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2019 Novel Corona Virus (COVID-19): Mini-review of the Epidemiology, Pathogenesis, Prevention and Treatment

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ABSTRACT

SARS-CoV-2 is a single-stranded RNA virus of 27-32kb genome size which belongs to the family of Coronaviridae and genus Coronavirus. It has emerged in China and has been reported as pandemic disease by World Health Organization. The virus can cause respiratory illness; termed as COVID-19 (coronavirus virus disease 2019). Common signs of infection include cough, fever and respiratory difficulties like shortness of breath. Serious cases of COVID-19 can lead to kidney failure, pneumonia and death. Worldwide efforts are being made via public health emergencies to identify the suspected COVID-19 cases and quarantine them to prevent further spread of the infection. Different vaccines are now available in various countries. Vaccines are effective interventions that can reduce the high burden of diseases globally. However, public vaccine hesitancy is a persistent problem for public health authorities. With the availability of COVID-19 vaccines, limited but increasing information is available on the public attitudes and acceptability towards the COVID-19 vaccines in Pakistan.

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INTRODUCTION

A novel coronavirus has recently emerged in December 2019 out of Wuhan City, China that affected the lower respiratory tract of patients (Adhikari et al., 2014). According to World Health Organization, the current reference name of the 2019 novel coronavirus is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the official name for the virus is coronavirus disease (COVID-19) (Tavakoli, Vahdat and Keshavarz, 2020). People with weakened immune systems, cardiopulmonary disease, older adults and infants are more prone to infection. It has quickly spread internationally, affecting more than 3,000 people and claiming over 57 lives in Pakistan till date (Regan, Renton and John, 2020). It continues to be a global health concern, with multiple countries declaring public health emergencies (Gostin and Hodge 2020) (Cui, Li and Shi, 2019).

HISTORY

Coronavirus (CoV) is the largest known RNA virus. The sub-family of Coronaviridae has four genera and each genus has a preference to infect a specific type of host. Coronavirus is an enveloped pathogen that is 27-32 kb in length and contains a single-stranded positive-sense RNA (Schoeman and Fielding, 2019). Six coronaviruses cause infections in humans before the new outbreak, the most serious, including MERS-CoV, SARS-CoV and four others that cause mild upper and lower respiratory symptoms (Chang et al., 2020). It had gained notoriety in the scientific and medical communities within the last 20 years due to the outbreaks of Middle Eastern respiratory syndrome CoV (MERS-CoV) in 2012 and severe acute respiratory syndrome (SARS-CoV) in 2003. MERS-CoV infected 2,254 patients with a 35% mortality rate while SARS-CoV infected 8098 patients with a 10% mortality rate (Chang et al., 2020). The mortality rate of SARS-CoV-2 is currently estimated to be about 2% (Song et al., 2019). The majority of infections by CoV were found in mammals and birds before these outbreaks (Zhao et al., 2012).

GENOMIC ORGANIZATION

Coronaviruses contain a non-segmented, positive-sense RNA genome of 27-32kb. The genome contains a 5′ cap structure alongside a 3′ poly (A) tail, that allow it to act as a messenger RNA for translation of the polyproteins (replicase). The replicase gene occupies two-thirds of the genome encoding the non-structural proteins about 20 kb, as opposed to the accessory and structural proteins, which make up only about 10 kb of the viral genome. The 5′ end of the genome contains untranslated region (UTR) and a leader sequence that contains multiple stem loop structures required for transcription and RNA replication. Transcriptional regulatory sequences (TRSs) are present at the beginning of each accessory or structural gene that is required for expression of each of these genes. The 3′ UTR also contains synthesis of viral RNA and RNA structures required for replication. The organization of the coronavirus genome is 5′-leader-UTR-replicase-S (Spike) – E (Envelope)-M (Membrane)-N (Nucleocapsid)-3′ UTR-poly (A) tail with accessory genes scattered within the structural genes at the 3′ end of the genome (Figure 1). Some of the accessory proteins have important roles in viral pathogenesis while others are almost exclusively non-essential for replication in tissue culture (Rothe et al., 2020).

EPIDEMIOLOGY AND PATHOGENESIS

Individuals of all ages are susceptible to infection. Infection is transmitted through large droplets generated during sneezing and coughing by symptomatic patients but

can also occurs before onset of symptoms and from asymptomatic people (Zou et al., 2020). Researches have shown higher viral loads in the nasal cavity as compared to the throat with no difference in viral burden between asymptomatic and symptomatic people (Chen et al., 2020). Patients can be infectious for as long as the symptoms last and even on clinical recovery. These infected droplets deposit on surfaces and can spread 1–2 m. The virus can remain viable on surfaces for days in favourable atmospheric conditions but are destroyed in less than a minute by common disinfectants like hydrogen peroxide etc. (Kampf et al., 2020). Infection is acquired either by touching surfaces contaminated by them and then touching the nose, eyes and mouth or inhalation of these droplets. The subsequent transmission via contaminated water supply, oral or faecal route is also hypothesized (Li et al., 2020). Neonatal disease due to post-natal transmission has also been described. However, trans-placental transmission from pregnant women to their fetus has not been reported yet (Wang et al., 2020). The incubation period of virus varies from 2 to 14 days. Studies have reported that virus can enter the respiratory mucosa through angiotensin receptor 2 (ACE2) (Singhal, 2020). The BCR (basic case reproduction rate) is estimated to range from 2 to 6.47 in various modelling studies (Singhal, 2020) (Jin et al., 2020).

DIAGNOSIS (Huang et al., 2020) (Russell et al., 2020)

A specific molecular test on respiratory samples (nasopharyngeal swab/ throat swab/ bronchoalveolar lavage /sputum and endotracheal aspirates) is used for specific diagnosis. Virus may also be detected in the blood and stool in severe cases. However, other laboratory investigations are usually non-specific and multiplex PCR panels currently available do not include the COVID-19. The white cell count is usually low or normal. Lymphopenia; a lymphocyte count <1000 has been related with severe disease. The platelet count is usually low or normal. The prothrombin time, creatinine, ALT/AST, D-dimer, LDH and CPK may be elevated and high levels are associated with severe disease. The procalcitonin levels are usually normal but ESR and CRP are generally elevated. A high procalcitonin level may indicate a co-infection of other bacteria. The chest X-ray (CXR) normal in early disease and usually shows bilateral infiltrates in severe infections. The CT is more specific and sensitive. CT imaging generally shows ground glass opacities, infiltrates and sub segmental consolidation. However, it is also abnormal in asymptomatic patients with no clinical evidence of lower respiratory tract infection. In fact, suspect cases with negative molecular diagnosis reported to have abnormal CT scans; many of these patients had positive molecular tests on repeat testing. The differential diagnosis includes all types of respiratory viral infections (parainfluenza, influenza, adenovirus, respiratory syncytial virus, non-COVID-19 coronavirus, human metapneumovirus), bacterial infections and atypical organisms (chlamydia, mycoplasma). It is quite challenging to differentiate COVID-19 from these infections through routine lab tests or clinically.

PREVENTION AND TREATMENT

It is mandatory to take all the precautionary measures to prevent infections. The first step is to ensure adequate isolation to prevent transmission to other person and healthcare workers. Clean/wash your hands often with soap and water or hand sanitizer for at least 20-30 seconds. Avoid touching mouth, eyes or nose with

unwashed hands. Mild illness can be managed at home with proper guidelines by physicians. The usual principles are maintaining nutrition and hydration and controlling cough, sneezing and fever. Routine use of antivirals and antibiotics such as oseltamivir should be avoided in confirmed cases. Provision of oxygen through face mask, nasal prongs or non-invasive ventilation is indicated in hypoxic patients (Zhao et al., 2020). Renal replacement therapy has been reported in some cases. Moreover, extra corporeal membrane oxygen support or mechanical ventilation even may be needed. Antifungals and antibiotics are required in case of suspected co-infections. Chinese guidelines suggest short term therapy with low-to-moderate dose of corticosteroids in COVID-19. However, World Health Organization advocate against their use (Zhao et al., 2020). Moreover, detailed guidelines for critical management of COVID-19 patients have been published by World Health Organization (Chen et al., 2020). No approved treatment for COVID-19 has been reported so far. Antiviral drugs such as lopinavirritonavir, ribavirin have been used based on the experience with MERS and SARS. Patients treated with combine dose of lopinavir-ritonavir with ribavirin had better outcomes as compared to those given ribavirin alone (Chen et al., 2020).

COVID-19 VACCINES

Vaccines stimulate human immune system using attenuated form of the virus which causes coronavirus. Each vaccine works differently to introduce antigen in our body which helps to fight against COVID-19. The antigen activates a specific immune response and this response forms immune memory, so our body can fight off COVID-19 in future.

Viral vector vaccines for COVID-19

This type of vaccine uses a harmless viral vector to deliver COVID genetic material. When administered, our cells use the genetic material to produce a specific viral protein, which is recognised by our immune system and activates a response. The University of Oxford/AstraZeneca vaccine uses this technology to protect against COVID-19.

Genetic vaccines for COVID-19

The Pfizer/BioNTech and Moderna vaccines use this type of technology to activate the immune system. The vaccines contain a segment of genetic material (RNA) of the SARS-CoV-2 virus, which causes COVID-19. When administered, our cells use the genetic material from the vaccines to make the protein, which is recognised by our immune system and activates a specific response.

Inactivated vaccines for COVID-19

This type of vaccine contains the killed SARS-CoV-2 virus, which is recognised by the immune system to trigger a response without causing COVID-19 illness.

Attenuated vaccines for COVID-19

This type of vaccine contains the weakened SARS-CoV-2 virus, which is recognised by the immune system to trigger a response without causing COVID-19 illness.

Protein vaccines for COVID-19

This type of vaccine contains proteins from the SARS-CoV-2 virus, which are recognised by the immune system to trigger a response.

WHO Approved Vaccines

Six vaccines including; Pfizer/BioNTech (RNA), CanSino (Non-Replicating Viral Vector), Sputnik V (Non Replicating Viral Vector), Oxford/AstraZeneca (Non Replicating Viral Vector), Sinopharm (Inactivated) and Sinovac (Inactivated) have

been approved for use in Pakistan and two vaccines; Anhui Zhifei Longcom (protein subunit) and CanSino (Non Replicating Viral Vector) are currently under clinical trials in Pakistan.

POLICY RECOMMENDATIONS FOR PAKISTAN

- Healthcare providers should take travel history of international travel in the past two weeks and all patients with any respiratory symptoms as well as any contact with infected people. Non-essential international travel should be avoided during pandemic.
- Triage centres for patients with respiratory illness should be set up in the outpatient department. Healthcare practitioners should practice hand hygiene frequently and wear personal protective equipment while examining corona patients.
- Suspected cases of COVID-19 should be referred to designated centres for testing isolation organized by government.
- Patients admitted with acute respiratory distress syndrome and severe pneumonia should be placed under isolation and evaluated for travel history. Decontamination of surfaces should be done regularly. They should be tested for SARS-COV2 and other co-infections using multiplex PCR panels.
- All the health-cares practitioners should be updated about guidelines of COVID-19 and recent development in the diagnosis and treatment of COVID-19.
- People should avoid spreading false information about the disease which might lead to anxiety and panic of the public.
- Non-essential international travel should be avoided at this time

CONCLUSION

The new COVID-19 outbreak has challenged the public, medical and economic health infrastructure of Pakistan and other countries. Time alone will tell how the virus will impact our lives here in Pakistan. More so, future outbreaks of viruses and pathogens of zoonotic origin are likely to continue. Therefore, apart from curbing this outbreak, efforts should be made to devise comprehensive measures to prevent future outbreaks of zoonotic origin. Vaccines perceived safety concerns and cost were associated with this refusal. Hence, the health care providers should design interventions in terms of awareness campaigns via all types of multimedia to spread more authentic information about the safety and efficacy of the vaccines. The awareness campaigns should also shed the light over the new technology that was utilized in the production of few of them in order to boost COVID-19 vaccines acceptance. Making the vaccine available for free by the government could as well enhance vaccines acceptance among the population.

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