





Journal of Experimental Biology and Agricultural Sciences

<http://www.jebas.org>

ISSN No. 2320 – 8694

A REAL-TIME UPDATED PORTRAYAL OF COVID-19 DIAGNOSIS AND THERAPEUTIC OPTIONS

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Received – August 27, 2020; Revision – September 14, 2020; Accepted – September 27, 2020

Available Online – October 08, 2020

DOI: [http://dx.doi.org/10.18006/2020.8\(Spl-1-SARS-CoV-2\).S21.S33](http://dx.doi.org/10.18006/2020.8(Spl-1-SARS-CoV-2).S21.S33)

KEYWORDS

COVID-19

Diagnosis

Immune response

Pathogenesis

Prevention

Treatment

ABSTRACT

The outbreak of COVID-19 seems to be the worst pandemic of history. The pandemic sprouting from China has created an uncertain situation globally. The rapid prevalence of this infectious agent has severely paralyzed every discipline of life at the domestic and international global levels within a few months after onset. The exponential growth of COVID-19 infected admissions in hospitals has oversaturated hospitals capacity, especially in developing and third world countries. Despite efforts of global communities and organizations, several developed countries are especially more affected due to a good economy and more intercontinental traveling. Due to extensive geographical spread, rapid transmission inclination, and severity of disease caused by COVID-19, the World Health Organization (WHO) declared “Public Health Emergency of International Concern”. The ripple influence of this pandemic has brought potential challenges to worldwide health-care systems. It might trigger a “*far-reaching*” *global economic* crisis if the virus spread is not strictly curbed. Therefore, the scientific concern has heightened on this novel Corona virus. This review intends to show a complete, updated, and streamlined picture of the COVID-19 pandemic. The first half of this review discusses the basic molecular virology of COVID-19, pathogenesis, immune response, and its transmission. The second part light on clinical features, diagnostic techniques, and facilities in Pakistan. Finally, along with the prevention and possible treatment of COVID-19, the opportunities and future perspectives are also discussed. In particular, the aim of this review is the true portrayal of RT-PCR testing in Pakistan.

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Peer review under responsibility of Journal of Experimental Biology and Agricultural Sciences.

Production and Hosting by Horizon Publisher India [HPI]
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1 Introduction

COVID-19 is the major health concern of the 21st century affecting all the countries of the world. The duration between the onset of the outbreak and the declaration of pandemic ranges just three months (Keam et al., 2020; Ciotti et al., 2020). By the end of August, WHO reported that 38000 deaths and 1.8 million cases were reported during the last week of August. At the same time, WHO mentioned that after the addition of these new cases total global figure of deaths reached 800000, while making 25 million confirmed cases have been reported since December 2019 (WHO, 2020). COVID-19 is the term referred to the current pandemic of novel SARS-2 (corona virus)-mediated respiratory infection, which erupted in late 2019 in Wuhan, China. Corona viruses are positive-sense, enveloped RNA (as genetic material) virus with diameter 60- 140 nm, outer surfacing like a crown when viewed through an electron microscope, hence got the name “corona” due to crown-like appearance (Richman et al., 2016).

Two major respiratory problems similar to the current pandemic occurred in the first quarter of the 21st century, where animal origin beta-viruses crossover to human beings resulted in major respiratory infections. First, highly infectious corona viruses emerged in 2002, when a novel beta-type SARS virus having bat origin (intermediate host-palm civet cats) caused severe respiratory syndrome that affected more than 8000 peoples with over 900 deaths (Chan-Yeung & Xu, 2003). The second major health event was caused by bat origin MERS (Middle East Respiratory Syndrome virus) corona virus in Saudi Arabia (intermediate host-camel) that cause serious respiratory problems in approximately 2500 individuals and taken the lives of 858 individuals (Memish et al., 2020).

The first confirmed COVID-19 case was reported in Wuhan, city of China, in December 2019 (Bilal et al., 2020; Dong et al., 2020; Yang et al., 2020). In the following days, infection not only spread in China but also in other countries in the world. On Jan 30, 2020, the WHO declared this disaster as a Public Health Emergency of International Concern. Therefore, health institutions called for a collective response at national and international levels to create the desired and systemized health system to stop this unstoppable (Holshue et al., 2020; Phan et al., 2020). On 26 February 2020, the first confirmed COVID-19 case (a student returned from Iran) was reported in the Sindh province of Pakistan. By the 10th of April, had 4695 cases; among them, 15.5% of patients had already recovered, 1% were critical, while 1.4% were under critical care (Abid et al., 2020). According to the WHO update, by the end of August, the figure of confirmed cases in Pakistan reached 288717, with 498 deaths (WHO, 2020).

In the earlier days, when we looked at the prevalence in Pakistan via national and international statistics of COVID-19 patients, we

found that the number of patients were going on increasing exponentially. According to the fresh WHO reports, Pakistan is recovering as compared with previous statistics. For instance, during the last week of August, a 20% reduction in new cases and a 24% reduction in death has been observed (WHO, 2020). Government and research institutes are trying to play their role in screening the majority of the population, but due to limited resources, only a small fraction of the population is screened daily. New initiatives are being taken to establish more diagnostic centers, and working institutions are trying to enhance their capacity to increase screening capacity daily. This review is done to show a complete, updated, and streamlined picture on the COVID-19 pandemic, especially in Pakistan. The first part of this review will discuss basic molecular virology of COVID-19, pathogenesis, immune response, and its transmission. The second part will shed light on clinical features, diagnostic techniques, and facilities in Pakistan and finally, the prevention and possible treatment of this novel SARS-CoV-2. The aim of this review is the true portrayal of RT-PCR testing in Pakistan.

2 Virology of COVID-19

Corona virus has a big family of viruses that cause infections of variable intensity ranging from commonly ignored common cold to acute, severe, scary, and painful respiratory syndromes (Keni et al., 2020). COVID-19 is the term referred to as the current pandemic of novel SARS-2 (corona virus) mediated respiratory infection, which erupted in late 2019 in Wuhan, China (Yang et al., 2020). Corona viruses are positive-sense, enveloped RNA (as genetic material) virus with diameter 60- 140 nm, outer surfacing like a crown when viewed through an electron microscope, hence got the name “corona” due to crown-like appearance (Richman et al., 2016). Some are known to cause significant respiratory issues (like SARS-CoV, MARS, etc.). In contrast, few other corona viruses are present in human circulation, known to cause low to mild respiratory infection, namely OC-43, NL-63, HKU-1, and 229-E.

The COVID-19 is a single-stranded positive-sense 30kb RNA that encodes 9860 a.a (Chan et al., 2020; Chen et al., 2020). Its genome is arranged as 5'-R-S-E-M-N-A-3' (where R stands for replicas, S for the spike, E for the envelope, M for membrane, N for Nucleocapsid, and A for poly-adenine), as shown in Figure 1 (Chan et al., 2020). The SARS-CoV-2 virus is a member of the order “Nidovirals” and family “Coronaviridae” subfamily “Coronavirinae”. This subfamily has further four genera (1) Alpha-coronavirus includes H-CoV-NL63 and H-CoV-229E (human corona viruses); (2) Beta-coronaviruses contains SARS-H-CoV, HCV- OC43, MERS-CoV, and HCoV-HKU1; (3) Gamma-coronaviruses contains birds and whales viruses; (4) Delta-coronaviruses contains viruses found in birds and pigs. SARS-CoV-2 is a peculiar beta-coronavirus that infects humans (Lu et al., 2020).

Coronavirus Structure and Protein Visualization

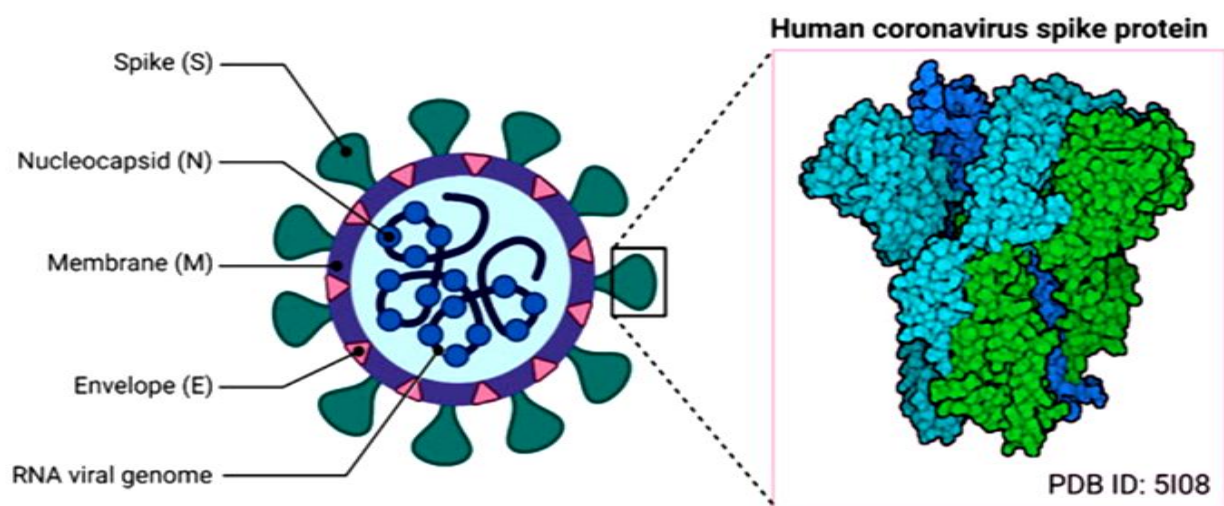


Figure 1 The 2019-nCoV structure and its protein visualization for active vaccine development. Coronaviruses belong in the family Coronaviridae and can cause disease in mammals and birds. The coronavirus spike (S) protein mediates membrane fusion by binding to cellular receptors (Bilal et al., 2020).

COVID-19 is a member of the family “Coronaviridae” and genera “Betacoronavirus” (Burrell et al., 2016). Coronaviruses are globally present in vertebrates, especially humans, and cause neurological, respiratory, hepatic, and enteric diseases. Most notable are the major epidemics of 2003 (SARS-CoV) and 2012 (MERS-CoV) infecting thousands of peoples. Comparative analysis indicates significant similarities and differences with the current outbreak; COVID-19 shows 79 % genome similarities with SARS-CoV (de Wit et al., 2016). Both viruses require ACE2 (angiotensin-converting enzyme 2) receptors for gaining entry into the host’s alveolar epithelial cell, induce cytokine storm in pulmonary endothelial cells, and predominantly attack and pass the infection to lower airways (Wan et al., 2020; Zhou et al., 2020). A mechanistic representation of endocytosis and exocytosis-based Corona virus entry and exit to and from the host, respectively, is shown in Figure 2.

3 Transmission of COVID-19

Corona viruses engage diverse subunit transcription/replication molecular machinery for its mechanism of action. Assembling of a group of non-structural proteins (that are cleavage products of viral proteins ORF-1ab and ORF-1a) aids in COVID-19 transcription and replication (Bilal et al., 2020; Buckman et al., 2020). Viruses require ACE2 (angiotensin-converting enzyme 2) receptors for gaining entry into the host’s alveolar epithelial cell, induce cytokine storm in pulmonary endothelial cells, and predominantly attack and pass the infection to lower airways. RNA dependent RNA polymerase (a key nsp12, also known as RdRp) plays a vital

role in the synthesis of RNA, thus playing a major role in viral transcription and replication with the help of other non-structural proteins like nsp7 and nsp8as cofactors (Subissi et al., 2014; Buckman et al., 2020).

Interestingly, molecular analysis has shown that the receptor for COVID-19 is an angiotensin-converting enzyme similar to SARS-CoV (Hoffmann *et al.*, 2020). These corona viruses use surface protein S to identify the required receptor on host cells; to gain entry into the target cells and results in infection. A genetic model study states that SARS-CoV-2 has a ten-fold higher affinity to bind with ACE-2 than SARS-CoV, at a slightly higher level than the infection threshold (Wrapp et al., 2020). The detailed molecular study for binding of protein with receptor strength of their interaction and infection and how this novel virus causes organ damage are still unknown and more research in this area is needed. These detailed studies will explain the higher transmission capability of COVID-19, enhanced number of confirmed cases, the affinity of ACE2 for S protein, and potential treatment candidate (Wang et al., 2020).

Of all ages, regions, and cultures are susceptible. The novel viral infection spread through sneezing and coughing droplets by the symptomatic patient, even from asymptomatic and early-stage infection with the disease (Rothe et al., 2020). Research and diagnostic studies show a higher level of corona virus in the nasal cavity than in the throat with a similar viral burden in asymptomatic and symptomatic patients (Zou et al., 2020). Symptomatic patients are considered infectious even in clinical

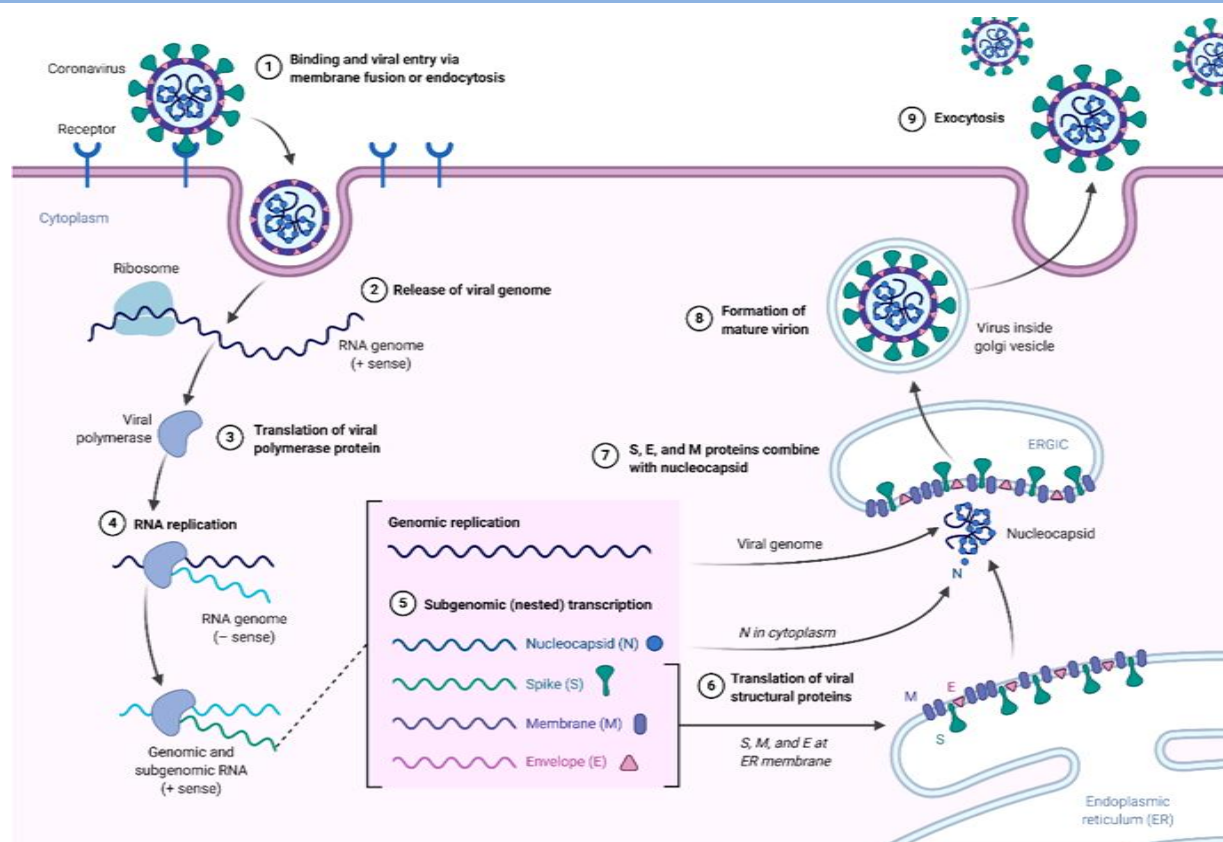


Figure 2 Representation of endocytosis and exocytosis-based Coronavirus entry and exit to and from the host, respectively(Iqbal et al., 2020).

recovery. The infected sneezing and coughing droplets can be deposited on the host surface even from a distance of 1-2 m. COVID-19 is viable for days if the environment is favorable; the viral infection is either spread through infected droplets inhalation or by touching infected surfaces and then nose or mouth. They are easily killed within seconds by general disinfectants like hydrogen peroxide, hypochlorite, etc. (Kampf et al., 2020). As RNA of infectious agent has been detected in stool, researchers are also suggesting its enteric route (fecal-oral route of infection) of infection (Chen et al., 2020; Ding & Liang, 2020).

4 Pathogenesis and immune response

Beta-coronaviruses, like the majority of the corona-virus family, exhibit unique pathogenesis capability and specie specificity, fine genetic changes can significantly change their host range, tissue tropism, and pathogenicity. A prominent example of fit in changed circumstances human exposure to deadly zoonotic MERS-CoV (Zaki et al., 2012) and SARS-CoV diseases (Peiris et al., 2004). In both outbreaks, the natural reservoirs were bats, and terminal hosts were humans with intermediary hosts for MERS-CoV and SARS-CoV were camels and palm civet, respectively (Guan et al., 2003; Alagaili et al., 2014). Intermediate hosts played the leading role of

this cross-species transmission, as they enhance terminal host and virus contact and permit necessary adaption for efficacious replication in new humans (Brennan et al., 2014).

As novel SARS-COV-2 have pandemic prospects, careful watch and scrutiny are highly important to evaluate its viral evolution, pathogenicity, host adaption, and transmissibility. Molecular relationships (like receptor interaction) govern the viral host range. The receptor-binding domains (S-protein on the envelope) of SARS-CoV and SARS-CoV-2 were similar structurally despite the variation of amino acids at key places (Lu et al., 2020). Research studies predict that ACE2 is used by the novel virus to enter the host cells(Wan et al., 2020). Molecular analysis suggests that the COVID-19 spike protein has two domains S1 and S2, in which receptor binding is done by S1 and fusion of cell membrane by S2. S1 domain is more conserved in different corona viruses, whereas the S2 domain shows more variations (Lu et al., 2020).

In addition, recognition of Gln493 and Asn501 (key residues on COVID-19 receptor binding domain) that control binding with ACE2 of host cell supports that this novel virus has acquired the ability for transmission from person to person (Wan et al., 2020). Although spike proteins and pattern of COVID-19 is similar to

SARS-CoV, at RNA level, it is jointly similar to SL-CoV-ZXC-21 and SL-CoV-ZC-45 (Harapan et al., 2020). However, specie specificity not only depends on binding efficacy with the receptor, encountering, and evading the host innate immune response is essential to drive pathogenesis. Research is being done to find the mechanism by which these novel viruses trickily dodge the defense system of the host (Chen et al., 2020). Due to unique features, corona infection is expanding at exponential rates. For example, if we took COVID-19 statistics of Pakistan for the last three months, we found that in starting, there were very few cases, but now thousands of patients get infected by this pandemic. In a viral infection, cellular and inflammatory responses are mediated by the host defense (immune) system to inhibit viral dissemination and replication (Felsenstein et al., 2020; Golonka et al., 2020). However, enhanced immune activation, together with the viral lytic effect on host cells, ultimately led to vicious pathogenesis. Clinical studies show that patients with viral infection suffer from fever, pneumonia, and dry cough as symptoms (Ali Shah et al., 2020; Chen et al., 2020). A considerable ratio of patients undergoes rapid septic shock or respiratory stress followed by organ failure, which led to the death of 1 in 10 serious patients.

Investigations suggest that critical patients in COVID-19 are presented with respiratory failure induced by hyperinflammatory response and flood of cytokines. Poorly controlled and dysregulated cytokines release, which is synergized by the effect of immune responses, develop other clinical complications and give rise to a vicious cycle. This complicated and disorganized interaction of the immune system and several other regulatory substances consequently leads to multiple organ failures and ultimately leads towards death (Keam et al., 2020). Old age adult males are comparatively more prone to be infected with COVID-19 and develop these complications more frequently (Malik et al., 2020).

5 Clinical features and diagnosis of novel SARS-CoV-2

Although COVID-19 has given diagnostic challenges in earlier stages of pandemic (Dinnes et al., 2020). Technological advances have made it possible to fight against and overcome the pandemic of COVID-19 of the 21st century. This has made it possible to investigate the routes of transmission, survival, and factors affecting the prevalence and possible ways to reduce the spread of infection and its possible ways to reduce the complications associated with various phases of infection (Afzal, 2020; Ai et al., 2020; Dhama et al., 2020; Dhama et al., 2020; Malik et al., 2020). This novel SARS-CoV-2 shows varied clinical features, commences with asymptomatic stage and ends with severe respiratory distress and organ damage. The clinical characteristics include dry cough, headache, fever, sore throat, breathlessness, conjunctivitis, and fatigue. Thus, they are similar to other respiratory infections. After seven days from onset of infection, a

fraction of patients progressed to severe pneumonia, organ failure, and ultimately death. This continuance is linked with the upsurge of inflammatory cytokines, including IP10, TNF α , IL-10, IL-2, MIP1A, IL-7, and GCSF (Guan et al., 2020; Wang et al., 2020). Severe complications due to COVID-19 include ARDS, major lung injury, acute kidney injury, and shock. The patients who persist this viral attack starts recovering in the second and third week, with the median treatment duration at the hospital was ten days. Adverse results are more frequent in the elderly with low immune response and those with fatal medical complications (Wang et al., 2020).

Specific COVID-19 diagnosis is made by specified molecular tests on samples (sputum, nasopharyngeal swab, throat swab, and endotracheal aspirates). Initially, national labs are offering these tests in case of emergency, but now a vast scale diagnosis is made even on a commercial level to screen the patients for infection from this novel virus. Other diagnostic investigations like blood chemistry, including RBC, WBC, Platelets, CRP, ESR counts, are non-specific and are not taken into consideration. WBC count is generally normal or low, platelet count may be low or normal, procalcitonin level is routinely normal, but ESR and CRP levels are usually elevated. D-dimer, LDH, prothrombin time, ALT, AST, and CPK levels may be raised, and high up levels are indications for the severe disease (Singhal, 2020).

Computerized tomography (CT) scan investigations are more specific and sensitive for COVID-19. CT findings show abnormality in patients with no respiratory track clinical record/asymptomatic individuals. In many cases, many suspected negative patients with abnormal CT values were found positive on repeat testing (Huang et al., 2020; Zhang et al., 2020). C-reactive protein, creatinine kinase, and lactate dehydrogenase elevation were demonstrated in most COVID-19 patients, but a small fraction of patients show high levels of serum creatinine and transaminase with an abnormal spectrum of the myocardial enzyme (Guan et al., 2020; Guan et al., 2020). Elevated IL-6 and IL-10 levels, and CD4⁺ T and CD8⁺ T low levels have been shown in COVID-19 patients (Wan et al., 2020). Another molecular research study shows elevated IFN, MCP1, IL1, and IP10. Highly serious patients admitted in ICU show increased levels of granulocyte colony-stimulating factor (GCSF), TNF α , MCP1A, IP10, and MIP1A. Radiological test results differ with immunity status, disease progression, comorbidity, previous medication, and patient age (Jin et al., 2020).

SARS-CoV-2 produces severe viral respiratory infection with three days of incubation period in humans. The characteristic attributes of the novel corona virus in adults are noticeable. Most common are fever (88 %), cough (68 %), fatigue (38 %); vomiting (5 %) and diarrhea (4 %) are infrequent (Yang et al., 2020). In addition to this, serious cases are susceptible to diversified complications,

including secondary infections, acute respiratory syndrome, and drastic heart injury. Scientific research verifies that this virus not only damages the lungs but also major organs and tissues of the body. In a research study on 214 COVID-19 patients, the neurological epitome was found in 35 % of the patients (Mao et al., 2020; Mao et al., 2020). In addition, ocular infections were also evident in COVID-19 patients, and eye secretions were tested positive for viral RNA in these patients (Ai et al., 2020). Serious COVID-19 patients admitted to hospitals had an unusual liver function, abnormal renal function, arrhythmia, and serious heart injury (Li et al., 2020). Tissue samples rectal mucosa, duodenum, and stomach of patients showed a positive result for COVID-19 RNA (Xiao et al., 2020).

As there is no prior exposure and proper treatment against COVID-19, health institutes devised the Initial Response Plan (IRP) based on recommendations of WHO. The health commission of major countries devised the diagnosis and isolation plan for suspected cases. Steps were taken to setup diagnostic labs to confirm the presence of COVID-19 in suspected cases, and a person with the required symptoms, the positive test, and exposure history is categorized as a suspected case. RT-PCR is regarded as a major confirmatory test by WHO, while chest CT scan and other symptoms are secondary diagnosis factors. Negative patients are considered free of virus, and positive patients are classified as 'critical' with an extreme medical condition, 'Severe' with apparent symptoms and airways obstruction, 'mild' and 'moderate' with low viremia and fewer symptoms (Zu et al., 2020).

Different diagnostic techniques are employed to screen the individuals for COVID-19. Commonly used diagnostic procedures include PCR, ELISA, CT Scan, Lamp scan, and X-RAY (PCR being most specific). Hou et al. suggested diagnostic technology based on CRISPR because of certain limitations of these tests (Hou et al., 2020; Hu et al., 2020; Lu et al., 2020; Yu et al., 2020). Diagnostic screening properly ensures the isolation of infected and suspected cases from a negative (normal) population. Negative patients are either screened for different infection or sent back home, whereas infected cases are first isolated and then treated for viral infection and secondary complications, in term resistance to the spread of this disastrous viral infection

6 RT-qPCR for SARS-CoV-2 detection

In the current situation, a pandemic requires accurate diagnosis with a short turnaround time. Various testing strategies are used to diagnose infections. Molecular techniques such as nucleic acid testing and detection are considered to be the gold standard, and positive nucleic acid confirms the presence of an infectious agent or pathogen (Carter et al., 2020; Cheng et al., 2020; Farfan et al., 2020; Lübke et al., 2020; Wu et al., 2020). In addition, certain diagnostic parameters can initially support the early detection of viral liberated particles

such as point of care testing antigens, antibodies against an infectious agent, nucleic acid, etc. (Dinnes et al., 2020).

In the early stages of this pandemic, the SARS-CoV-2 complete genome was sequenced, and that genome clear the way for the synthesis of different primers and standardized assays for COVID-19 (Lu et al., 2020; Wu et al., 2020). The first Real-time PCR protocol targeting viral envelope (E), RNA dependent RNA polymerase (RDRP), genes (G), and Nucleocapsid (N) of COVID-19 were documented on January 23, 2020 (Corman et al., 2020). The following generalized steps are followed for RT-PCR detection of SARS-CoV-2: extraction of RNA, probes, and primers targeting specified regions on viral genome, standard and controls making, and finally, real-time PCR assay.

PCR analysis is highly specific and regarded as the most accurate diagnostic analysis for COVID-19 but it has some limitations like false-positive and false-negative results. Molecular biologists worked on these and recommended some critical steps to overcome this problem. False-negative results are caused by poor sample quality, handling, storage, extraction, transportation, and time of collection. Suggested measures to overcome this problem are to use extraction control, optimize the sample collection period, and RNasePin CDC assay (human housekeeping gene) quantitative detection. Factors that cause false-positive results are less-specific kits, which can be overcome by the use of highly specified assays and kits, sample contamination, which can be reduced by decontamination procedures and following proper SOPs. The final factor is cross-contamination, which can be diminished by the use of adequately designated areas for each step and use of appropriate negative and positive controls (NIH, Pak recommendations) (Carter et al., 2020; Farfan et al., 2020; Lübke et al., 2020).

7 COVID-19 Real-time PCR testing facility in Pakistan

At the end of February, the government of Pakistan and health institutes takes initiatives to set-up diagnostic labs to detect Corona virus in suspected patients. Initially, the turn-out was very low, COVID-19 kits were imported from different countries, but there is a shortage of required labs. The majority of diagnostic labs worldwide are employing PCR, ELISA, Lamp-based detection, and radiological based diagnosis for COVID-19. Each type of testing has its pros and cons. Radiological readings are manipulated by multiple factors like the immune condition of patients, recent medication, age of patients, and many other, ELISA based testing is sensitive but less specific. In contrast, PCR based diagnosis is the most particular technique to detect viral RNA in the patient but has less sensitivity and prone to false-negative results. A practical approach and advanced skills are required to reduce false-negative results and to enhance its sensitivity, which some research laboratories are employing by use of specific primers, reagents, and real-time analysis of viral RNA in the sample.

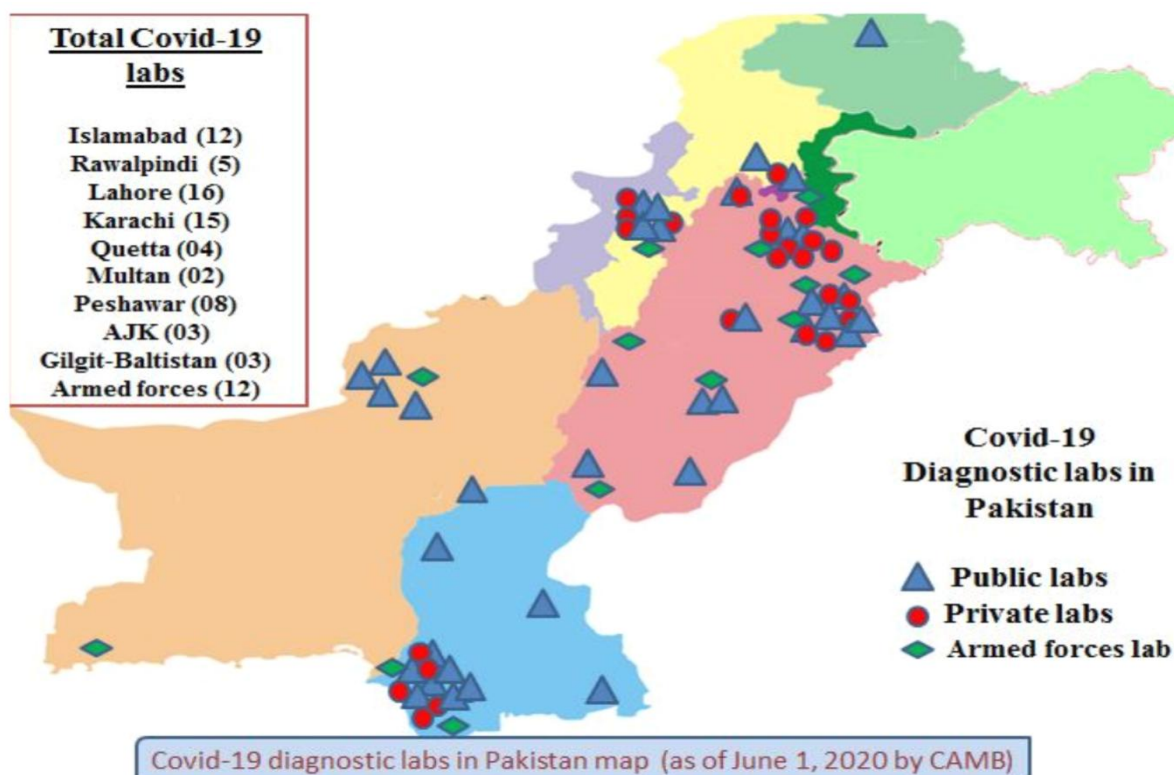


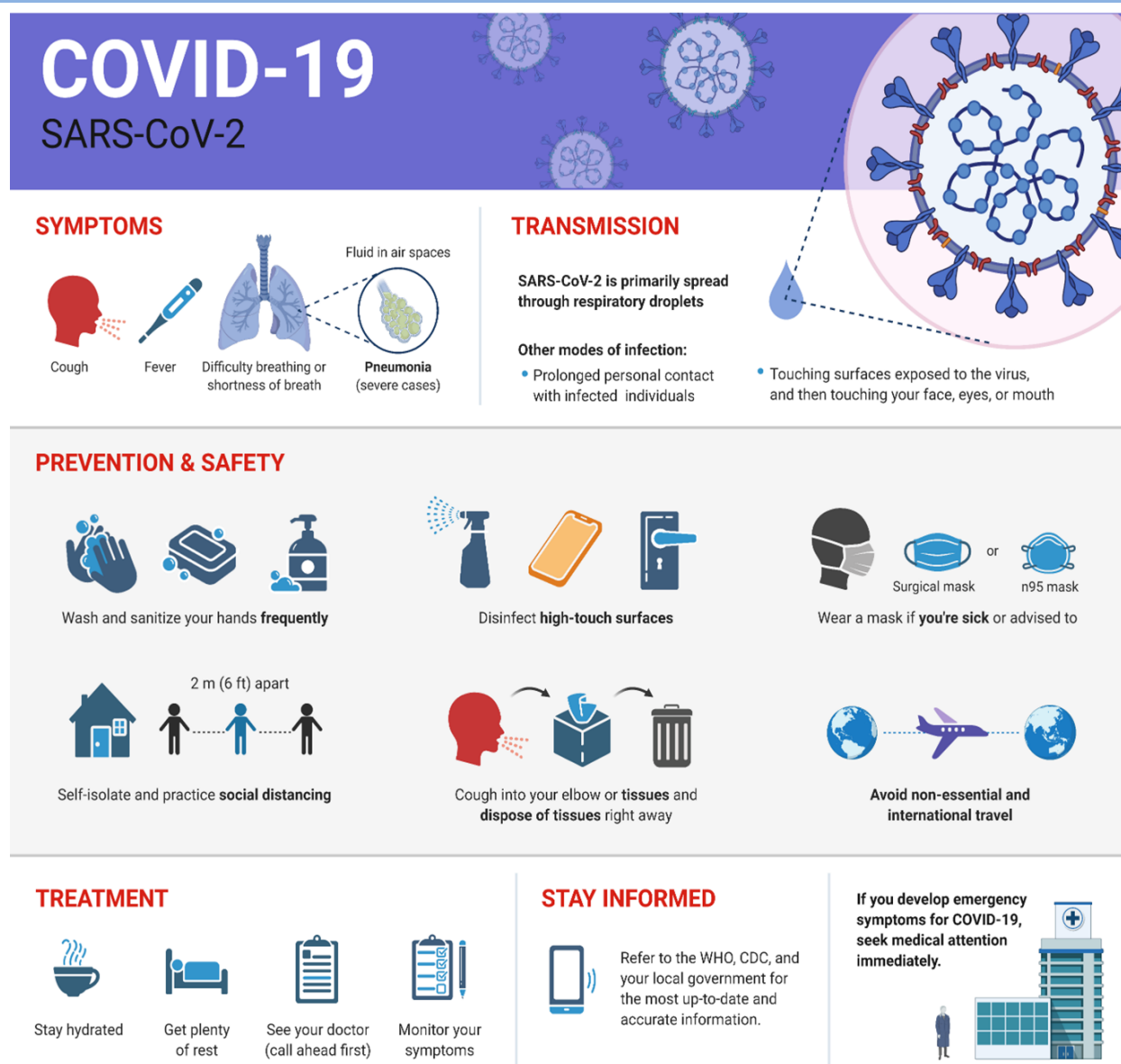
Figure 3 COVID-19 diagnostic labs in Pakistan map

According to recommendations by the National Institute of Health, Pakistan COVID-19 is expeditiously growing, and specified and timely diagnosis of this novel corona virus is ultimately require to control and properly manage this pandemic. By looking at statistics, there is widespread demand for the creation of rapidly COVID-19 diagnostic testing labs in Pakistan. Scientists and healthcare workers work day and night and created 100 COVID-19 diagnostic labs in just 100 days with a total capacity greater than 30,000 tests per day. Area wise distribution of Public, private, and Armed forces diagnostic labs are shown in Figure 3. To support this initiative of the government of Pakistan, many research and molecular institutes come forward and dedicate their services to this emergency issue. Renowned CAMB Institute of Punjab University voluntarily has created the first institutional COVID-19 BSL-2 level laboratory. Punjab University (renowned and oldest institute of Pakistan) responded promptly to this call, and scientists worked hard day and night to play their role in curbing this disaster. Renowned Virologist Dr. Idrees Khan (Head of Virology division, Center for Excellence in Molecular Biology) created an indigenous COVID-19 detecting kit with cost 10X lower than the imported kits. Dr. Nazim (Head of Virology, therapeutic and diagnostic division, Center for Applied Molecular Biology, PU), with his tireless efforts, created the first-ever institutionalized Real-Time COVID-19 detection

lab of Pakistan in no time. This lab is equipped with modern research facilities and is categorized in the BSL-3 level. This lab was inaugurated by Vice-Chancellor of Punjab University and Special Secretary Health on March 30, 2020. From that, this lab is regularly working and conducts more than 100 tests daily to aid the health department of the Punjab government. Due to this and many other initiatives, Pakistan is operating more than 17,000 COVID-19 diagnostic tests daily and have a total capacity of 30,000 tests daily.

8 Treatment and prevention of COVID-19

By the start of this pandemic, no previous therapeutic approach was available. The vaccine has not been developed yet. The fast COVID-19 spread has stressed the demand for discovery and development of efficient vaccine and potential treatment (Sharun et al., 2020). Research is being done in different domains with unique approaches to treat the COVID-19 virus, nsp12 and RdRp are excellent targets to inhibit the virus, and clinical trials are being done with new therapeutics. At present, supportive treatment is provided for secondary complications to isolated and quarantined positive patients like antibiotic infusion, fluid management, and oxygen therapy for secondary medical conditions is recommended (Habibzadeh & Stoneman, 2020; WHO, 2020).



Information sources: CDC: <https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/steps-when-sick.html> | WHO: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>

Figure 4 Safety information and precautionary measures to put the current 2019-nCoV/COVID-19 outbreak in perspective (Shahbaz et al., 2020).

At present, there is no ultimate and approved treatment against COVID-19, so prevention is a practical approach to protect ourselves. Various therapeutic strategies have been being considered, and several drugs are being applied to reduce the severity of symptoms. Dexamethasone is considered to be useful in critically ill patients (Patel et al., 2020; Sharun et al., 2020). An old modality of therapy that almost had been forgotten, but this modality has shown a great promise during the pandemic of COVID-19 and has reduced the mortality significantly (Cunningham et al., 2020; Sharun et al., 2020). Several characteristics of the virus hinder the prevention

procedure, namely, asymptomatic transmission, non-specific attributes of disease, infectivity before the symptomatic stage, high incubation time, prolonged illness, relapse, and post-recovery transmission (Jin et al., 2020). Of the effective approaches, recommended is the proper isolation of suspected, symptomatic, and confirmed cases. Individuals should follow personal protection, wear surgical masks, gloves, and frequent use of sanitizers, and follow cough hygiene (Figure 4). Homes should have enough access to sunlight to knockdown virion. Caregivers take proper protection and distance from suspected cases, wash their hands before entering and

leaving their room, and should have the least contact with anything in that specified room. Confirmed and suspected patients should be isolated in separate vicinity having negative air pressure. Regular contamination should be done on equipment, rooms, and surfaces with disinfecting agents like hypochlorite. Practitioners should be protected with N95 respirators, shoe cover, and full gown; precautions should be taken while dealing with patients and are monitored and examined regularly for indications of COVID-19 (Chu et al., 2020; WHO, 2020).

The only way to prevent the spread of COVID-19 is to adopt social distancing strategies and preventive measures recommended by local and international experts. Until now, these strategies have proved to be the most worthy (Morawska & Cao, 2020; Zhang et al., 2020). Experts suggest that good and balanced nutrition can helpfully maintain our immunity. It is considered to be essential to prevent and manage viral infections (Jaggers et al., 2020; Jayawardena et al., 2020). These steps to minimize the escalation of corona virus includes indoor and outdoor measures, dig out and isolate cases, identifying the latest contacts of the patient, travel check, social distancing initiatives and quarantine, and vaccines preparation, trials of medicines and treatments. As specific therapies and vaccines are present yet, other initiatives are playing an indispensable role in limiting the number of patients by many folds. These actions play their part by breaking the COVID-19 chain of transmission and intercepting the appearance of new cases.

9 Conclusions and perspectives

COVID-19 has challenged the medical, social, and financial infrastructure of the world in no time. At present, we can only predict the impact of the virus in the short and long run. Initially, the virus shows exponential growth in terms of the number of patients. Statistics of Pakistan and the world have shown that we are on the verge of disaster, as thousands of new cases are reported daily. Advanced diagnostic facilities across the globe that helped in identifying infected individuals and so breaking the chain of transmission, currently there are more than 100 COVID-19 diagnostic labs in Pakistan. Parallel to this, scientists are doing great to discover potential vaccine and treatment, and that will be available in a few months. This is just the first phase; such outbreaks of particular origin will continue to occur; efforts and research should be made in this regard to prepare and equip in advance to prevent a similar disaster from future outbreaks.

Conflict of interest

The listed author(s) declare no conflict of interest in any capacity, including competing or financial.

Funding

No funding was received for this study

Authors' contribution

All listed author(s) have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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