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Review Article on the Coronavirus disease (COVID-19)

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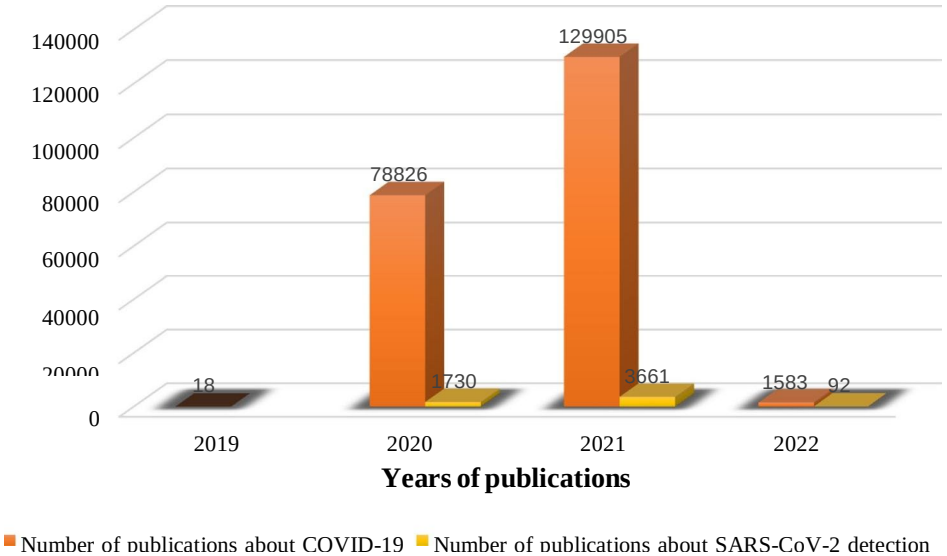
Abstract: ***Coronaviruses are a group of enveloped viruses with nonsegmented, single-stranded, and positive-sense RNA genomes. Coronaviruses belong to the "Coronaviridae family", which causes various diseases, from the common cold to SARS and MERS. In March 2020 the World Health Organization declared the SARS-Cov-2 virus a global pandemic. We performed a review to describe existing literature about Corona Virus Disease 2019 (COVID-19) history, Symptoms, Epidemiology, Clinical features, Clinical manifestations, Diagnosis, Treatment, Prevention.***

Keywords: COVID-19, Symptoms, Epidemiology, Clinical features, Clinical manifestations, Diagnosis, Treatment,Prevention

I. INTRODUCTION

The world health organization declared an epidemic on january 30, 2020, following the outbreak of the sars- cov-2 virus in wuhan, hubei province, china, and its rapid spread to 25 countries. This happened just 1 month after the announcement of the first case of the disease on december 31, 2019. Coronaviruses are positive single- stranded rna viruses that belong to the coronavirus family and are genetically classified into four genera: α, β, γ and δ coronavirus these viruses often infect animals such as birds and mammals and usually cause mild respiratory infections in humans. Due to the sars- cov-2 rna content and its high potential for emergence, respiratory infections caused by the virus have recently led to deadly endemics in humans, such as sars and mea- sles. The first case of mid- dle east respiratory syndrome (mers) was observed in saudi arabia in 2011–2012, of which 2495 cases have been reported since then, of which 858 cases were associated with death and the death rate was estimated at 34.4%. While no new mers-cov cases have been reported since 2004, the sars-cov-2 outbreak occurred unexpectedly in 2020. Sars-cov-2 is the seventh member of the coronavirus family, which, like mers-cov, sars-cov causes respiratory disease in humans with a genome size of 27–35 kb and belongs to the beta-coronavirus species. Like other coronaviruses, it encodes several structural proteins and non-structural proteins. Spike glycoprotein (s) of and nucleocapsid protein (n), membrane protein (m) and coating protein (e) are among its structural proteins



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COVID-19 is a rapidly growing pandemic with its first case identified during December 2019 in Wuhan, Hubei Province, China. Due to the rampant rise in the number of cases in China and globally, WHO declared COVID-19 as a pandemic on 11th March 2020. The disease is transmitted via respiratory droplets of infected patients during coughing or sneezing and affects primarily the lung parenchyma. The spectrum of clinical manifestations can be seen in COVID-19 patients ranging from asymptomatic infections to severe disease resulting in mortality

II. HISTORY

Coronaviruses are enveloped positive sense RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance under the electron microscope; hence the name coronavirus [3]. Four corona viruses namely HKU1, NL63, 229E and OC43 have been in circulation in humans, and generally cause mild respiratory disease. There have been two events in the past two decades wherein crossover of animal betacorona viruses to humans has resulted in severe disease. The first such instance was in 2002–2003 when a new coronavirus of the β genera and with origin in bats crossed over to humans via the intermediary host of palm civet cats in the Guangdong province of China. This virus, designated as severe acute respiratory syndrome coronavirus affected 8422 people mostly in China and Hong Kong and caused 916 deaths (mortality rate 11%) before being contained. Almost a decade later in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV), also of bat origin, emerged in Saudi Arabia with dromedary camels as the intermediate host and affected 2494 people and caused 858 deaths (fatality rate 34%)

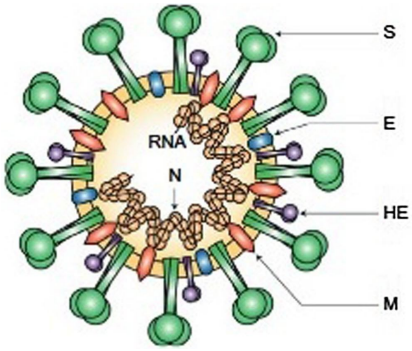


Fig.1 Virion structure and its genome

III. SYMPTOMS

A wide range of symptoms are found in COVID-19 patients, ranging from mild/moderate to severe, rapidly progressive, and fulminant disease. Symptoms of COVID-19 are non-specific and disease presentation can range from asymptomatic to severe pneumonia. Incidence of asymptomatic cases ranges from 1.6% to 51.7% and these people do not present typical clinical symptoms or signs and do not present apparent abnormalities in lung computed tomography. The most common symptoms of COVID-19 are fever, cough, myalgia, or fatigue and atypical symptoms include sputum, headache, haemoptysis, vomiting, and diarrhoea. Some patients may present with sore throat, rhinorrhoea, headache, and confusion a few days before the onset of fever, indicating that fever is a critical symptom, but not the initial manifestation of infection. Furthermore, some patients experience loss of smell (hyposmia) or taste (hypogeusia), which are now being considered early warning signs and indications for self-isolation.

The most common symptoms of COVID-19 are

- Fever.
- Dry cough.
- Fatigue.

Other symptoms that are less common and may affect some patients include

- Loss of taste or smell.
- Nasal congestion.
- Conjunctivitis (also known as red eyes).
- Sore throat.
- Headache.

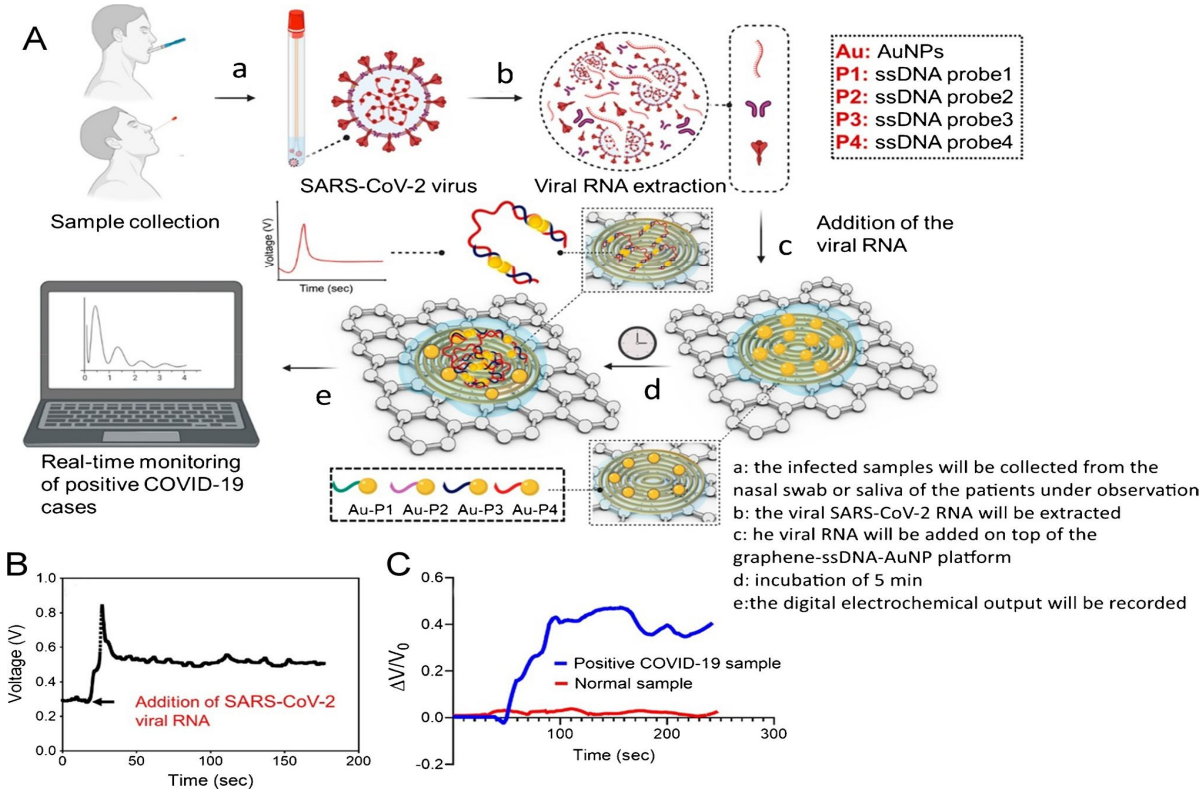
- Muscle or joint pain.
- Different types of skin rash.
- Nausea or vomiting.
- Diarrhea.
- Chills or dizziness.

Symptoms of severe COVID-19 disease include:

- Shortness of breath.
- Loss of appetite.
- Confusion.
- Persistent pain or pressure in the chest.
- High temperature (above 38 °C).Other less common symptoms are
- Irritability.
- Confusion.
- Reduced consciousness (sometimes associated withseizures).
- Anxiety.
- Depression.
- Sleep disorders.

People of all ages who experience fever and/or cough associated with difficulty breathing or shortness of breath, chest pain or pressure, or loss of speech or movement should seek medical care immediately. If possible, call your health care provider, hotline or health facility first, so you can be directed to the right clinicrological complications such as strokes, brain inflammation, delirium and nervedamage.

IV. SAMPLE COLLECTION & ANALYSIS



[1]

Fig. 2 A Schematic illustrations of the principle of the COVID-19 electrochemical sensing platform. B Sensor output signal as a func- tion of time with the addition of SARS-CoV-2 viral RNA load.

A. *Transmission*

Zoonotic transmission initially appeared to be a plausible cause as majority of early cases had a history of exposure to wet markets. However, by the end of January 2020, the number of people who developed the disease without exposure to the market or another person with respiratory symptoms increased. The spread of the disease among persons who did not visit Wuhan and among healthcare workers suggested a person-to-person spread of the virus. The exact mode of transmission of this virus is unknown. But, as with other respiratory viruses, droplet borne infection, either directly or indirectly, through fomites is probably the predominant mode of transmission. At present, there is no evidence for airborne transmission of the virus.12 13 Although virus particles have been detected in stool samples of both symptomatic and convalescing patients, the risk of feco-oral transmission is unclear

V. DURATION OF VIRUS

The duration for which a patient with COVID-19 remains infective is unclear. Viral load in the oropharyngeal secretions is highest during the early symptomatic stage of the disease [13,14]. The patient can continue to shed the virus even after symptom resolution [13]. In a study from China, the median duration of virus shedding was 20 days (interquartile range [IQR] 17.0–24.0) amongst the survivors [15]. A study of viral dynamics in mild and severe cases revealed that mild cases tend to clear the viruses early, while severe cases can have prolonged viral shedding [16]. Data from studies using twin respiratory and fecal sampling have shown viral shedding can persist in stools for more than 4 weeks even when respiratory samples are negative [17]. Xu et al identified male sex, delayed hospitalization after illness, and invasive mechanical ventilation as risk factors for prolonged viral shedding [13]. Transmission during the asymptomatic phase has also been reported. In a study from Singapore, 6.4% of the 157 locally acquired cases of COVID-19 were attributed to transmission during the asymptomatic phase of the disease .***Severity of Covid-19 Virus:***

A. *Spectrum of Infection Severity*

The spectrum of symptomatic infection ranges from mild to critical; most infections are not severe [19,39-44]. Specifically, in a report from the Chinese Centre for Disease Control and Prevention that included approximately 44,500 confirmed infections with an estimation of disease severity [45]:

1) Mild disease (no or mild pneumonia) was reported in 81 percent.
2) Severe disease (eg, with dyspnea, hypoxia, or >50 percent lung involvement on imaging within 24 to 48 hours) was reported in 14 percent.
3) Critical disease (eg, with respiratory failure, shock, or multiorgan dysfunction) was reported in 5 percent.
4) The overall case fatality rate was 2.3 percent; no deaths were reported among noncritical cases.

Similarly, in a report of 1.3 million cases reported to the United States Centers for Disease Control and Prevention (CDC) through the end of May 2020, 14 percent were hospitalized, 2 percent were admitted to the intensive care unit (ICU), and 5 percent died [46]. The risk of severe illness varied by age and underlying comorbidities.

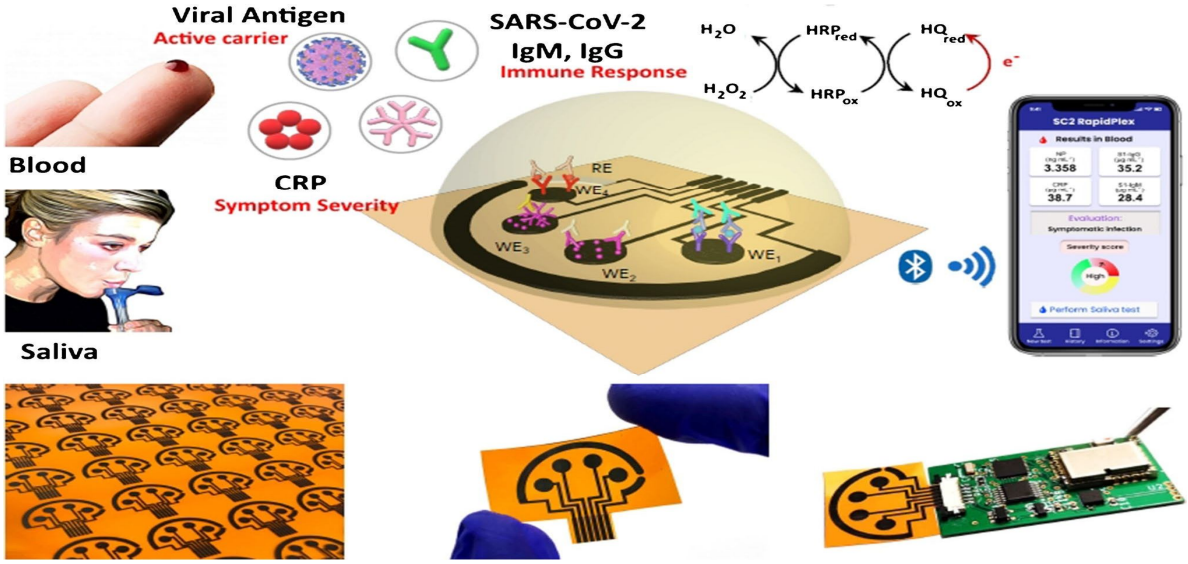


Fig. 3 Schematic illustration of the SARS-CoV-2 RapidPlex multisensor telemedicine platform for detection of SARS-CoV-2 viral proteins. Reproduced with permission from [93]

B. Infection Fatality Rate

The case fatality rate only indicates the mortality rate among documented cases. Since many severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections are asymptomatic and many mild infections do not get diagnosed, the infection fatality rate (i.e., the estimated mortality rate among all individuals with infection) is considerably lower and has been estimated in some analyses to be between 0.15 and 1 percent, with substantial heterogeneity by location and across risk groups [47-50].

C. Fatality Rate Among Patients Hospitalized

Among hospitalized patients, the risk of critical or fatal disease is high. In a study from early in the pandemic that included 2741 patients who were hospitalized for COVID-19 in a New York City health care system, 665 patients (24 percent) died or were discharged to hospice Of the 647 patients who received invasive mechanical ventilation, 60 percent died, 13 percent were still ventilated, and 16 percent were discharged by the end of the study. The in-hospital fatality rate associated with COVID-19 has been higher than that for influenza. As an example, in an analysis of hospital data from the United States Veterans Health Administration, patients with COVID-19 were five times more likely to die during the hospitalization than patients with influenza (21 versus 3.8 percent).

Over the course of the pandemic, declining in-hospital fatality rates have been reported [61-64]. As an example, in a retrospective study of a national surveillance database in England that included over 21,000 critical care patients with COVID-19, ICU survival improved from 58 percent in late March 2020 to 80 percent by June 2020 [61]. The reasons for this observation are uncertain, but potential explanations include improvements in hospital care of COVID-19 and better allocation of resources when hospitals were not overburdened.

In resource-limited settings, in-hospital mortality rates may be higher than those reported elsewhere. As an example, in a study from 10 countries in Africa, where there was a median of two intensive care specialists in each hospital and a minority of facilities did not have pulse oximetry, the in-hospital 30-day mortality rate following critical care admission was 48 percent [65]. Mortality was associated with underlying comorbidities as well as resource shortages.

D. Excess of Death During Pandemic

Neither the case fatality rate nor the infection fatality rate account for the full burden of the pandemic, which includes excess mortality from other conditions because of delayed care, overburdened health care systems, and social determinants of health [66-68].

E. Incubtion Period

The mean or median incubation period of the disease ranges from 5 to 6 days [69,70]. Laueret al estimated that 2.5% of the patients will develop symptoms within 2.2 days (95% CI, 1.8 to 2.9 days) and 97.5% of patients will develop symptoms within 11.5 day(95% CI, 8.2– 15.6 days).

Serial interval refers to the time interval between the onset of symptoms in the primary case and the secondary case. The mean serial interval is estimated to be approximately 4 to 5 days [71,72]. By analysing data from 468 infector–infectee pairs, Du et al noted that 59 secondary cases had symptoms earlier than their primary case. This suggested that there is a possibility that the transmission of the disease occurred during the asymptomatic phase of illness in this group of patients [73].

F. Period of Infectivity

The duration for which a patient with COVID-19 remains infective is unclear. Viral load in the oropharyngeal secretions is highest during the early symptomatic stage of the disease [74].

The patient can continue to shed the virus even after symptom resolution. In a study from China, the median duration of virus shedding was 20 days (interquartile range [IQR] 17.0–24.0) amongst the survivors [75].

A study of viral dynamics in mild and severe cases revealed that mild cases tend to clear the viruses early, while severe cases can have prolonged viralshedding [76].

Data from studies using twin respiratory and fecal sampling have shown viral shedding can persist in stools for more than 4 weeks even when respiratory samples are negative [77]. Transmission during the asymptomatic phase has also been reported. In a study from Singapore, 6.4% of the 157 locally acquired cases of COVID-19 were attributed to transmission during the asymptomatic phase of the disease.

VI. DIGNOSIS

A. When is a COVID 19 Diagnostic Test Required?

Diagnostic testing for COVID-19 is conducted to find out whether a person is infected with the SARS-CoV-2 virus, responsible forCOVID-19 infection.

Your healthcare practitioner may recommend you the same if:

1) You are experiencing symptoms of COVID 19 such as high fever, cough, shortness of breath, excessive fatigue, etc.
2) You have long-term health conditions such as asthma,heart diseases, etc. and experience a sudden worsening of symptoms.
3) You have come in contact with someone testedpositive for COVID 19 recently.
4) You are a healthcare worker working in a hospitalenvironment.
5) You require hospitalization for treatment or surgery of existing medical conditions.

B. Different Laboratory Test Available for Dignosis

In general, there are two types of tests for diagnosing COVID-19 namely, Antigen or rapid testing and Molecular or PCR testing. The antigen test is often used as a point- of-care test, less expensive and yields quicker results within minutes. However, there is a higher chance of false-negative results as compared to molecular testing. Molecular testing yields more accurate results but are time-consuming [79].

C. Tretment

Initially, early in the pandemic, the understanding of COVID-19 and its therapeutic management was limited, creating an urgency to mitigate this new viral illness with experimental therapies and drug repurposing. Since then, due to the intense efforts of clinical researchers globally, significant progress has been made which has led to a better understanding of not only COVID-19 and its management but also has resulted in the development of novel therapeutics and vaccine development at an unprecedented speed [80].

D. Prevention

Preventive measures are the current strategy to limit the spread of cases. Early screening, diagnosis, isolation, and treatment are necessary to prevent further spread.

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 [81]. Important COVID-19 prevention and controlmeasures in community are summarized in Table 2.

Quarantine	Other Measures
Voluntary quarantine (self-quarantine)	Avoiding crowding
Mandatory quarantine	Hand hygiene
Private residence	Isolation
Hospital	Personal protective equipment
Public institution	School measures/closures
Others (cruise ships, etc)	Social distancing
	Workplace measures/closures

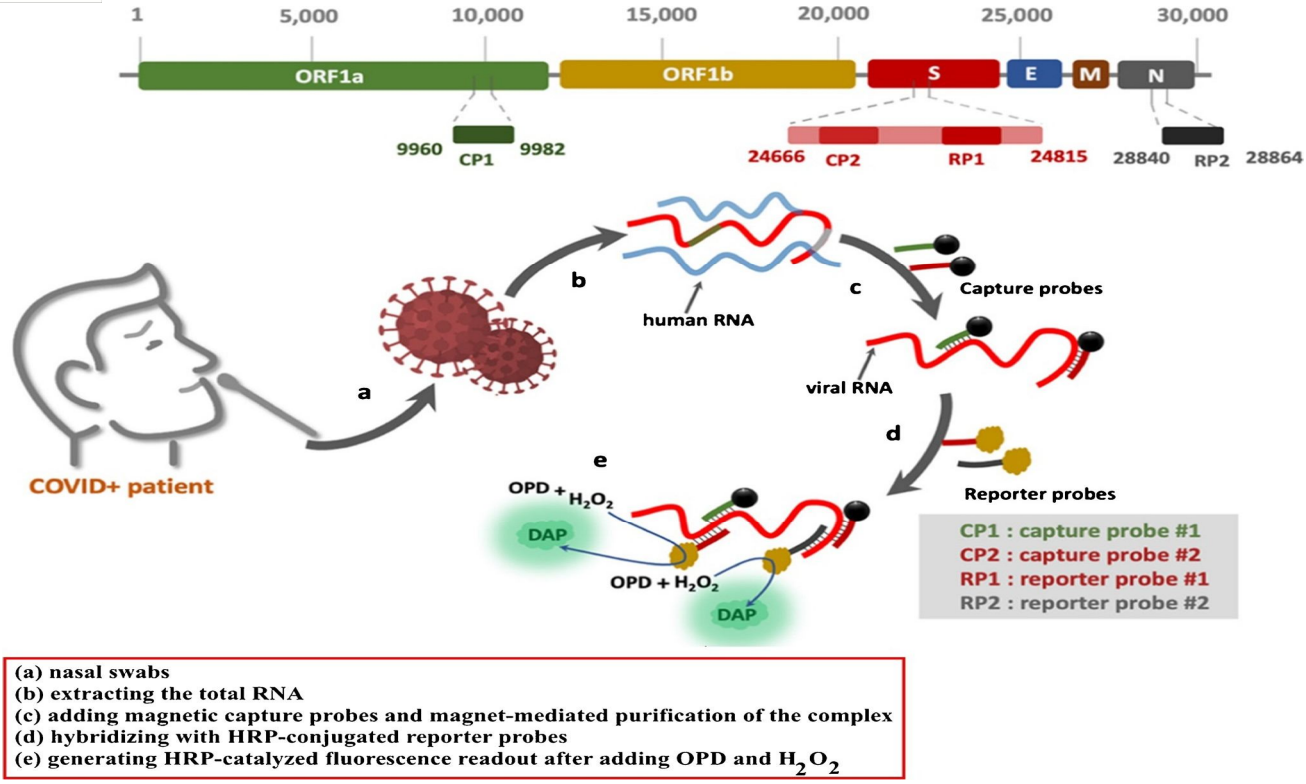


Fig. 4 The schematic depicts the step-by-step process for capturing and detecting viral RNA using magnetic probes and HRP-terminated reporters. Reproduced with permission from [124]

AuNPs to congregate. The quantity of target RNA is ren- dered into a shift and intensity change of the absorbance peak, a change in the Raman signal of AuNPs coupled with residue DNA probes and a variation in the fluorescence intensity of the supernatant. Each operating mode in the suggested biosensor may detect single-base mismatches in the target gene, reducing false positive/negative readings. The suggested biosensor does not need the extraction and purification of viral RNA. The suggested biosensor provides a relatively easy detection method when compared to PCR- based detection. Due to the long-term stability, the reaction solution conjugated to the DNA probe may be stored in the reaction chamber and ready for diagnosis. The operator only needs to load the detection sample and then centrifuge the supernatant to separate it from the aggregated AuNPs after adding the SSC buffer. A photoluminescence system is used to test the fluorescence intensity, and an automatic, portable microplate reader is used to test the absorption spectrum, while a micro-Raman spectrometer is used to record the Raman spectrum. Using 96 or 384 microplates, the proposed detection method can detect 96 or 384 samples simultane- ously. In all triple modes, the sensor reaches a femtomole level detection limit of 160 fM in absorbance mode, 259 fM in fluorescence mode and 395 fM in SERS mode. The sug- gested sensing platform offers a novel method for detectingCOVID-19 and other infections that is rapid, sensitive and selective [123].

In another work, Zayani et al. described the develop- ment of a magnetofluorescent bioplatform to detect SARS- CoV-2 viral RNA directly in total RNA collected from COVID-19-positive patients' nasopharyngeal swabs. Two capture probes attached to magnetic beads through a biotin/streptavidin linkage, targeting two particular loca- tions in the ORF1a and S genes, yielded a greater fluo- rescence response (Fig. 12). Through the oxidation of o-phenylenediamine to fluorescent 2,3-diaminophenazine, two horseradish peroxidase (HRP)-conjugated reporter sequences, corresponding to the loci of the S and N genes, were utilized to detect the presence of viral RNA. The bio- platform possesses a linear dynamics range from 0.01 up to 3.0 ng (1×10^3 to 9×10^7 copies/µL) with a low LOD of 0.01 ng of viral RNA (1×10^3 copies/µL) under optimum conditions. This platform is highly selective and sensi- tive that can distinguish SARS-CoV-2 RNA from similar viruses such as West Nile, hepatitis C, measles and non- polio viruses. In addition, 46 clinical samples verified the proposed biosensor (36 COVID-19-positive and 10 COVID-19-negative samples, as assessed with the gold standard RT-qPCR method). The sensitivity and specificity of the proposed technique achieved 100%. Finally, hav- ing such a simple and specific technique available in the field, at a main point of care, can aid in the identification of SARS-CoV-2 infection in resource-limited situations [124].

Pramanik et al. showed the ability to quickly diagnose, within 10 min, specific SARS-CoV-2 spike recombinant antigen or SARS-CoV-2 spike protein pseudo-type bacu- lovirus using Rhodamine 6G (Rh-6G) dye-coupled DNA aptamer-adhering gold nanostar (GNS) spectroscopy. Because the Rh-6G-attached single-stand DNA aptamer enveloped the GNS, the NSET method quenched 99% of the dye's fluorescence. The fluorescence signal remains in the presence of spike antigen or virus due to aptamer–spike protein binding. In particular, 130 fg/mL for antigen and 8 particles/mL for virus were established as a limit of detec- tion of the NSET test. Finally, it was proven that GNSs with DNA aptamer may terminate the infection by inhibiting the receptor-binding capacity of angiotensin-converting enzyme2 (ACE2) and dissolving the virus' lipid membrane [125].

VII. CONCLUSIONS AND FUTURE PROSPECTS

COVID-19 is a serious and dangerous infectious disease with symptoms similar to SARS in the form of fever, cough and fatigue. The disease is mostly transmitted through respiratory droplets and close contact. This dis- ease is a major threat to world health and safety. Bioana- lytical methods designed to diagnose COVID-19 disease are superior to other diagnostic methods due to their lower cost, higher accuracy, better detection limit and lower error. The advantages and disadvantages of various bio- sensing methods used to detect the SARS-CoV-2 virus are given in Table S2. Electrochemical methods can be used in further studies of this disease and similar diseases, and even by simulating the disease using relevant biosen- sors due to their high response speed, which in addition to helping the advancement of science, also offers the pos- sibility of rapid diagnosis and achievement. It provides the appropriate treatment method, so it is recommended to use the simulation and design of appropriate biosen- sors to make the necessary predictions to prevent or even diagnose and treat similar emerging diseases that may occur. Nanotechnology has the potential to accelerate the development of unique diagnostic sensors, the integra- tion of novel devices, improved optimization/validation and improvements in sensing performance at the point of care. Future research should focus on developing novel and next-generation non-invasive, specific, inexpensive and quick biosensing techniques and technologies for diag- nostic applications, particularly in the management of pan- demics and life-threatening infectious illnesses. However, certain difficulties require further investigation and atten- tion. For starters, the majority of these technologies and materials have been studied on a laboratory scale, imply- ing that employing
them in real-world circumstances may not be as precise as in the lab [126]. Furthermore, none of these biosensors has yet been developed for detecting the SARS-CoV-2 virus. As a result, the commercialization of numerous efficient biosensors should be hastened. Aside from the approaches and biosensors given, innovative methods such as AI-based technologies, wearable biosen- sors for continuous public monitoring and single-use dis- posable sensors for individual testing should be researched for SARS-CoV-2 mass screening [49].

A. *Supplementary Information*

The online version contains supplemen- tary material available at https://doi.org/10.1007/s00604-022-05167-y.

B. *Declarations*

Conflict of interest: The authors declare no competing interests.

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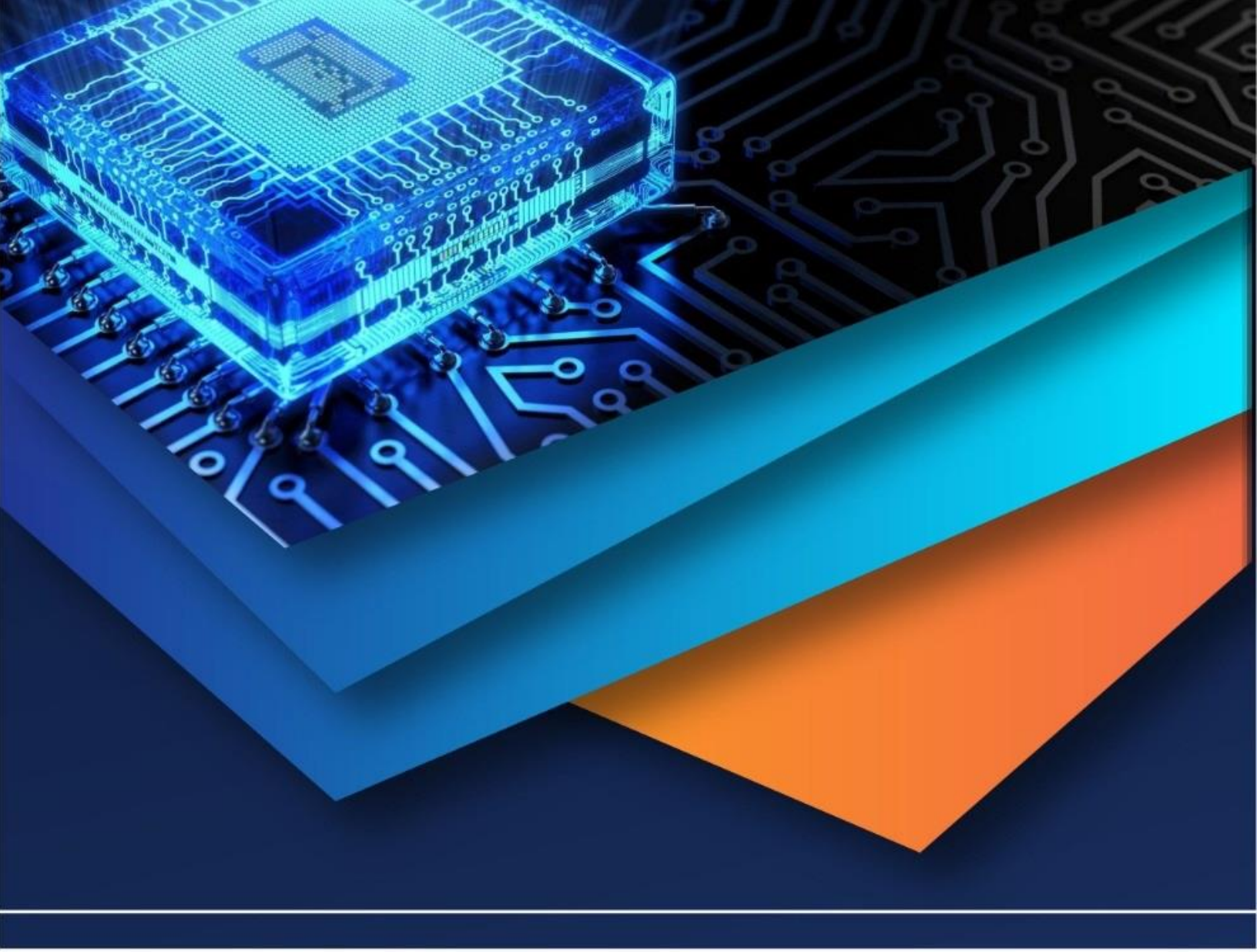

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