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Clinical epidemiology and advancement in diagnostics of SARS-CoV-2 infection

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Abstract

Severe acute coronavirus 2 (SARS-CoV-2) respiratory syndrome has spread to almost every part of the globe, causing social unrest. Coronavirus 2019 (COVID-19) causes fever, sore throat, cough, muscle pain, dyspnea, confusion and headache. This can lead to life-threatening breathing failure and can also damage the heart, lung, liver and nervous systems. SARS-CoV-2 infections are also misleadingly diagnosed with influenza infection, and bacterial seasonal high-breath infections. For the interpretation of epidemiology, contract-tracing, case control and for the repression of SARS-CoV-2 diagnostic assessments for COVID-19. Diagnostic testing in terms of disease and outbreak control, laboratory diagnosis of SARS-CoV-2 is highly significant. The development of rapid treatment tests with greater sensitivity and specificity is the key diagnostics as this helps prevent SARS-CoV-2 infection from spreading. Early diagnosis of viral infections is a strong improvement for the application of particular interventions in public health such as outbreak prevention, and closing of high-risk specific areas. At present, the gold standard procedure for routine diagnosis for COVID-19 infection is a Nucleic Acid Amplification Test (NAAT)-based RT-PCR technique. There have been many other advances such as bio-sensor and nanomaterial bases diagnostics. The creation of genome archives and open access genomic libraries for global researchers is simple for managing the outbreak of COVID-19 and speeding up the diagnosis and drug processes. This study summarizes numerous molecular diagnostic approaches, techniques and innovative research strategy, and clarifies the rapidly increasing range of diagnostic tests available and in-depth, including nanomaterial-based instruments to be used by health practitioners as resources guidance.

Keywords: COVID-19, epidemiology, RT-PCR, NAAT, biosensor, nanomaterial

Introduction

The Coronavirus genus belongs to the Corona-viridae family. These viruses are known as coronavirus and have a crown-like spike on their surface [1]. CoVs are generally widespread among human beings, birds and other mammals and induce infectious, neurological, enteric and hepatic diseases [2]. Currently, seven different forms of human HCoVs are found to affect people and result in diseases ranging from moderate or common cold to serious and/or lethal infections [3]. In some extreme cases, diseases related to common cold may be causing severe infections in children, teenagers and elderly communities, including four HCoVs, including HCoV-OC43, HCoV-229E, HCOV-HKU1 and HCoV-NL63 The remaining three coronaviruses, including SAR-CoV, MERS-CoV and Coronavirus-2 (SRC-SR2) will damage human respiratory tracts and lead to extreme respiratory disorders and pneumonia. The remaining three viruses are associated with SARS-CoV [4].

CoVs are a single-strand RNA (ssRNA) positive-sense with a genome length from 20 to 32 kb (125 nm) which belongs to the Nidoviral Family (subfamily Coronavirinae) [5].The CoV is classified into four subgroups, i.e. α-CoVs, β-CoVs, β-CoVs and α-CoVs based on the genomic structure [6].Among them, the α and β-CoVs only infects mammals, which usually contribute to human respiratory disease and other animals with gastroenteritis [7].The other two subgroups, µl and µl, have birds and rodents infected [8].HCoV229E and HCoV-NL63 out of the seven HCoVs are α-CoVs, while β-coVs are β-HCoVs are HCoV- OC43, HCoV-HKU1, SARS-coV and SARS-CoVs-2 [9].

Clinical Epidemiology of SARS-CoV-2

COV-2 of SARS In early December 2019 a group of local health workers in Wuhan city, Hubei Province, Mainland China, confirmed pneumonia-like unexplained causal symptoms epidemiologically linked to the demand for seafood. The infection was temporarily identified by the WHO on January 7, 2020 as a 2019-nCoV (2019-nCoV); the International Committee of Taxonome Taxation (ICTV) has renamed it SARS-CoV2 and the SARS-CoV-2 study group (CSG) as 'COVID-19' on 11 February 2020.

On the 30th January 2020, the WHO declared the 2019-nCoV outbreak to be the sixth and latest in the chronological order, the Public Health Emergency of International Concern (i). H1N1 (2009), (ii). Polio (2014), (iii). Western Africa Ebola (2014), (iv) Zika, 2016, & (v). Ebola in the Republic of Congo (2019). COVID-19 was declared 'pandemic' on 11 March 2020 by WHO. By 25th April 2021, this emerging highly infectious disease has spread globally enormously specifically to India, and for the ninth consecutive week new COVID-19 cases increased, with almost 5.7 million cases registered last week in April 2021. There were more than 87 000 new deaths recorded for the sixth week in a row. In addition to the south-east Asia and western Pacific areas, all regions have recorded declines over the last week. The Southeast Asia area recorded the

highest relative changes in all cases and death rates for the third consecutive week. Although several countries around the country record increasing patterns, the vast majority of these regional trends are in India and 38 percent of global cases have been recorded in the past week. Similarly, there have been decreases in new deaths this week in all but two countries, South-East Asia and East Mediterranean. The largest numbers of new cases are registered in India (2 172 063 cases, 52% more), the United States (406 001 new cases, 15% less), Brazil (404 623 new cases, 12% less cases), Turkey (378 771 new cases, 9% more cases), and France. The new cases are reported as having increased in the last three years (211 674 new cases; 9 percent decrease) [38].

Disease transmission

SARS-CoV, MERS-CoV and SARS-CoV-2 are spread through contact between the human and human being or by aerosol delivery to the surfaces polluted by the infected person [10].The most frequent report of transmission through direct human-to-human interaction is among health workers and the primary care providers of the ill patient [11].

These viruses scatter over the respiratory driplets as they sneeze or coughe. These infected areas may also be transmitted by humans after contact [12]. Aerosol absorption is when the ill person coughs or sneezes and droplets filled with this virus are pushed by air up to 3 foot towards the neighboring mucous membranes [13].

Clinical pathology

Medical pathology can be divided into three moderate, serious and critical stages in relation to SARS-CoV-2 infections. In the moderate stage of infection, patients with mild febrile disease such as dry cough, sore throat, etc. may or may not have pneumonia, often with signs of high respiratory infection. In serious cases, due to dyspnea, productive coughing, shortness of breath and hypoxia, the rate of respiration exceeds 30 minutes. This symptoms establish initial symptoms within a brief period of time (24–48 h). Finally, death is due to the critical stage of acute pneumonia, breathing loss, heart arrest and/or multiple organ failure.

Clinical Diagnosis

The clinical suspected COVID-19 criteria include: The following: Influenza-like Illness cases are classified as those with acute fever infections and toxin, severe acute respiratory infection and necessary hospitalization; other symbols include temperature, cough, sneeze, running nose, breathlessness, uneasiness, gastroenteritis, and trouble breathing. SARS-CoV presence is recognizable by laboratory experiments centered in antigen or nucleic acid, such as fast testing and RT-PCR in real time, respectively. In the cases of potential virus nucleic acid-based identification tests for the latest infection COVID-19, throat swab or nasopharyngeal swab is obtained where blood/serum is used to diagnose IgM (current/recent infection) or IgG (paste infection) for serosurveillance studies to measure the incidence of population infection. For the comprehension of the epidemis, contract tracking, casemanagement and dissemination of the SARS-CoV-2, diagnostic testing of COVID-19 is important. Hence, swift, highly precise and highly sensitive molecular diagnostic tests are urgently required.

More specifically, precise and speedy diagnosis of infection with SARS-CoV-2 can help diagnose patients, separate and cure them to mitigate public contamination risks and dramatically reduce mortality rates. According to current recommendations, physicians can organize laboratory diagnoses of COVID-19 with their local and state health departments by state labs [14].

Advancement in Laboratory-based tools for Covid-19 diagnosis

WHO currently suggests the identification of specific sequences of the RNA virus for laboratory diagnosis COVID-19 based on the Nucleic Acid Amplification (NAAT) test, such as a real-time polymerase reverse transcriptase chain reaction (rRT-PCR). The Indian Council of Medical Research (ICMR), in conjunction with the Drug Controller of India (DCGI) and the Dept. of Health and Family Welfare, have proposed the use of rRT-PCR-based tests that had been authorized in the U.S. FDA EUA/CE-IVD certified kits (MoH&FW). The FDA EUA/CE-IVD certified RT-PCR-kits are extremely accurate, detecting or not using the presence or lack of SARS-CoV-2 virus nucleic acid. The Gold Standard Diagnostic Test for COVID-19 is the latest gold PCR test. Other molecular approaches like virus antigen or serological testing of antibodies are actually only advisable in the laboratory environment and not in clinical decision-making [15].

Overview of SARS-CoV-2 detection

First of all, the fast and reliable identification of SARS-CoV-2 by the reverse transcription–polymerase chain reaction (RT–PCR) in real time is used in COVID-19 management [16]. SARS-CoV-2 nuclear acids found in nasopharyngeal liquids are detected by RT–PCR. Testing is used to discourage contagious propagation by asymptomatic individuals and populations where virus discharges will unwittingly propagate the infection to aged persons and people with co-morbidities [17]. Precise viral identification is the basis for a COVID-19 pandemic [18]. Lapses impair public protection and facilitate the dissemination of infection with false negative outcomes of the test. It continues to be a pressing need to improve test sensitivity and specificity. Serological tests accompany the identification of viruses, showing previous infections and may be used for treatment purposes. Antibodies are identified through a qualitative detection of IgG or IgM antibodies with an enzyme-like immunosorbent assay [19]. These studies will identify an immune reaction to the viral spike (S) protein and can be helpful to evaluate defense against subsequent viral exposure and/or for the purpose of touch tracking [20]. The value of these tests cannot therefore be overestimated. This also applies to epidemiological assessments and extensive global clinical requirements [21].

Future studies will include the advancement of immune sensitivity and specificity diagnostic tests13. In reality, these tests eventually show viral defense when reinfections develop [22]. The next boundary for COVID-19 control is inducing immunity against SARS-CoV-2. To this end, our aim in this review is to summarize the clinical disease presentation, which focuses on the optimal use at human, population and social levels of nanomaterial and other diagnostic tests. Present and prospective COVID-19 nanomaterial diagnostics are outlined in the study. The aim is to help curb the global spread of the virus.

RT–PCR

Current diagnostic testing for nuclear, antibody and protein-based identification of the pandemic use of SARS-CoV-2 remains the golden norm for the viral detection of nucleic acid by the RT–PCR. The sensitivity and virus identification characteristics of nuclear acid testing have increased over the serological tests currently available. RT–PCR is a responsive, accurate, and certain viral identification depending on SARS-CoV-2 recognition against common breathing pathogens. Although the consistency of the procedure, findings have still not enabled the viral infection to be contained [22]. Regulated laboratories were authorized to report on in-house SARS-CoV-2 diagnostic testing in February 2020, the United States Food and Drug Administration (FDA). The treatment starts when viral RNA is isolated and converted into complementary DNA (cDNA). Next, cDNA with Taq DNA polymerase will be amplified. The last overall workflow for the RT-PCR test is shown in Figure 2a and quantifies the viral load.

The average turnaround period is more than 2 d and is at risk by cross contamination with reduced specificity. The experiments are usually done in hospital labs. Real-time RT-PCR results using primers that target various portions of the viral genome can be impacted by variations in viral RNA sequence. Moreover, due to viral evolution, false negative findings can arise [23]. The RT–PCR experiments also have drawbacks of storage samples, poor purification of nucleic acid, cost and time of wait [24]. The gold standard for SARS-CoV-2 diagnostics remains the RT-PCR test, despite these limitations. The processing of large quantities of samples is essential for alternative in situ hybridization and immunohistochemistry and aerosols and protection limits can be created [25]. The option and special characteristic of the antibody and the consistency of the assay depend on immune histo-chemistry.

The virus sequencing is the most conclusive process, but the expense, equipment and expertise needed are limited to follow this approach. Isothermal amplification is a good alternative to nucleic acid amplification dependent on thermal cycling [26]. Simplify SARS-CoV-2 genome regions can now be found with a Simplified RT-PCR. The proteins S and RNA (RdRp)/helicase (Hel) depending on the RNA and the genes N of SARS-CoV-2 are detected. The RdRp/Hel tests are extremely sensitive ways of detecting viruses. In combination with the correct handling of large sample numbers with automated and cobas 6800 systems, fast and accurate results are obtained [27].

RT loop-mediated isothermal amplification (RT–LAMP)

Diagnostic checks based on LAMP are detected either by turbidity thresholds or colorimetric or fluorescent measurements. This technique has a low background interference and is easy to execute and envision. Experience, perception and reaction [28]. are the key drawbacks of LAMP testing. The signal reading properties of EvaGreen were higher than the properties of SYBR Green [29]. for two fluorescent dyes studied. In order to have laboratory viral diagnostics, RT-LAMP is built on paper/strips combined as part of a microfluidic platform [30]. The test assigns fluorescein to a single primer series and catalyzes its substance by labeled RT [26].

SARS-CoV-2 can be confidently characterized by using an alternative LAMP violet leuko crystal coloration that allows 100 copies to be observed per reaction. A Closed Penn-RAMP tunnel, which combines the RT-recombinant polymerase enhancement with the RT-LAMP in one vacuum, increases the detection limit of the test [31]. RT–LAMP research workflow. The 3-stage RT-LAMP products will form the basis for the LAMP reaction. In stage LAMP transcriptase solutions for the preparation of amplification mixtures of deoxyribose adenosine (dATP), polymerase (Bst 2.0) and avian myeloblastosis virus (AMV). The biotin-labelled nucleoprotein (np), backward (LB) loop primer (np-LB*) reaction of the LAMPs and open-reading frame1a/b labelled fluorescein isothiocyanate (FITC) (F1ab). The isothermal amplification begins (RT–LAMP reaction in phase (ii) -forward loop primer (LF) (F1ab-LF*)). (iii) Detectable COVID-19 products RT–LAMP are supplied step by step.

The findings of labelling F1ab-LAMP* and F1ab-LB * or np-LF * and Np-LB* for digoxigenin and biotin, respectively are seen on stage FITC/ Biotin-labeled np-LAMP and FITC/biotin-labeled F1ab-LAMP amplicons. The F1ab-RT–LAMP product, in turn, is labeled with FITC and biotin, while np-RT–LAMP is labeled with digoxigenin and biotin. In addition, FITC is assigned to the f1ab primers set.

Moreover, under optimized conditions, the marked F1ab-LF* and F1ab-LB* premiers will respond and SARS-CoV-2 RNA with AMV-RT in 40 minutes will be transformed to cDNA. The RT–LAMP mechanism consists of the FITC and digoxigenin components to detect F1ab, np primer [32]. This reaction is the material for the further LAMP amplification. RNA removal is time consuming, costly and involves centrifugation steps which are not needed for Easy COV RT–LAMP testing. Without RNA extraction from the sample, EasyCOV is a quick and straight-forward test. Easy COV findings have proved to be 72 % sensitive. LAMP saliva strategies can detect infection profiles in humans. EasyCOV can diagnose SARS-CoV-2 in Saliva and it is viable with a simple, quick and painless treatment for large-scale screenings for the general public [32].

SARS-CoV-2 diagnostics using Nanomaterials

Nanomaterials-based FET bio sensors have enabled high sensitivity, selectivity and detection limits to achieve high biosensor efficiency. Nanowires for exposed gated FET micro regions for very high SARS-CoV-2 and SARS-CoV electrochemical identification, respectively have been used as graphene and In 2O3 nanos. For the development of an immunosensor and a MERS DNA sensor and COVID-19, with fempto-pico molar detection limit, other nanomaterials such as the gold nanoparticles and the gold nanoislands were employed effective.

The possibility of their miniaturization on cost-efficient and integrated platforms, similar for handheld electrochemical readers, used for POC diagnostics is an essential element of nano biosensors with electrochemical and FET transduction. In addition, the affinity biosensors can easily be multiplied by inserting several electrodes on the same platform that are accessible individually, enabling simultaneous detection. Naturally, more efforts would be necessary before realistic implementations of miniaturized POC multiplex testing are possible.

Despite these positive characteristics, very few cases of SARS, MERS and COVID-19 nanobiosensors have so far been developed and implemented successfully in real-life clinical analysis. Naturally, several trials are under way for

COVID-19. SARS-CoV-2 antibodies are under production with nanosensors for treatment. At this moment, the commercial availability of anti-SARS-CoV-2 antibodies is limited to lateral immunoassays developed by different companies as single use POC tests. They are paper-like membrane stripes covered in the conjugation pad and antigens of the membrane of nitrocellulose with gold nanopart-antigen conjugations. A patient's blood drop is placed on a sample pad and capillary activity translates into the examination. Realize and bind both IgG and IgM human immobilized antibodies. However, the clear colored line is only made by human IgG-IgM/gold nanoparticles-antgen conjugates [33].

Detection of SARS-CoV-2 antibodies

Serological tests for the evaluation of antigen-specific plasma antibodies are normally carried out by fast lateral flow test bands, lacking in quantitative results or by time- and labor-intensive, albeit semi-quantitative, immunocompromised assays. Here, we discuss a novel use of biolayer interferometry for rapid antigen identification in plasma samples and its usefulness for quantifying SARS-CoV-2 antibodies. This biolayer immunosorbent assay uses a single use biosensor in an automatic "dip-and-read" configuration, which provides antigen loading, plasma antibody binding and isotype detection in real-time optical measuring. In less than 20 minutes, all semi-quantitative data can be collected. Highly complex techniques such as the Enzyme-Linked Immunosorbent Assay and the Chemiluminescent Immuno-assay (ELISA), achieve or surpass their efficiency. This methodology is particularly important for the timely implementation of current COVID-19 emergency platforms, such as serosurveillance and vaccine candidate assessment. In a wider context, BLI-ISA is a new tool for evaluating therapeutic antibodies and other specimens of biomolecules [34].

SARS-CoV-2 antigens

A quick diagnostic test was also carried out to identify the presence in samples from the respiratory systems of infected persons of viral antigens expressed by SARS-CoV-2. Antigen in the sample binds to antibodies attached to a paper strip in a plastic box for this assay. In less than half an hour, this response produces a physically visible signal. The antigen(s) detected are expressed only if the virus replicates active, therefore acute or early infections may be identified by the testing. A more general form of rapid diagnostic test was also advertised by Abbott for COVID-19, which measures the presence of anticorps in the blood of infected people.

The Abbott test is able to detect the antibody SARS-CoV-2 on laboratory devices ARCHITECT i1000SR and i2000SR which can run around 100–200 hourly trials [35]. SARS-CoV-2 antibodies are manufactured after an illness week [36]. The intensity of any anti-body reaction depends on age, diet, seriousness of illness, co-morbidity and drugs.

Biosensor based diagnostic

Electrical ultrasensitive biosensor for the rapid identification of SARS-CoV-2 based on isothermal rolling circle amplification (RCA). The test entails hybridization of RCA amplicons with redox active labels that are visible by an electrochemical biosensor, which have been functionally functionalized. The one-step hybridization test will detect at less than 2 hours as small as 1 copy/μL of N and S genes. In a study 106 clinical sample sensors, including 41 positive and 9 positive SARS-CoV-2 for other respiratory viruses, showed a 100% match with the qRT-PCR, and had a total association between current biosensor signals and the Cq (quantitative cycle). This biosensor can be used as a real-time COVID-19 test on-site [37].

Conclusion

SARS-CoV-2 a worldwide pandemic, and is currently the world's worst infectious outbreak. In several other countries, including India, the government and ICMR, the virus spreads by interventions including national shutdown, isolation of infected people, care, main and secondary touch tracking's, decontaminations and screening for infected areas. Previous lack of test access has slowed outbreak controls but is rapidly growing in the monitoring of this new virus. In the diagnosis of the infection, epidemiological awareness, case control and suppressing spread, the COVID-19 diagnostic testing is crucial. For faster screening approaches in the global battle against the pandemic, universal operating procedures and coordination of the available diagnostic assays are essential. The development of fast, more sensitive and more precise point-of-care testing is the key time requirement since this helps to reliably determine and assist in the containment of SARS-CoV-2 infection spreading. Early diagnosis of infection significantly increases the execution of specific interventions in the public health sector including controlling infection, decontaminating the soil and closing specific high risk areas. There are several things still being explored of the COVID-19 virus and illness. A greater knowledge of virus dynamics and the immunological reaction can help determine for molecular tests the best form and timing of therapeutic content and help decide the procedure.

In order to enhance the class-based specificity and sensitivity of antibody and antigen-based testing the university scientists and biotechnologists are tasked with describing additional SARS-CoV-2 strains. Significant nanomaterial-based virus detection will aid in the production of CO VID-19 tests that provide on-demand diagnostic capabilities effectively in the pandemic that are highly sensitive, quick, portable, rapid and cost-effective. The SARS CoV-2 genome isolated from infected populations worldwide needs to be sequenced at large scales in order to detect mutations that could influence molecular test results. The establishment of genome repositories and open-source genomic libraries for global scientists is simple for managing the COVID-19 epidemic and speeding up progress in diagnostics. This study provides a road map for diagnostic methods in connection with epidemiological diseases, COVID-19 prevention and regulation.

Conflict of interest

Nil

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