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MODEST REVIEW ON HUMAN NOVEL CORONAVIRUSINFECTION (NCOVID 19) AND ROLE OF CLINICAL PHARMACIST IN PANDEMICOUTBREAK

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ABSTRACT

Human Novel Coronavirus (ncovid-19) is an important pathogen globally. In the days and weeks ahead, we expect to see the number of cases, the number of deaths, and the number of affected countries climbs even higher. We have therefore made the assessment that COVID-19 characterized as a pandemic. This review provides a comprehensive, up-to-date assessment on current issues of the basic virology, pathogenesis, clinical epidemiology, and laboratory features, treatment and prevention strategies for ncovid-19. However, current evidences on ncovid-19 demonstrate that these viruses effectively spread via infected droplets, aerosols, contacts, hands and surfaces. It is transmitted between individuals. Previously, two coronaviruses infecting animals have evolved and caused outbreaks in humans i.e. SARS-cov (Severe Acute Respiratory Syndrome) and MERS-cov (Middle East Respiratory Syndrome). Coronavirus is responsible for a substantial proportion of upper respiratory tract infections. These viruses traditionally associated with dry cough, cold, shortness of breath, sore throat and fever. So, optimal treatment involves prompt diagnosis and it is slightly manageable with current technologies. Indeed, whether the clinical manifestations of coronavirus are related directly to viral pathogenicity or secondary to the host immune response is the subject of ongoing research. There are currently no approved antiviral therapies and treatment remains primarily supportive.Pharmacists are a trusted and accessible resource for the public during this public health emergency.Role of pharmacists is to ensure the availability and timely provision of the safest and most effective therapy in pandemic disease.

INTRODUCTION

The term modest usually refers to provide the limited data and to prove the widespread of COVID-19 in an effective manner. On January 31, 2020, the World Health Organization (WHO) designated the outbreak of new coronavirus in the Wuhan, China as a "Public Health Emergency of International Concern" (PHEIC). On February 13, 2020, the WHO officially named the 2019-ncov as Coronavirus Disease-2019 in Geneva, Switzerland.[1] The human coronaviruses history was first isolated in the 1960s, is responsible for a substantial proportion of upper respiratory tract infections in children. Since 2003, new human coronaviruses including NL63, 229E representing a group of newly identified group- I coronaviruses, has been identified worldwide. The global distribution of a newly identified group - II coronavirus (OC43, HKU1), has not yet been established. Corona virology has advanced significantly in the past few years. [2] In addition to those viruses, other human

coronaviruses that have emerged to cause fatal infections include[3, 4]:

- The MERS virus, or Middle East respiratory syndrome, which first appeared in Saudi Arabia. [3,5]
- The SARS virus, or severe acute respiratory syndrome, which first occurred in the Guangdong province in southern China. [3]
- A novel coronavirus designated as 2019-ncov first appeared in Wuhan, China. [6]

Coronavirus is a virus that is found in animals and rarely transmitted from animals to humans. It is also spread from person to person. [3]Coronaviruses are zoonotic, meaning they are transmitted between animals and people. Upon detailed investigations found that SARS-cov was transmitted from civet cats to humans and MERS-cov from dromedary camels to humans. Several known coronaviruses are circulating in animals that have not yet infected humans. [7]

BASIC VIROLOGY AND STRUCTURE

Coronaviruses (cov) are large group of *enveloped, positive-stranded RNA viruses,[8, 9]* in the order of family *Coronaviridae.*These viruses having virions which are spherical in shape with the diameter of 125 nm. The name coronavirus so called, because the club-shape spike projections that are emerge from the surface of the virions which is the prominent feature of coronaviruses, give them the appearance of a solar corona.[9] The genome of the virus is packed inside a helical capsid formed by the nucleocapsid protein (N) and further surrounded by an envelope. The coronavirus envelope is associated with three structural proteins: The membrane protein (M) and the envelope protein (E) are involved in virus assembly, whereas the spike protein (S) mediates virus entry into host cells. Some coronaviruses also encode an envelope-associated hemagglutinin-esterase protein (HE). [9] All enveloped proteins and N proteins in all virions but HE is only present in some beta corona viruses. [10]

Nucleocapsid proteins are phosphoprotiens plays an important role in virion structure, replication and transcription, **membrane proteins** are glycosylated protein crucial for the virion to fuse into the cell and to make protein antigenic and plays a key role in regenerating virirons in the cell**,** [10]**envelope (E) protein** is a small, integral membrane protein involved in several aspects of the virus life cycle, such as assembly, budding, envelope formation, and pathogenesis. [11] **spike proteins (S)** are glycoproteins locate outside the cell which mediates virus entry into host cells and give the virion the typical shape, mediates virus entry into host cells. All enveloped protiens and N protiens in all virions but HE is only present in some beta corona viruses. [10]

Coronavirus was divided into 4 genera: alpha, beta, delta, and gamma. [8]

• Alpha covs (229E, NL63) and beta covs (OC43, HKU1) infects humans, gamma covs infects avian species, and delta covs infects both humans and avian species. [8]

• Four hcovs [hcov229e (green), NL63 (blue), OC43 (orange), and HKU1 (red)] endemic globally. [8, 12]

- ✓ Hcov 229E was first isolated in 1967 and shares only 65% nucleotide identity with other human alpha corona virus. [13]
- ✓ Hcov-NL63 was first isolated in 2003 from a 7- months old child suffering from bronchiolitis and conjunctivitis. [13]
- ✓ Hcov-OC43 is already known since 1960s. [13]
- ✓ Hcov –HKU1 was discovered in 2005 in a 71- year old man with pneumonia. [13]
- ✓ The present novel-cov was identified in 2019, in a 55year old individual with pneumonia. [14]

EPIDEMIOLOGY

The data on global outbreak of 2019-n cov, SARS-cov, and MERS-cov were obtained from World Health Organisation (WHO) and Centre for Disease Control and Prevention (CDC). [15]

- **Middle East Respiratory Syndrome (MERS):** At the end of November 2019, a total of about 2494 confirmed cases, 858 (35%) people have died worldwide from MERS [16]. It was first appeared in Saudi Arabia in 2012 with majority of cases (2102) and deaths (780) and then in

other countries in the Middle East, Africa, Asia, and Europe. [17] In May 2015, there was an outbreak of MERS in South Korea with 180 cases and 38 deaths,[18] which was the largest outbreak outside of the Arabian Peninsula.[17]

- **Severe Acute Respiratory Syndrome (**SARS)**:** In 2003, a total of about 8098 people were affected and 774 (11%) people died from an outbreak. [16, 17, 19] as of 2015, no further cases of SARS were reported. [17] The SARS epidemic put the animal coronaviruses in the spotlight. [2]

The novel coronavirus COVID-19 is affecting 207 countries and territories around the world and 2 international conveyances (the diamond princess cruise ship harbored in yokohama, Japan and the Holland America's *MS Zaandam* cruise ship).[17, 20] the early reports predicted the onset of potential outbreak from Wuhan Hubei Province, China. The first case was reported in December 29, 2019. [21] According to WHO situation report, the status of n-COVID Cases (Table-**1**). [22]

GLOBAL SPREAD

The outbreaks experiencing from Severe Acute Respiratory Syndrome (2003) and Middle East Respiratory Syndrome (2015) tolls to raise upto full extent and its severity leads to the emergence of global ncovid-19. The rapidity of global outbreak by commercial air travel is another feature of COVID-19 common to SARS and MERS.The rapid spread of COVID-19 is likely to be driven by the phenomenon of 'super-spreading'. Super-spreading describes the escalation of transmission of the disease to a large number or at least eight contacts can get infected from a common source. Experience from MERS suggests the transmissibility of the virus is not just due to its inherent infectivity but also due to influence of hygiene practices, crowding, and infection control standards. Any delay in the screening of disease and implementation of preventive control measures, increases the likelihood of spreading the pathogen. [23].

CORONAVIRUS –TRANSMISSIBILITY[24]

- Infected droplets : >5µm, travel <1m
- Aerosols: <5µm, travel>1m
- Contact
- Hands, surfaces

Three main transmission routes for the nCOVID-19:

1) **Droplets transmission:** When someone who is infected coughs or sneezes, they send droplets containing the virus into the air.
2) **Contact transmission:** A healthy person can catch the virus if the person touch the surface or object that contains virus and by touching their mouth, nose or eyes. [25]
3) **Aerosol transmission:** When the droplets get mix into the air, forming aerosols and may cause infection when inhaled into the lungs. [26]

Survivability outside body: The survivability of coronavirus depends on the material and the surface is made from. The coronavirus lives up to hours to days on surfaces like countertops and doorknobs. It is not air borne disease and it is not clear whether exposure to heat, cold, or sunlight affects how long it lives on surfaces.[25],

- 1-2 days on nonporous surfaces. [24]
- 8-12 hours on porous surfaces. [24]

Non-Porous Surfaces: Metal (doorknobs, jewelry) 5 days, Wood (furniture, decking) 4 days, Plastics (Packaging like milk containers and bus seats) 2-3 days, Stainless steel (Refrigerators, pots, pans, sinks) 2-3 days, Copper (teakettles, cookware) 4 hrs, Glass (drinking glasses, mirrors, windows) up to 5 days, Ceramics (Dishes, pottery) 5 days.[25]

Porus Surfaces: Cardboard (shipping boxes) 24hrs, Aluminum (soda cans, tinfoil) 2-8hrs, Paper: the length of times varies. Some strains of corona virus live for only a few minutes on paper, while others live for up to 5 days.[25]

INCUBATION PERIOD

Current estimates of the incubation period of sarscov-2 range from 2-14 days. '[27]'

RISK FACTORS AND COMPLICATIONS

Older people and people with co morbid conditions have a higher risk for severe complications if they contract the virus. These health conditions include:

- Lung conditions, such as COPD and asthma
- Certain heart conditions
- Immune system conditions, such as HIV
- Cancer that requires treatment
- Severe obesity
- Other health conditions, if not well-controlled, such as diabetes, kidney disease, or liver disease. '[28]'

The complications include:

- Pregnant women have a higher risk of complications.
- The virus can lead to pneumonia, respiratory failure, septic shock, organ failure, '[26]' and death... '[26,29]'

CLINICAL FEATURES

Most common symptoms include: Fever'[26]' Fatigue'[26]', Dry cough, and Breathing difficulty.

If anyone experiences the following symptoms, they require medical attention right away:

- Trouble breathing or shortness of breath
- Ongoing chest pain or pressure
- New confusion
- Can't wake up
- Bluish lips or face. '[25,28]'

If the person exposed and infected, symptoms will appear within 2 days or as many as 14 days. It may vary from person to person. The most common symptoms and the percentage of people who have them include: '[25, 26, and 30]'

- Fever: 88%
- Dry cough: 68%
- Fatigue: 38%
- Coughing up sputum, or thick phlegm, from the lungs: 33%
- Shortness of breath: 19%
- Bone or joint pain: 15%
- Sore throat: 14%
- Headache: 14%
- Chills: 11%
- Nausea or vomiting: 5%
- Stuffy nose: 5%
- Diarrhea: 4%
- Coughing up blood: 1%
- Swollen eyes: 1%

PATHOGENESIS:

Human Coronaviruses: Prior to the SARS-cov outbreak, Two of the coronaviruses were only thought to cause mild, self-limiting respiratory infections in humans are α-coronaviruses (hcov-229E and hcov-NL63) while the other two are β-coronaviruses (hcov-OC43 and hcov-HKU1) '[31, 32]'

SARS-cov is a group of 2b β-coronavirus, which causes the most severe disease- Severe Acute Respiratory Syndrome (SARS).SARS-cov primarily infects epithelial cells within the lung, which is capable of entering macrophages and dendritic cells but only leads to an abortive infection.'[33, 34]'Despite this, infection of these cell types may be important in inducing pro-inflammatory cytokines.'[35]'in fact, many cytokines and chemokines are produced by these cell types and are elevated in the serum of SARS-cov that may contribute to disease. '[36]' MERS-cov is a group of 2c β-coronaviruses, which are highly related to two previously identified bat coronaviruses-HKU4 and HKU5,'[37]'and likely an intermediate host as humans, but rarely comes in contact with bat secreta. Serological studies have identified, providing evidence that dromedary camels may be the natural host. Because MERS-cov antibodies in dromedary camels in the Middle East,'[38]'and cell lines from camels have been found to be permissive for MERS-cov replication.'[39]'.MERS-cov utilizes Dipeptidyl peptidase 4 (DPP4) as its receptor. '[40]'the virus is only able to use the receptor from certain species such as bats, humans, camels, rabbits, and horses to establish respiratory infection.

LIFE CYCLE AND REPLICATION OF CORONAVIRUS: Coronavirus shows replicative phase of lifecycle. The stages of coronavirus lifecycle include Attachment and Entry, Replicase Protein, Replication and

Transcription, Assembly and Release are the expressions that are essential for viral replication. '[41]'

1. Attachment and Entry: Viruses are obligate intracellular pathogens because they cannot replicate without the machinery and metabolism of a host cells. So Spike Proteins are glycoproteins located outside the cell which mediates virus entry into host cells. The initial attachment of the virion to the host cell is initiated by interactions between the **S** protein and its receptor. Amino peptidase N, SARS-cov and hcov-NL63 use angiotensin-converting enzyme 2 (ACE2) are the receptors of Alpha, SARS-cov and hcov-NL63 respectively, MHV enters through CEACAM-1receptor and MERS-cov binds to dipeptidyl-peptidase 4 (DPP4) to gain entry into human cells. After binding to its specific receptor, the virus must next gain access to the host cell cytosol which is accomplished by acid-dependent proteolytic cleavage of S protein by a cathepsin, TMPRRS2 or another protease. Cleavage occur at two sites, first cleavage for separating the RBD and fusion domains of the S protein, the second for exposing the fusion followed by fusion of the viral and cellular membranes takes place. Fusion generally occurs within acidified endoscopes, but some coronaviruses, such as MHV, can fuse at the plasma membrane resulting in fusion and ultimately release of the viral genome into the peptide cytoplasm. '[9]'

2. Replicase Protein Expression: After the release of the viral genome inside the cell cytoplasm, the genome serves as an mRNA for the first open reading frame (ORF1), from which the viral replication proteins are translated and processed. These proteins induce and assemble on double-membrane vesicles and become the sites for viral RNA synthesis, and thus comprise the replication complexes. These replication complexes are likely responsible for all viral RNA synthetic activities in the viral life cycle. '[9]'

3. Replication and Transcription: Viral RNA synthesis follows the translation and assembly of the viral replicase complexes. Viral RNA synthesis produces Sub-genomic RNAs serve as mrnas for the structural and accessory genes which reside downstream of the replicase polyproteins. Cis-acting sequences are also important for the replication of viral RNA.

Coronaviruses are also known for their ability to recombine using both homologous and non-homologous recombination. Recombination likely plays a prominent role in viral evolution and is the basis for targeted RNA recombination, a reverse genetics tool used to engineer viral recombinants at the 3′ end of the genome. '[9]'

4. Assembly and Release: The viral structural proteins are translated and inserted into the endoplasmic reticulum (ER) after the replication. These proteins move along the secretary pathway into the endoplasmic reticulum-Golgi intermediate compartment (ERGIC). However, viral envelopes produced when the M protein is expressed along with E protein suggesting these two proteins formed vlps. These M protein directs most protein-protein interactions and also binds to the nucleocapsid, which are required for enhancing the envelope maturation and also promotes the completion of virion assembly. It is unknown how E protein assists M protein in assembly of the virion. N protein enhances VLP formation. There, viral genomes encapsulated by N protein bud into membranes of the ERGIC containing viral structural proteins, forming mature virions. '[9]' Following assembly, virions are transported to the cell surface in vesicles and released by exocytosis. This leads to the formation of large, complex and multinucleated cells, which allows the virus to spread within an infected organism without being detected or neutralized by virus-specific antibodies. Released virus can infect other cells and can replicate within the parent cell through binding to CEACAM-1. '[42, 43, 44]' Viral spike glycoprotiens binds to host cell suface, then the virus enters into host cell by the process of endocytosis. Release of genomic RNA into cytoplasm through uncoating, followed by translation of positive-strand RNA on host cell ribosome leads to formation o large proteins. The proteolytic process occurs by RNA dependent RNA polymerase it forms Antisense negative-strand template (sub genomic negative strand template) and release of sub genomic RNA takes place. Transational process leads to formation of viral proteins. Following

assembly, virions are transported to the cell surface in vesicles and released by exocytosis.

DIAGNOSIS:

Doctors are making some suggestions to detect the viruses through

- Physical examination. '[45]'
- Imaging examination include CT imaging, X-ray imaging. '[45]'
- Laboratory examination: Blood tests include total WBC, C-reactive protein, prolactin, Erythrocyte sedimentation rate. '[45]'
- Samples from sputum, throat swabs, lower respiratory tract secretions, stool and blood etc. Are tested positive for n-COVID. '[46]'
- Other breathing tests.
- Polymerase chain reaction: Routine confirmation of cases of COVID-19 is based on detection of unique sequences of virus RNA by nucleic acid amplification test (NAAT) such as real-time reverse-transcription polymerase chain reaction (rrt-PCR),'[47,48,49]' with confirmation by nucleic acid sequencing.'[47]' The CDC developed a protocol for RT-PCR that included specific primers designed to bind to key areas of the novel coronavirus. FDA authorized CDC's test via an Emergency Use Authorization (EUA), through which the FDA permits use of a non–FDA-approved drug to respond to a declared emergency. The CDC quickly shipped the test to state and local public health laboratories to support public health surveillance by identifying new cases around the country. '[50]'
- Serological testing: Serological surveys can aid investigation of an ongoing outbreak and retrospective assessment of the attack rate or extent of an outbreak. '[47]'Serological assays are important in cases where RNA is difficult to isolate,'[9]' and also in cases where NAAT assays are negative and there is a strong epidemiological link to COVID-19 infection, paired serum samples (in the acute and convalescent phase) could support the diagnosis.'[47]'

THERAPEUTIC STRATEGIES FOR THE TREATMENT OF nCOVID-19:

Till now, there is no drugs are currently FDA-approved for treatment of COVID-19. Efforts to treat in humans are still ongoing. But a number of drugs approved for other indications are of great interest for repurposing for COVID-19 treatment.However, from earlier experience of the management of SARS-CoV and MERS-CoV, many agents are being used in the treatment of 2019-nCoV.

Examples of drugs used for these illnesses include:

- Antiviral or retroviral medications such as Nucleoside analog, Neuraminidase inhibitors, Protease inhibitor
- Antimalarial agents such as Chloroquine, and Hydroxychloroquine
- Steroids to reduce lung swelling such as corticosteroids
- Immunomodulators such as interferon and immunoglobulins[51]
- Blood plasma therapy[52]
- Breathing support, such as invasive mechanical ventilation.[51]

Antivirals:

Among nucleoside analogs ribavirinand remdesivirare evaluated in 2019-nCoV. Ribavarin and Remdesivir were initially evaluated for the treatment of Ebola and are now being investigated for COVID-19 treatment, given its activity against RNA viruses.[51] 200mg once daily on the first day followed by 100mg daily for 9 days. Generally adverse effects include: hemolytic anemia, hypocalcemia, and hypomagnesemia and are contraindicated in hypersensitivity reactions, hepatic impairment. Increased liver enzymes and serum electrolytes are of monitoring parameters. '[53]' Neuraminidase inhibitors are oseltamivir indicated in the management of influenza and also used in the management of 2019-nCoV. It is given as empirical form and can be started in suspected MERS-CoV. Lopinavir and ritonavir are recommended protease inhibitor for the treatment of 2019-nCoV.[51]These drugs inhibit the action of 3-chymotrypsin- like protease enzyme which plays a vital role in processing of viral

replication. It is recommended in the dose of 400mg/100mg twice daily for 14 days. Adverse effects include diarrhea, dyslipidemia, hepatic disorders, abdominal pain, and headache and are contradindicated in porphyria, hemophilia, cardiovascular diseases, and pancreatitis. Monitoring of blood glucose, LFTs, serum lipid profile is required. [54]

Corticosteroids and anti-malarials:

Corticosteroids were widely used in the management of the current epidemic of 2019-nCoV and also used for the treatment of SERS-CoV and MERS-CoV. Use of corticosteroid is reported to be associated with delayed clearance of viral RNA and other steroid-related complications such as psychosis. [51] Antimalarial agents such as Chloroquine and Hydroxychloroquine in the dose of 100mg/400mg are used for the treatment of SERS-CoV and MERS-CoV.Adverse effects include gastrointestinal upset, retinal toxicity and are contraindicated in patients with liver diseases, porphyria, and renal toxicity. Monitoring of electrolytes, renal and hepatic functions is required.[55]

Immunomodulators:

a) Interferons

Interferons are antivirals, primarily used in the treatment of hepatitis B infection and are recognized to play critical role in inhibiting viral infection by directly interfering with viral replication. IFN-αs, IFN-β, combinations of IFN-α/β and IFN-γs are effective in inhibiting SARS-CoV replication. For the treatment of 2019-nCoV, IFN-α (5 million U bid inj) is recommended. [56] Adverse effects include neutropenia, fatigue, and flu-like syndrome and are contraindicated in patients with rheumatoid arthritis, severe depression or psychosis. Monitoring of serum bilirubin, ALT, AST and alkaline phosphatase is required.

b) Immunoglobulins:

In case of critically ill SARS, who show signs of deterioration, further escalation of immunomodulation is indicated and intravenous (i.v.) immunoglobulin may be considered. Patients who show poor response to initial empirical therapy may get benefit from i.v. immunoglobulin.Adverse effects include chest tightness, blood pressure changes and anaphylactic reactions and are contraindicated in patients with diabetes, chronic heart failure, a condition with abnormal proteins in blood. Monitoring of vital signs and liver and renal function tests, CBC count with differential count. Apart from immune modulators, metformin, atorvastatin, fibrates, as well as nutritional supplements may help in treating acute respiratory distress syndrome (ARDS) by boosting immunity.Some of the host-directed therapies basically target improvement of host immune response, or handling of host-related factors associated with viral replication.Zinc also having antiviral effect and it inhibits CoV RNA polymerase activity and thus hampers replication in cell culture experiments.Other treatment options, which are either used rarely or in experimental state, are SiRNA, tumor necrosis factor-alpha inhibitors, neutralizing antibodies, pentoxifylline, etc., due to poor level of evidences these are not recommended for routine care. [51]

Blood plasma transfusions as plasma therapy. ‘[52]’

Plasma therapy has been effective in Ebola and also in other coronavirs infections like MERS and SARS. This therapy is not proven to be coronavirus cure; it is only being tested as one. The concept of plasma therapy is based on the premise that using antibodies from the blood of a recovered COVID-19 patient, to treat those who are critically ill after being infected with the virus.Thepatient who has recovered from COVID-19 contains antibodies has the ability of targeting and fighting the novel coronavirus in the second patient.While adding that at least 72 hours are required for the patient to show a response to this therapy. Some may take up to 10 days. The best results can be obtained when it is used within the first 14 days of symptoms. There could be minor risks which are associated with transfusion of blood. One donor can donate 400ml of plasma which can save two lives, as 200ml is sufficient to treat one patient.

Table –1: Spreading rate of Covid-19 (weekly) confirmed and death cases as per WHO reports

WHO reports	GLOBALLY (cumulative)		CHINA		INDIA		Affected countries
	Confirmed cases	Death cases	Confirmed cases	Death cases	Confirmed cases	Death cases	
March-8	1,09,586	3685	80,859	3,100	34	--	101
March-15	1,53,517	5735	81,048	3,204	107	2	143
March-22	2,92,142	12783	81,498	3,267	283	4	167
March-29	6,34,813	29891	82,341	3,306	979	25	203
April-4	10,51,635	56,985	82,875	3,335	2,301	56	207
April-11	16,10,909	99,690	83,369	3,349	7,447	239	207
April-18	21,60,207	1,46,088	84,180	4,642	14,378	480	207
April-25	27,19,896	1,87,705	84,324	4,642	24,506	775	210
May -2	32,67,184	2,29,971	84,388	4,643	37,336	1,218	212
May-9	38,55,788	2,65,862	84,416	4,643	59,662	1,981	212
May-16	44,25,485	3,02,059	84,478	4,644	85,490	9,752	215

According to world health organisation the following are the comination of drugs used in the treatment of coronavirus:

1. Ribavirin along with corticosteroids became a standard regimen for the treatment of SARS-CoV.
2. In SARS-CoV infection, compared to ribavirin or interferon (IFN) alone, the combination of IFN-α + high-dose corticosteroids.
3. IFN-α (5 million U bid inh) is recommended along with lopinavir + ritonavir combination. [51]

Not yet, but clinical trials are under way in the U.S. and in China to test vaccines for SARS-cov-2/COVID-19. '[17]'One vaccine called mRNA-1273 (which was developed by using messenger RNA) would tell cells to pump out a protein that will kick-start immune system to fight the virus. It's worked well in animals and is ready to test in humans.'[17]'Only supportive care. '[26]'

PREVENTIVESTRATEGIES OF COVID-19'[57]':

Everyone has to take strict precautions to prevent the coronavirus spreading day by day. Knowing symptoms of this virus first and foremost will keep you away from it. Reduce the risk by preventing it from spreading in humans. To reduce coronavirus everyone must follow the following precautions:

1. Cleaning of hands:

- Wash off the hands often with soap and water for at least 20 seconds especially after being in a public place or after blowing off the nose, coughing, or sneezing.
- If soap and water are not readily available, use a hand sanitizer that contains at least 60% alcohol. Cover all surfaces of hands and rub them together until they feel dry.
- Avoid touching the eyes, nose, and mouth with unwashed hands.

2. Avoid close contact:

- Avoid close contact with people who are sick

Maintain distance between one people from another if COVID-19 is spreading in the community. This is especially important for people who are at higher risk of getting very sick.

3. Take steps to protect others

- ✓ Stay home if one gets sick, except to get medical care.
- ✓ Cover coughs and sneezes
  - Cover the mouth and nose with a tissue while coughing or sneezing or cover with the elbow.
  - Throw used tissues in the trash.
  - Immediately wash hands with soap and water for at least 20 seconds. If soap and water are not readily available, clean hands

with a hand sanitizer that contains at least 60% alcohol.

- ✓ Wear a face mask if anyone gets sick.
- ✓ Clean and disinfect
    - Clean and disinfect frequently touched surfacesdaily. This includes tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks.
    - If surfaces are dirty, clean them: Use detergent or soap and water prior to disinfection. '[57]'

Preventive strategies are focused on the isolation of patients and careful infection control, including appropriate measures to be adopted during the diagnosis and the provision of clinical care to an infected patient. For instance, droplet, contact, and airborne precautions should be adopted during specimen collection, and sputum induction should be avoided. The WHO and other organizations have issued the following general recommendations:

- Avoid close contact with subjects suffering from acute respiratory infections.
- Frequent hand wash, especially after contact with infected people or their environment.
- Avoid unwanted contact with farm or wild animals.
- People with symptoms of acute airway infection should keep their distance, cover coughs or sneezes with disposable tissues or clothes and wash their hands.
- Strengthen, in particular, in emergency medicine departments, the application of strict hygiene measures for the prevention and control of infections.
- Individuals that are immune-compromised should avoid public gatherings. '[58, 59]'

Pharmacists play an essential role in reviewing and interpreting the information for their clinician colleagues, particularly when physician colleagues may be experiencing increased patient volume and thus may have limited time to read and evaluate new data as they are published.

EFFECTIVE ROLE OF CLINICAL PHARMACIST IN PANDEMIC OUTBREAK

Pharmacists have a vital role within the healthcare team to optimize patient care during COVID-19. While enthusiasm for any drug that could aid in this disease may run high, it is important to take an appropriate critical approach in evaluating risks and harms. One of the fundamental roles of pharmacists is to ensure the availability and timely provision of the safest and most effective therapy. In this role, pharmacists must plan for, identify, and mitigate drug shortages during the COVID-19. This is crucial, that drug shortages can lead to prescribing of suboptimal therapy and have been associated with patient harm'[60]' Therefore, pharmacists must work proactively, identify effective therapeutic alternatives, enforce the implementation of drug shortage mitigation strategies, and if needed, prioritize drug supply to the patients who are most likely to benefit. Pharmacists are the drug information experts in evaluating literature related to new or repurposed therapies and can help make system-level and patient-specific treatment decisions, as well as ensure access to these therapies and other drugs on shortage due the pandemic. By serving as a resource to physicians and other medical providers, patients, and the public, pharmacists are essential in mitigating adverse consequences. Pharmacists are a trusted and accessible resource for the public during this public health emergency. '[61]' Pharmacists must educate their patients and the public on effective strategies to prevent acquisition and further spread of infection (eg, optimal hand hygiene, social distancing, staying home if having respiratory symptoms).

CONCLUSION

This review concludes that, covid-19 is a pandemic respiratory disease with high spreading rate throughout the world than other coronavirus infections like SARS and MERS but mortality is comparatively less. The exact incubation period and clinical presentation of this virus is not yet completely known, it differ from one region to another region of the world.

The defined curative or prophylactic therapy is not yet developed/available and an empirical therapy is being practiced and an extensive research is underway with variety of potential options.Proper eduction by the pharmacists related to preventive measures like quarantine, social distance and proper sanitization techniques and use of medication to the patients and to the public on effective strategies to prevent acquisition and further spread of infection is vital in controlling the spread.

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