Deep Insights of COVID-19: Perception of Current Infection and Anticipation of Potential Immunity

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Abstract

The outbreak of COVID-19 caused by coronavirus SARS-CoV-2 laid its tremendous effects on a national, regional, and global levels. This overview discusses current diagnostic tests to assist management of the disease. Diagnosis of SARS-CoV-2 is approached throughout two main policies; virus detection in body fluids and anti-virus antibody tests. PCR is considered the most reliable test and is carried out in different types of swabs, the most common of which is the nasopharyngeal swab. Antibodies are detected in the plasma using ELISA, especially anti-nucleocapsid and surface spike protein to confirm past infection and investigate presumed immunity. Tracing neutralizing antibodies indicates inhibition of viral replication. Vaccines based on different viral components are examined in many laboratories. Russia declared the first approved vaccine in August 2020, while the United States prompt vaccine production by January 2021. Diabetic patients showed serious complications during the course of the COVID-19 infection, the degree of which was correlated to the type of diabetes although exact mechanism is still under studying. Patients with no history of diabetes were diagnosed with diabetes post-COVID-19 treatment. Periodontal diseases in diabetic patients and COVID-19 may entail systemic interactions.

Introduction

Multiple series of coronaviruses have been reported, ranging from the common cold to much more serious viruses as Severe Acute Respiratory Syndrome (SARS-CoV), and Middle East Respiratory Syndrome (MERS) named in 2003, 2012 respectively. The aforementioned viruses were delivered from animals to humans. The novel coronavirus outbroken in late 2019, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It belongs to the subfamily β–coronaviruses and shares 79.5% of the genetic sequence of SARS-CoV. The clinical disease caused by SARS-CoV-2 is called Coronavirus disease 2019 (COVID-19)[1].
COVID-19 is a rapidly spreading disease that almost infected all age ranges and showed

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higher rates of mortality. These alarms made the World Health Organization (WHO) declare COVID-19 pandemic on the 11th of March 2020[2]. With the clinical and economic impact of this pandemic taken into consideration, it is essential to have highly specific and sensitive tests to uncover the infection even in asymptomatic patients. With the aim of effective treatment and development of vaccines, the potential response of the human immune system to the virus is explored.

The aim of this review is to reveal the current diagnostic tests, its reliability, sensitivity, and specificity. The tests that are being developed and improved on a population level to detect and diagnose infection, thus assist in the management and containment of the disease. As well as explore the immune response of the body in convalescent patients and the keen efforts to develop an effective vaccine.

Importance of COVID-19 diagnosis

When SARS-CoV-2 infects an individual, multiple factors determine the body's response and development of COVID-19 disease. These include viral factors as viral number and virulence,

host factors as the health state, host immune system and nutrition, and environmental factors. Consequently, definite infection by SARS-CoV-2 ranges from mild to severe, or even death, based on the capability of the immune system to fight against the virus. Up till now, there is no proven effective treatment for COVID-19, though dozens of existing compounds were suggested, and thus there is a need for natural supplements that may be beneficial to prevent COVID-19 infection by boosting the immune system, and to prevent and modulate cytokine storm in severe forms of COVID-19[3].

Accordingly, it is imperative to control spreading of the infection as long as no definite treatment is reported. The key to controlling the spread of SARS-CoV-2 and its clinical expression as COVID-19 is to test individuals according to the WHO statement [4]. Screening permits assessment of risk and rapidly implement necessary measures at the appropriate scale to reduce both virus transmission as well as economic, public health, and social impacts. In the early stages of this pandemic, there was inadequate access to suitable diagnostic tests globally. This led to confusion among healthcare professionals and the public, about the prioritization of testing and interpretation of results. Taking also into consideration the incubation period of the virus to the first symptom is typically 5 to 7 days, with a range of 4-14 days [5].

Early screening facilitates the management and control of infection especially in vulnerable patients as old aged and critical medical conditions; diabetes, heart disease, and asthma [6].

Who should be screened for SARS-CoV-2?

In countries such as Singapore and South Korea, aggressive programs of testing, contact tracing, and isolation have been implemented to early control of infection. As the pandemic progresses, the focus has been on symptomatic patients, and key workers and their families.
Testing symptomatic patients for current infection enhances contact tracing, and thus infection prevention and control. Key workers, especially those in healthcare, maybe self-isolating for long periods if a household member has symptoms. Exclusion of infection in the household enables staff to return to work, as would be proof of staff immunity[7].

Testing methods:

The SARS-CoV-2 infection could be approached throughout two main policies; virus detection in various body fluids and anti-virus antibody tests. Antibody detection tests are used to confirm past infection and presumed immunity to reinfection.

Accordingly, the most common diagnostic tests in use for SARS-CoV-2 infections are reverse transcriptase-polymerase chain reaction (RT-PCR), and IgM and IgG enzyme-linked immunosorbent assay (ELISA).

Interpretation of test results depends on the type of the biological sample, timing of collection. As well as, recognition of both intermittent viral shedding and variation in the sensitivity and specificity of different test systems. Diagnostic tests should be accurately investigated and legalized before use in clinical set-ups, as tests of unreliable results would cause worse outcomes than when not applying any examinations[8].

Reverse transcriptase-polymerase chain reaction RT-PCR

RT-PCR is very commonly used in the diagnosis of COVID-19 using nasopharyngeal swabs or other upper respiratory tract specimens, including throat swab or, more recently, saliva. Viral load peaks by the end of the first week post-infection, where minimal symptoms are just being developed. Values may be fluctuating, so a single negative swab is not indicative and deceiving, and tests should be repeated for confirmation. Swabs must be collected accurately and conveyed in a proper viral transference medium[9].

With respect to sensitivity, nasopharyngeal swaps are preferred over oropharyngeal ones. Nasopharyngeal swabs are better taken as the symptoms first emerge. However, swabs from both sites could be combined to enhance sensitivity. Deeper respiratory secretions such as sputum and bronchoalveolar fluid contain more viruses, and yields increase over 2-3 weeks in more severe cases. Fecal virus shedding can persist after the resolution of diarrhea [8].

Different manufacturers direct their work towards different RNA gene material such as envelope nucleocapsid proteins (NC), spike protein (S), RNA-dependent RNA polymerase (RdRp), and ORF1genes. Despite differences in the targeted virus proteins, sensitivity does not

differ to a great extent between different tests, except the RdRpSARSr (Charité) primer-probe, which has a slightly lower sensitivity[10].

The cycle threshold (Ct) is used to measure viral RNA in the nasopharyngeal swabs. Ct is the number of replication cycles required to produce a fluorescent signal. Low Ct values designate higher viral loads, while Ct value less than 40 is clinically reported as PCR positive. In most symptomatic individuals of COVID-19 infection, Ct is positive as early as day one of symptoms and reaches a maximum within the first week. This positivity starts to retreat by the third week and subsequently becomes undetectable. PCR positivity may persist beyond the third week which reflect only the detection of viral RNA without the presence of a viable virus[11,12].

Interestingly, viral RNA has been detected by RT-PCR beyond week six following the first positive test. Few cases have also been reported positive after two consecutive negative PCR tests and it was difficult to interpret the results if it was a testing error, reinfection, or reactivation. However, it was recommended that in a situation of lack of testing resources, patients might be re-tested only after the 20th day from the first positive test and beyond [13].

In a study of nine patients, attempts to isolate the virus in culture were not successful beyond day 8 of illness onset, which was linked with the decline of infectivity beyond the first week. Based on this fact, the "symptom-based strategy" of the Centers for Disease Control and Prevention (CDC), indicated that health care workers can return to work, if at least 3 days (72 hours) have passed in recovery. The recovery is characterized by resolution of symptoms as the fever without the use of fever-reducing medications, and improvement in respiratory complications (as cough or shortness of breath). This recovery is acceptable when at least ten days have passed since the onset of symptoms [14].

The timeline of PCR positivity differs with the type of swap collected where it declines more slowly in sputum swaps and may still be positive while nasopharyngeal swabs are negative [12]. PCR positivity was reported positive in the stool beyond the nasopharyngeal swabs by a median of 4 to11 days in 57% of infected patients and was not correlated to clinical symptoms [11]. The persistence of PCR in sputum and stool was found to be similar as assessed by Wölfel et al [15]. In a study of 205 patients with confirmed COVID-19 infection, RT-PCR positivity was highest in bronchoalveolar lavage specimens (93%), followed by sputum (72%), nasals swab (63%), and pharyngeal swab (32%) [16]. False-negative results were likely due to untimely sample collection in relation to onset of symptoms and/or scarcity of samples especially nasopharyngeal swabs [12].

Delays in transporting samples to the laboratory and returning results to the originator mean that the overall test turnaround often exceeds 48 hours. The decentralization of laboratories helps reduce these delays and provide more timely information for both diagnosis and public health interventions. Novel systems are being assessed for faster detection of key viral sequences and a variety of point-of-care antigen detection devices have been developed, but their performance varies widely. Some antigen detection devices have poor sensitivity, indicating that infections are missed, and infectious individuals might not be managed appropriately [17].

RT-PCR tests reported 100% specificity owed to the primer design that is selective to the SARS-CoV-2 genome sequence. Nevertheless, false-positive results have been spotted which might be due to technical mishandling or reagent contamination [15].

Detection of SARS-CoV-2 Antibodies:

When patients are of mild- moderate symptoms, or already recovered from COVID-19 infection, viral loading is not an applicable tool, alternatively anti-virus antibodies could be investigated demonstrating the host immune response to SARS-CoV-2 infection. Serological diagnosis provides a viable tool to understand the extent of COVID-19 in the community and to recognize immunized individuals who are potentially "protected" from becoming reinfected.

The most sensitive and earliest serological marker is the total antibodies [18]. Immunoglobulin M (IgM) and immunoglobulin (IgG) ELISA tests have been found to be positive as early as the fourth day after symptom onset, and higher levels occurred in the second and third week of illness[19].

Guo et al[18], found that the combined sensitivity of PCR and IgM ELISA directed NC antigen was 98.6% versus 51.9% when only the PCR test was used. Quantitative PCR had a

higher positivity rate than IgM ELISA during the first 5.5 days of illness, after which ELISA test positivity became higher.

The Specificity recorded of ELISA-based IgM and IgG antibody tests in the diagnosis of COVID-19, was around 95%. The most prevalent protein of the virus is the NC, to which most antibodies are directed. Consequently, tests detecting NC-antibodies would be more sensitive. On the other hand, the receptor-binding domain S (RBD-S) protein is the host attachment protein to the virus, and anti-RBD-S antibodies would be more specific and are expected to be neutralizing. Consequently, using NC and/or RBD-S antigens to detect the presence of IgM or IgG antibodies is expected to be highly sensitive[20].

The main drawback of antibodies tests is the cross-reactivity with SARS-CoV and possibly other coronaviruses. Antibody tests are purely qualitative in nature and can only indicate the presence or absence of anti-SARS-CoV-2 antibodies. The presence of neutralizing antibodies can only be confirmed by plaque reduction neutralization test. However, high titres of IgG antibodies detected by ELISA, have been shown to positively correlated with neutralizing antibodies. Neutralizing antibodies inhibit viral replication in vitro and have been considered as a key immune product for protection or treatment against viral diseases. Virus-specific neutralizing antibodies are provoked either through infection or vaccination. The long-term persistence and duration of protection developed by the neutralizing antibodies remain unknown[12].

Antibody detection tests may also be limited by poor specificity, so people are wrongly identified as having been infected and have a false sense of security.

Human response to SARS-CoV-2

The adaptive immune response of the body to viral infections is manifested in virus-specific T-cells, for cell-mediated immunity responsible for the inflammatory response. In addition to B-lymphocytes response for humoral immunity and production of antibodies. IgM provides the first line of defense during viral infections, while higher affinity IgG aims for long-term immunity and immunological memory. Consequently, the detection of IgM in the serum indicates recent infection, while the detection of IgG suggests that exposure occurred several days before[6].

Studies on antibody development against SARS-CoV back in 2006, showed that anti-virus specific IgM and IgG antibodies were not detected until the tenth day of infection. IgM appeared first showing detected positivity to one month and then dropped gradually until it was untraceable at 180 days. On the other hand, IgG titre reached its maximum after a month and remained higher than IgM and lasted up to 720 days. At that time, the viral neutralizing potential through neutralizing antibodies against consequent infection peaked after thirty days, then, unfortunately dropped gradually to a minimum in most cases and was completely undetectable indicating a lack of virus immunity [21]. In addition, patients infected by SARS-CoV were reported to have an imperfect expression of types I and II interferons, indicative of poor protective immune responses [22].

Experiments in Rhesus Macaques monkeys were carried out during the early phase of recovery from initial infection by SARS-CoV-2. Monkeys were challenged for reinfection with an identical viral strain. Clinical, radiographic, and histopathological observations did not show any detectable viral dissemination, clinical manifestations, or histopathological changes. The only elevation detected was the specific anti-SARS-CoV-2 antibodies. Average titers of neutralizing antibodies showed a linear increase since the primary infection and could be responsible for the protection against subsequent reinfection by SARS-CoV-2[23].

Immune responses to mild-moderate SARS-CoV-2 infection triggered increased antibody-secreting cells, follicular helper T cells, activated CD4^{+} T cells and CD8^{+} T cells, and IgM and IgG antibodies in the blood even before symptomatic recovery. These immunological changes persisted for at least seven days after full resolution of symptoms[24].

Antibodies were detected as early as two days of illness onset in human plasma serum [25]. Reports by Xiao et al [26], indicated that in week 3 after the onset of symptoms, all patients were positive for IgM and IgG. By time IgM dropped back while IgG continued to go up. For an observational period of 7 weeks, all patients were positive for IgG indicating a humoral immune reaction defending the body against the SARS-CoV-2 virus. Longer periods of observations are mandatory if vaccine development to SARS-CoV-2 is desired.

Ni et al[27], detected SARS-CoV-2-specific

humoral and cellular immunity in convalescent subjects. Most subjects displayed serum neutralizing antibodies that were correlated with the numbers of virus-specific T cells. IgG antibody titer was maintained for at least 2 weeks after discharge from hospitals where the period of hospitalization ranged from 11-45 days.

Zhou et al [28], monitored infected patients 18-20 days after onset of symptoms and all patients exhibited NP-specific antibody response. Virus-specific IgM peaked at day nine after disease onset, and the transition to IgG occurred within the second week. Over time, IgM titre decreased while all patients were strongly positive for anti-viral IgG. They also reported that sera from several patients succeeded in impeding SARS-CoV-2 entry in target cells.

Xiang et al [19], identified anti-SARS-CoV-2 IgM and IgG antibodies in 85 patients with a confirmed diagnosis and 24 patients with the suspected diagnosis. IgM and IgG antibodies were confirmed at less than 5 days of symptoms onset in 60% and 40 % of the patients respectively. For more than 30 days, IgM appeared in 87.7% of patients and IgG in 100% of the patients.

An increase of IgM and IgG seropositivity was detected in 23 patients of age range 37-75. against NP and RBD for most patients at 10 days or later of symptom onset. More patients had earlier seropositivity for anti-RBD than anti-NP for both IgG and IgM, a fact that was correlated with virus neutralization titer[20].

Xun et al [29], collected plasma of 175 COVID-19 recovered patients of age range 16-85 of mild symptoms. SARS-CoV-2-specific neutralizing antibodies were traceable in patients' plasma within the second week of symptoms onset and remained thereafter, although their titers were variable in different patients. Elderly and middle-aged patients had significantly higher plasma titers than young patients and 30% of the patients failed to develop any detectable levels of neutralizing antibodies.

Surprisingly, SARS-CoV-2 T-cell reactivity has been reported in non-exposed donors, mostly associated with CD4+ T cells, and to a lesser extent CD8+ T cells; 40-60% of unexposed donors in the United States[30], 20% of healthy controls in the Netherlands[31], 34% of SARS-CoV-2 seronegative healthy donors in Germany[32], 50 % of unexposed subjects with no history of infection or contact with patients in Singapore[33]. Although definite data on the source of these memory T-cells in unexposed individuals remains unavailable speculations suggest that it might originate from exposure to 'common cold' coronaviruses. It is expected that people with a high level of pre-existing memory T-cells could deliver an immune response on exposure to SARS-CoV-2 and thereby limit disease severity and could also enhance vaccination outcomes[34].

SARS-CoV-2 Vaccine

Researchers worldwide have been busy and over stimulated working around the clock to develop a SARS-CoV-2 vaccine. Under normal circumstances, the process of developing an efficient vaccine passing through animal experiments then human trials to reach an official approval and marketing, takes years. Nevertheless, in the outstanding current situations, experts estimate that a boosted vaccine development process could speed an effective product to appear in approximately 12-18 months[34].

Studies on SARS-CoV and MERS-CoV vaccines showed that the spike (S) protein on the surface of the virus is an ideal target for a vaccine. In SARS-CoV-2, this protein interacts with target cell ACE2 receptors to gain entry to the cells and cause infection, thus antibodies targeting the spike can interfere with this binding and neutralize the virus[35].

Despite that, re-infections are unlikely in the short term, recurrences were reported in Shangqiu, Henan Province, China, in which all patients were females of age range 30-56[36]. Re-infections after days of recovery in four patients with age range 30-36, have been reported by Lan et al[37] and were interpreted as consequences of false-negative test results.

Researchers around the world are developing more than 165 vaccines against SARS-CoV-2, and 27 of which reached human trials. While in normal circumstances, vaccines require years of research and testing before reaching the clinical phase, but scientists are racing to produce a safe and effective vaccine[38].

Different strategies are advocated in vaccine development to stimulate body response. Virus genetic material has been used to provoke an immune response in which viral proteins are produced in the body. Messenger RNA based vaccine has been reported. Early human trials provoked SARS-CoV-2 antibodies, as well as immune T cells in the United States, and other

countries including Argentina, Brazil, and Germany[39-40].

Circle DNA (plasmid DNA) encoding for target protein in the pathogen is being investigated as well, as an anti- SARS-CoV-2 vaccine. The trial vaccine did not show any pathological affinity and was considered a safe alternative to hinder infection that varies from introducing attenuated virus in the human body, but yet no results of human trials are announced[41].

On the other hand, viral vector vaccines that use attenuated virus to deliver coronavirus genes into cells and provoke an immune response is being investigated. University of Oxford researchers announced COVID-19 vaccine testing in human volunteers. The investigated vaccine is based on an adenovirus vaccine vector and the SARS-CoV-2 spike protein. Genetic material and viral protein SARS-CoV-2 is formulated to form Spike glycoprotein (S)[42]. The results of phase I/II trials of the Oxford vaccine encourages strong immune responses in which the vaccine provoked T cell response within 14 days of vaccination and neutralizing antibody response within 28 days. Participants were supplied with a booster dose which resulted in neutralizing activity against the coronavirus in 100% of participants[43].

On the other hand, a coronavirus protein or a protein fragment could be introduced in the human body to elicit an immune response. The state-owned Chinese company Sinopharm announced Phase III trials in July/2020 in the United Arab Emirates. Abu Dhabi's health minister was the first volunteer to be injected, and thousands of volunteers were scheduled to participate. Vaccine found no severe adverse effects and produced an immune response[44].

To date, just one coronavirus vaccine has been approved. Sputnik V – formerly known as Gam-COVID-Vac. It was developed by Gamaleya Research Institute of Epidemiology and Microbiology, run by the Health Ministry of the Russian Federation. It was approved by the Ministry of Health of the Russian Federation on the 11th of August 2020. This vaccine consists of two components, administered 21 days apart: Component 1 consists of a recombinant adenovirus vector based on the human adenovirus type 26, containing the SARS-CoV-2 S protein gene. Component 2 consists of a vector based on the human adenovirus type 5,

containing the SARS-CoV-2 S protein gene. Both components are designed to enter human cells and produce an immune response that is estimated to last for two years, according to Mikhail Murashko, Minister of Health of the Russian Federation. As the reported vaccine has not yet entered Phase 3 clinical trials, experts have raised considerable concern regarding the vaccine's safety and efficacy[45].

On the other hand, United States government has chosen three vaccine candidates to fund for Phase 3 trials under Operation Warp Speed: Moderna's mRNA-1273, The University of Oxford, AstraZeneca's AZD1222, and Pfizer and BioNTech's BNT162. The Operation Wrap speed aims to using the resources of the federal government (FDA) and the U.S. private sector to accelerate the testing, supply, development, and distribution of safe and effective vaccines, therapeutics, and diagnostics to counter COVID-19 by January 2021. Despite the fact that developing a safe controlled human infection models for human trials could take 1-2 years, FDA guidance issued that a sponsor should provide data from placebo-controlled trials indicating their vaccine is at least 50% effective against COVID-19, in order to be authorized for use[46].

COVID-19 in diabetic patients and the impact in oral health:

Day by day there is an increased improvement in the understanding of the dangers caused by COVID-19 that are associated with additional hazards in the human body in those individuals with chronic non-infectious diseases. Diabetic patients are on top of the patients who face the problem of worse outcomes, and a limited chance of disabling the virus, accordingly diabetic patients show higher incidence of serious complications and death than non-diabetics. Although scientists expect that death rate (which means the number of people who die from the virus as a percentage of the total number of people who contract the virus), would decline as we get better at detecting and treating this pandemic virus, diabetic patients are more prone to experience severe symptoms and complications when infected especially if they do not manage their diabetes well and experience fluctuating blood sugars. And by this viral infection, they may suffer from increased inflammation, or even an internal swelling may occur which is originally produced by over limit

blood sugars. Both the infection and uncontrolled sugar levels could result in more severe complications. Another issue in diabetic patients is ketoacidosis, which is commonly experienced in type 1 diabetes. Ketoacidosis complicates the management of fluid intake and the control of electrolyte levels that are important in managing sepsis. Consequently, diabetic patients may develop septic shock as a highly serious complication of COVID-19 infection[47].

The correlation of diabetes and COVID-19 is being recently studies especially the impact of diabetes type and preliminary data from England suggests higher risk in people with type 1 diabetes compared to type 2[48].

There are limited data to date on the association between blood glucose control and COVID-19 outcomes. A retrospective study of 451 people with COVID-19 with diabetes and/or hyperglycemia from the united states reported that people with uncontrolled hyperglycemia had a longer length of illness and higher mortality compared with people without diabetes or with uncontrolled hyperglycemia[49]. Another retrospective study of people with type 2 diabetes from China reported that well-controlled blood glucose is evident to be correlated with improved outcomes in infected patients[50]. On the other hand, severe infection may predispose to a more difficulty managing of blood glucose, so the causal mechanism behind correlations between glucose control and COVID-19 outcomes is unclear. Two recent studies in the United Kingdom reported that diabetes was independently associated with a higher risk of death that increased with higher HbA1c[51].

The medication of most COVID-19-related consensus statements recommend stopping metformin and sodium-glucose cotransporter 2 inhibitors (SGLT2i) during acute illness and following the sick-day rules. Dipeptidyl peptidase 4 inhibitors (DPP-4i), glucagonlike peptide 1 receptor agonists (GLP1RA), and insulin are the preferred options in particular for the hospitalized patient[52].

Recently, there is a growing concern in a percent of patients with no history of diabetes whom during COVID-19 treatment were diagnosed with diabetes at the follow up clinics. This phenomenon has been observed worldwide lately by experts, who are trying to understand whether and how COVID-19 might be eliciting diabetes among those who didn't have the disease before[53].

Periodontal diseases have been always associated with diabetes despite the fact that definite corelation has not been proven because of the confounding evidence, and few randomized trials[54]. Periodontitis is activated and sustained by an atypical host immune-inflammatory response to bacteria in the subgingival biofilm. It is characterized by alveolar bone loss, abscess formation, tooth mobility, and eventual tooth loss[55].

All of these complications were found to be driven by elevated recruitment of polymorphonuclear neutrophils (PMNs), which are primed and recruited from the circulation to the sites of inflammation. This recruitment supports the fact that periodontal tissue inflammation potentiates systemic effects that predispose toward an exacerbated innate immune response. Furthermore, peripheral PMNs can respond synergistically to simultaneous and remote inflammatory triggers and consequently contribute to the interaction between periodontal diseases and other inflammatory conditions.[56]

These influences imply that diabetic patients with COVID-19 and even after recovery necessitate special dental care, although that the Occupational Safety and Health Administration, describes the performance of aerosol-generating procedures on known or suspected COVID-19 patients as "very high risk"[57]. In addition, the CDC recommends that patients with symptoms of COVID-19 should avoid nonemergent dental care until the patient has completely recovered, and providers should stick to the protocols established by the CDC to limit infection transmission[58].

Conclusions

Sensitive and specific diagnostic tests are essential for population surveillance of COVID-19. Diagnosis of SARS-CoV-2 is commonly approached through PCR or ELISA serological tests. PCR is useful in early stages of active infection. Serological detection of anti-virus antibodies as ELISA is beneficial in patients who present late or show up with mild-moderate symptoms.

The time course of PCR positivity and seroconversion may vary in different age groups, and according to the type of sample being

collected. Infection by SARS-CoV-2 elicits both cellular and humoral responses. During late or after infection, serological tests of antibodies to nucleocapsid and viral spike proteins showed that the IgM antibody is usually detected earlier than IgG and the body can develop neutralizing antibodies that provide immunity against COVID19, but the longevity of these antibodies is still unknown.

Different vaccine approaches are being developed by researchers including viral genome whether RNA or DNA, modified viral genetic material, viral protein or protein fragments, or attenuated virus. Some of experimental vaccines have reached the third phase of clinical trials on thousands of human volunteers. However, many questions remain unresolved, particularly how long is the potential immunity of individuals, both asymptomatic and symptomatic, who were infected with SARS-CoV-2.

Serious complications of COVID-19 infection and higher death rate were observed more in diabetic patients and uncontrolled hyperglycemia than people without diabetes, and even linked to the type of diabetes. Patients with no history of diabetes were diagnosed with diabetes at the follow up clinics of COVID-19 treatment. Periodontal diseases in diabetic patients and COVID-19 should be taken seriously for fear of systemic interactions.

Acknowledgements

Declaration of Interest

The authors report no conflict of interest.

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