprising of about 7% mortality rate (<https://www.worldometers.info/coronavirus/>). The mortality rate in SARS-CoV was 10% and in MERS-CoV was 34% which is much higher than COVID-19 (Malik et al., 2020; Meng et al., 2020). In China about seventeen deaths took place on 22 January, 2020, & and increased to fifty six deaths increased in 25 January, 2020 (Wang et al., 2020d). Among 2684 COVID-19 cases 2.84% died as on 25 Jan, 2020 & the median age of deaths was seventy five years (Wang et al., 2020d).

Subjects at risk

There is no clear evidence yet which age group is more susceptible however among the subjects which are infected by COVID-19 the death rate is more in older subjects as compared to young. The current scene of COVID-19 depicts all age group of patients are equally susceptible. Although subjects who are in exposed hotspot work places like hospitals the prime example being the health care workers and the patients suffering from ailments other than COVID-19 are usually at high risk of getting infected (Meng et al., 2020). In the beginning of the pandemic about one thirty eight subjects which were hospitalized with corona virus in China, fifty seven comprising of forty one percent were assumed to have been infected in hospital only, including forty subjects which were health care workers consisting off twenty nine percent and seventeen patients hospitalized due to other causes comprising of twelve percent (Wang et al., 2020b). Out of 1,716 health care professionals in China (14, February, 2020) were infected with SARS-CoV2 comprising of three point eight percent subjects nationwide & six of that cluster who have died (Meng et al., 2020).

Clinical presentation

The large proportion of patients presented dry cough, breathlessness, muscle pain, fatigue, headache, sore throat, diarrhea, vomiting & confusion (Chen et al., 2020b; Guan et al., 2020). Subjects who were screened via CT scan demonstrated bilateral pneumonia having ground glass opacity & patchy shadows were the most prevalent (Guan et al., 2020; Wang et al., 2020b). The COVID-19 subjects in China who were hospitalized, near about 1/4 to 1/3 lead to dangerous complications like ARDS, arrhythmia & shock & were shifted to ICU (Chen et al., 2020b; Huang et al., 2020; Wang et al., 2020b). Generally subjects of

higher age (Older) group & the activeness of prevailing co-morbidities like hypertension, CVS disorders & Diabetes were connected with poor prognosis (Liu et al., 2020; Wang et al., 2020b; Yang et al., 2020)

Diagnosis

The first line methods to diagnose COVID-19 are the molecular based approaches and the nucleic acid testing is one of the specific diagnostic tests to confirm the suspected cases (Ahn et al., 2020). However in addition to nucleic acid testing there are various other assays like virus marker & serum antibody testing which can be done with short span of time to diagnose COVID-19 (Chen et al., 2015; Meyer et al., 2014). As the COVID-19 breakout took place in Wuhan China the genome sequence was rapidly released to the public database and it helped to diagnose it more appropriately (Zhu et al., 2020). The RT-PCR has demonstrated to be more accurate, specific and precise way to diagnose the respiratory pathogenic agents in subjects with ARI (Wang et al., 2020a). The earlier virus namely SARS-CoV was diagnosed by RT-PCR & NGS. The genome sequence of COVID-19 released was utilized to design specific primers & probes for its diagnosis (Corman et al., 2020). In many Countries the host institutes have standardized some protocols and provide some specific genome sequence which was later sheared on WHO database respectively (Ahn et al., 2020).

Pathogenesis

The subjects suffering with COVID-19 demonstrated increased leukocyte number, respiratory findings were not normal, and there were higher blood levels of inflammatory cytokine proteins (Rothan et al., 2020a). A COVID-19 subject at five days of high body temperature showed cough, coarse breathing sounds & temperature of thirty nine degree Celsius. The results from RT-PCR of sputum were positive leading to confirmation of COVID-19 (Lei et al., 2020). The leukocyte count was 2.91×10^9 cells per liter of which seventy percent were neutrophils declaring leucopenia. Higher levels of C-reactive protein were noted with level of 16.6mg/liter of blood. The RBC sedimentation rate was also higher (Lei et al., 2020). The COVID-19 pathogenesis starts from when the Corona virus attacks respiratory system causing pneumonia, RNAemia, incidence of ground glass opacities & ACI (Huang et al., 2020). The high blood levels of cytokine and chemokine in subjects with COVID-19 were IL1- β , IL1RA, GMCSF, IFN- γ , IP10, MCP1, IL7, IL8, IL9, IL10, basic FGF2, GCSF MIP1 α , MIP1 β , PDGFB, TNF α , and VEGFA. The severe cases of COVID-19 subjects had IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1 α , and TNF α pro-inflammatory cytokines in high levels and were responsible for the severity (Huang et al., 2020)

TREATMENT THERAPIES CURRENTLY IN PRACTICE

There is no specific antiviral treatment recommended for COVID-19, and no vaccine is currently available. The treatment is symptomatic, and oxygen therapy represents the major treatment intervention for patients with severe infection. Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy, whereas hemodynamic support is essential for managing septic shock. At present, the treatments of patients with SARS-CoV-2 infection are mainly symptomatic treatments. However several treatment options are currently employed to treat this pandemic:

Nucleoside analogues

The prominent antivirals are the nucleoside analogues are being increasingly used. They act by interfering with the nucleotide bio-synthesis causing termination of viral replication. In other way they generally act to inhibit production of viral RNA synthesis. Nucleoside analogues shoot the RNA dependent RNA polymerase which is key player in the replication of viral RNA (Debing et al., 2014; Leyssen et al., 2005; Wang et al., 2016).

Favipiravir

Favipiravir is one of the nucleoside analogue approved in Japan for the treatment of Influenza virus & can block the replication of viruses like Ebola, Yellow fever, Chikun-gunya, Noro-virus & entero-virus (De Clercq, 2019). A Study has demonstrated that Favipiravir is lead molecule for the treatment of SARS-CoV2 having efficacious anti-viral activities in Vero E6 cells with EC50 61.88 μ M (Wang et al., 2020c). Favipiravir was given in combination with IF- α (with clinical trial number ChiCTR2000029600) & or baloxavir-marboxil (with clinical trial number ChiCTR2000029544) to COVID-19 patients (Ahn et al., 2020).

Ribavirin

Ribavirin is the popular nucleoside analogue approved for the treatment of HCV and RSV & has been use for the treatment of subjects having SARS-CoV or MERS-CoV (Al-Tawfiq et al., 2014; So et al., 2003; Zumla et al., 2016). In addition to that ribavirin showed anemia at high doses and the efficacy and toxicity are also unpredictable (Al-Tawfiq et al., 2014; Zumla et al., 2016). Ribavirin was also given in combination with interferon (clinical trial number ChiCTR2000029387) to activate anti-viral response however it was given in low doses to prevent adverse effects. The drugs which are administered in combination forms should be monitored very carefully.

Remdesivir

Remdesivir is an approved anti-HIV-RT inhibitor has almost similar structures to that of Tenofovir & alafenamide (Choy, 2016). The Remdesivir has demonstrated potential therapeutic activity against SARS-CoV as well as MERS-CoV in HAE and has the potential to block the MERS-CoV replication in the mouse model (Sheahan et al., 2017). Remdesivir was targeted against the deadly Ebola and the therapeutic efficacy was drug remdesivir was approved to be given in patients having SARS-CoV2 in the USA (Holshue et al., 2020). The activity against SARS-CoV2 was investigated in Vero cells (Wang et al., 2020c). The 2 clinical phase III trials were carried out to investigate remdesivir in subjects suffering from SARS-CoV2 (clinical trial numbers as NCT04252664 and NCT04257656). However, the clinical efficacies, as well as toxicity profile, need to be validated via clinical output in subjects having SARS-CoV2.

Anti-malarial: Chloroquine

A prominent and cheap drug approved for malaria acts by sequestering the protons into suicidal bags to level up the pH intracellularly. The drug has broad spectrum anti-viral potential by blocking endosomal acidification which is essential for membrane fusion/melting between virus and host cell (Savarino et al.; Yan et al., 2013). In the previous investigations it has been elucidated that chloroquine is having in-vitro anti-viral potential against many viruses like nipah, Hendra, Ebola, SARS, MERS & HIV (Keyaerts et al., 2004; Kono et al., 2008; Savarino et al., 2003; Vincent et al., 2005). The blocking activity against SARS-CoV-2 of chloroquine is due to interference with the glycosylation of cell receptor (Vincent et al., 2005). In china chloroquine was administered to COVID-19 subjects to

investigate the clinical efficacy and toxicity and results showed that it blocks the exacerbation of corona virus (Gao et al., 2020). On the basis of strong pre-clinical and clinical investigations its concluded that it's a potential anti-viral candidate against SARS-CoV-2.

Protease inhibitors

The protease inhibitors are the main pillars in the anti-viral drug therapy act by binding with the viral protease enzyme that are required for breakdown of poly-proteins in-order to survive (Mukherjee et al., 2008; Wu et al., 2004). Lopanavir and Ritonavir are the two prominent examples of protease inhibitors are considered to have anti-SARS and MERs-CoV activities (Chu et al., 2004; Que et al., 2003). Clinical trials (ChiCTR2000029539) were carried out in SARS-CoV-2 subjects for anti-protease activity. Drug repurposing will be great alternative for COVID-19 disaster in addition to novel therapies to be developed against its specific antigens.

Vaccines

Vaccines have revolutionized the therapeutic all time in dealing with the deadly disease and by proper vaccination many of these deadly diseases have been vanished from the world the prime example being smallpox. The best way for safeguarding lives from infections as vaccines are more economical than drugs & reduction in mortality/morbidity without long lasting effects (André, 2001; Li et al., 2019). The therapeutic as well as preventive vaccines would be the best to safeguard the world health (André, 2001; Pronker et al., 2013). From the last 20 years 3 deadly viruses namely SARS-CoV, MERS-CoV, and SARS-CoV2 appeared globally & impacted every domain of life (Guarner, 2020) and from twenty years no vaccine has been developed yet. There is immense need of vaccines to combat against such corona viruses otherwise it can lead to destroy the health human lives one day. However various research groups are working on vaccines against COVID-19 by using many approaches & we are hoping to have it in the near time. The recognition mechanism of virus antigens & host surface proteins is the most crucial/critical way to understand cross-species transmission & host tropism and the development of in-vivo models for development of vaccine (Guarner, 2020). The most important shoot point on the COVID-19 are spike proteins to effectively develop vaccines as it makes the binding communication between virus and host cells (Coutard et al., 2020; Guarner, 2020; Li, 2016). The host receptors that are recognized by COVID-19 spike proteins are like ACE2, APN, and DPP4. The SARS-CoV and SARS-CoV2 are nearly 75% similar homology for the spike protein (Coutard et al., 2020). In the spike protein there are 2c subunits S1 and S2, S1 contains RBD and S2 is responsible for fusion of two membranes that is viral and host membrane (Graham et al., 2013; He et al., 2004).

Convalescent Plasma Therapy (CPT)

From more than 10 decades CPT has been used as a special adaptive immunotherapy for the safeguard and treatment of various infectious ailments. CPT from last twenty years was increasingly employed for the treatment of SARS-CoV, MERS-CoV and H1N1 pandemic with appreciable efficacy and safety profile (Cheng et al., 2005; Hung et al., 2011; Ko et al., 2018; Zhou et al., 2007). From the meta-analysis of about thirty two studies of SARS-CoV & influenza demonstrated statically dramatic decrease in the pooled odds of mortality following CPT as compared to inert preparation's (Mair-Jenkins et al., 2015). The CPT doesnot demonstrated any dramatic enhancement of survival in the Ebola virus (Van Griensven et al., 2016). The CPT could give a better therapeutic response in SARS-CoV-2 as

the virological properties of SARS-CoV, MERS-CoV and SARS-CoV-2 are almost similar (Chen et al., 2020a; Lee et al., 2020). Subjects recovered from SARS-CoV-2 can be the potential source of Convalescent plasma (Duan et al., 2020).

Melatonin

Melatonin is physiological molecule with many biological activities & has been promisingly used in the treatment of insomnia, delirium, atherosclerosis, respiratory disorders & viral diseases (Howlader et al., 2017). The melatonin has produced promisingly results previously against ARS caused by bacterial, viral or radiation (Huang et al., 2010; Wu et al., 2019; Yip et al., 2013). There is no direct evidence that melatonin exerts direct anti-viral effects however it exerts in-direct anti-viral effects & indirect effects are in the form of anti-inflammatory, anti-oxidative & the immune activation characteristics (Anderson et al., 2015; Boga et al., 2012; Junaid et al., 2020; Reiter et al., 2020a; Reiter et al., 2020b). In mouse model of encephalitis (by virus) on melatonin administration there was decreased viremia reduction in paralysis & death and even decrease in viral load (Ben-Nathan et al., 1995). There was reduction in ALOI, secretion of pro-inflammatory cytokines, inflammatory cells in RSV models, and these investigations were studied by Reiter et al. which supported the utilization of melatonin in viral infections (Reiter et al., 2020b). The melatonin exerts its anti-inflammatory effect by various pathways one being the sirtuin-1 which inhibits HMGB1 causing down-regulation of the polarization of macrophages to pro-inflammatory type (Hardeland, 2018). In acute lung injury due to sepsis the SIETI increase LI & inflammation and the administration of melatonin may prove therapeutically beneficial (Wang et al., 2019). The melatonin acts by inhibiting Nuclear factor kappa-B which is main key player in the production of pro-inflammatory cytokines and cause decrease in inflammation in acute respiratory distress syndrome (Ling et al., 2018; Sun et al., 2015). It also down-regulates Nuclear factor kappa-B stimulation in the T-lymphocytes and lung tissue (da Cunha Pedrosa et al., 2010; Shang et al., 2009).

CONCLUSION

The COVID-19 has tremendously hit every perspective of life from daily life to economic crunch worldwide. The drugs as well as vaccines are at early stage of development for the treatment of SARS-CoV-2 and a great progress in the elucidation of total genome sequence to initiate clinical trials with already existing anti-viral drugs and vaccines to plasma therapy. There is need of collaborative research throughout the world to combat the deadly virus by shearing the protocols, databases, unanswered questions about new corona virus pandemic. The globally sheared SARS-CoV-2 sequences and other information have helped to design specific, precise and fastest diagnostic methods that are need of hour. There is need of drug-repurposing as lot drugs like choloquine, Favipiravir, Remdesivir, Ribavirin etc. have shown promising results and there may many other drugs which need to be investigated in-terms of safety and efficacy. In addition to drug repurposing there is need of development of vaccines which can efficaciously combat with COVID-19. The development of rapid diagnostic tests and therapies many drug manufacturing companies initiated the development of vaccines against COVID-19. The public should also cooperate with health care professionals, government officials to prevent further spread of COVID-19 by remaining indoors, avoiding gatherings, maintain distances from each other.

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CONFLICT OF INTEREST

None.

ABBREVIATIONS

ARI: acute respiratory infection
 ALOI: acute lung oxidative injury
 ARS: acute respiratory stress
 ACI: Acute Cardiac Injury
 ARDS: acute respiratory distress syndrome
 CCDCP: Chinese Center for Disease Control and Prevention
 CC: Common Cold
 CT: Computed Topography
 HCV: hepatitis C virus ORF
 HMGB1: high mobility group boxchromosomal protein 1
 HAE: human airway epithelial
 HIV-RT: Human Immune deficiency Virus- Reverse Transcriptase
 ICU: Intensive care unit
 LM; Lung Injury
 MERS-CoV: Middle East respiratory syndrome
 NGS: next-generation sequencing
 ORF: Open Reading Frames
 RSV: respiratory syncytial virus
 RBD: receptor-binding domain
 RTPCR: Real Time Polymerase chain reaction
 RSV: respiratory syncytial virus
 SARS-CoV: severe acute respiratory syndrome

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