REVIEW

Road toward rapid-molecular point of care test to detect novel SARS-coronavirus 2019 (COVID-19): Review from updated literature

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Abstract   Coronavirus disease 2019 (COVID-19) named by the WHO as a result of the global public health emergency. COVID-19 is caused by a new coronavirus named as novel coronavirus (2019-nCOV). From the first case reported in December 2019 it is now a pandemic situation and a major public health emergency. The COVID-19 transmission rate is very high, infecting two to three persons on average with contact to an already infected person. There is a need for the health system, specially in developing countries such as in Pakistan, to combat such a novel disease by rapid, accurate, and high quality diagnostic testing in order to screen suspected cases and also surveillance of the disease. A rapid, accurate and low-cost diagnostic point-of-care device is needed for timely diagnosis of COVID-19 and is essential to combat such outbreaks for compelling preventive measures against the disease spread. This review is to highlight the importance of point-of-care diagnostics device for robust and accurate diagnosis of COVID-19 in physician offices and other urgent healthcare-type settings and encourage academics and stake holders towards advancement in order to control outbreaks and develop the public health surveillance system.

Introduction

The novel SARS- Coronavirus 2019 (nCOV-19) that causes the disease COVID-19, name given by the WHO on 30th of January and declared a public health emergency as the condition adapted to a pandemic situation. Globally, there are 5,657,529 confirmed cases of COVID-19, which includes 356,254 total deaths.[1] The Report of Ministry of National Health Services, Regulations and Coordination Field Epidemiology and Disease Surveillance Division (FEDSD), National Institute of Health (NIH), Islamabad reported the current scenario of disease burden as a total of 64,028 confirmed cases and death cases were 1,317 till May 28, 2020.[2] While 40,406 cases still had the status of active cases. The disease

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spread in 213 Countries and Territories around the world.[3] The Centers for Disease Control and Prevention (CDC) have reported SARS-CoV-2 as a respiratory virus, hence transmission is adhered to "respiratory droplets" when an infected or asymptomatic carrier coughs or sneezes and prevention is only possible by maintaining at least a six-foot distance between individuals. The virus also spreads by close contact, touching a surface or object that is already contaminated and then touching your own nose or mouth.[4] The most common symptoms of COVID-19 are fever, dry cough, tiredness followed by less common symptoms such as aches, sore throat, diarrhea, conjunctivitis, headache and loss of taste or smell. Patients with serious symptoms observe difficulty breathing or shortness of breath, chest pain or pressure, loss of speech or movement in clinical settings.[5] Developing countries needed surveillance of such an outbreak in order to combat the pandemic situation for prompt public health intervention and prevention. A robust and accurate Point-of-care diagnostic device is designed for achieving public health objectives of disease diagnosis and epidemiologic surveillance. Point-of-care (PoC) testing devices are used for rapid and timely diagnosis for various infectious diseases and do not require a trained or expert professional. PoC testing is a portable molecular test with the advantage of its availability at physician offices and other urgent healthcare-type settings. In the era of public health emergency, PoC testing will significantly contribute towards low cost, robust and economical diagnosis and early detection of COVID-19, as well as decreasing the cases of an infectious disease in controlling the outbreak. At present Reverse Transcriptase polymerase chain reaction (RT- PCR) is dominant for the diagnosis of nCOV-19. While there are other methods used by different PoC testing devices with most frequent and accurate being Loop Mediated Isothermal Amplification (LAMP) assay in closed tube with colorimetric detection and serologic detection of COVID-19 IgM/IgG by Rapid Test device. This review focuses on a PoC device integrated with the mobile phone in contributing public health response and control as well as highlighting the use of LAMP assay as a method of COVID-19 diagnosis.

Methodology

Published papers including those articles published from PubMed, WHO global database for COVID-19, Centers for Disease Control and Prevention guidelines COVID-19 transmission webpage to clarify information about types of spread were reviewed. Our review included those articles providing essential literature on PoC diagnostics for COVID-19 and LAMP assay as a molecular technique for the diagnosis of infectious agents. Our search terms and data base appropriate syntax are ''SARS corona Virus'', ''COVID-19'', ''Point of care diagnostics''. We included preprint, peer reviewed and retrieved full text articles and examined the citation chain for each article to be included.

Methods for diagnosis of COVID-19

The current diagnostic technique indicating current infection, which is use as the referenced method globally is the reverse real-time PCR assay (rRT-PCR) which require sophis-

ticated lab setup, expensive instrument, well trained and qualified staff, transportation efforts and deals with a broad variety of clinical specimens such as nasal swab, pharyngeal swab, Broncho alveolar lavage fluid, sputum, feces, fibro bronchoscope brush biopsies and blood.[6,7] Antibody testing in serum indicates previous infection of COVID-19 which involves the lateral flow method indicating in vitro qualitative detection of both IgM and IgG antibodies.[8]

Prof. Jinzhao Song[9] conducted a study in mid-February and reported a Single and Two-Stage, novel closed-tube COVID-19 assay at home, clinic or points of entry based on nucleic acid detection and amplification. Their method includes loop mediated isothermal amplification and is performed in a closed tube with calorimetric detection. Using bioinformatics tools, they designed primers for the conserved region of the viral genome such as open reading frame 1ab (ORF1ab) gene. For higher sensitivity, they address a two stage isothermal method known as dubbed Penn-RAMP.[9] They reported 10 times higher sensitivity with respect to LAMP and PCR on purified processed nucleic acid; however, their study was performed on synthetic samples and requires actual patient samples.

Yang T et al.[6] reported their invention of a PoC diagnostic device for COVID-19 in their research paper published on 18 March 2020. They integrate the mobile phone with a paper-based PoC testing device and also the method of PCR was loop mediated isothermal amplification. The concept behind their method of nucleic acid detection was adopted from previous research.[10] They combine a paper-based PoC device and LAMP technology integrated to a mobile phone app as an accessible COVID-19 diagnostic tool that a self-quarantined patent easily collects a nasal swab sample and performs this user-friendly test on such a device. The result will be shared through the mobile app to clinicians or the public health concerned.

Trieu Nguyen reported[7] in their opinion report on 14 March 2020 about PoC testing as paving the road for rapid detection of virus which proposed PoC diagnostic as a potential candidate for detecting COVID-19 as well as a response to the outbreaks. They integrate a mobile phone app with loop mediated isothermal amplification technology (LAMP) on a paper-based PoC device. LAMP has the advantage of being highly sensitive, easy and time efficient, characterized by a reaction catalyzed in isothermal condition. The technology uses strand displacement rather than the conventional heat denaturation principle and therefore the reaction has an advantage to be run on constant thermal environment. LAMP uses four different primers i.e., forward inner-outer primer and backward inner-outer primer which are complementary to the template sequence. Using strand displacement polymerases enzyme catalyze chain elongation with a displaced strand forming a cauliflower-like loop dumbbell structure. These loop structures contain multiple sites for the initiation or synthesis of other copies by providing binding sites for another set of primers. A swab sample containing COVID-19 was transferred in tube and a specific reagent added for LAMP reaction. After the reaction, the colorimetric reaction is detected on a mobile phone app specially designed to detect colorimetric changes on paper and the result is shared with the patient as well as with the public health department for epidemiologic surveillance. Having high sensitivity and specificity, LAMP technology is now a

popular method in the detection of pathogens in molecular biology.

Necessity and socioeconomic significance

Point-of-care (PoC) testing devices are used for rapid and timely diagnosis for various infectious diseases and do not require a trained or expert professional. PoC testing is a portable molecular test with the advantage of its availability at physician offices and other urgent healthcare-type settings. In this era of public health emergency, PoC testing will significantly contribute towards low cost, robust and economical diagnosis, and the early detection of COVID-19 as well as decreasing the cases of an infectious disease in controlling the outbreak. A rapid, accurate and cost-effective detection device with little requirement will benefit the individual and government by reducing transportation needs, lowering the spread of infection as well as mitigating the cost of testing.

Rapid and accurate testing significantly contributes towards epidemiologic surveillance and future outbreaks of such infectious diseases. In-house testing of reverse transcription-polymerase chain reaction (RT-PCR) is endorsed by the WHO and CDC and adopted by many reference laboratories.[11,12] However, in such a challenging time, when health care resources are insufficient to combat the situation due to having increasing numbers of patients infected seeking care, PoC testing shall be regarded as essential for testing viral genome nucleic acid thereby reducing the chances of spreading the infection to distant areas and eluding the consequences of delayed reporting of infectious disease such as COVID-19.

Various studies reported the dramatic effect of late reporting of infectious disease as stated by Elisabeth Reijn et al.[13] that timely and accurate diagnosis will radically contribute towards effective public health response as well as averting secondary cases and outbreaks of infectious diseases. Timeliness for infectious diseases is an important factor as delay mostly occurs in a situation of referring the cases by the general practitioner or diagnosing cases to the local municipal health service. Netherlands health care providers are strictly gratified for reporting to the surveillance department of infectious diseases in order to control secondary cases and develop prevention guidelines and precautionary measures. A PoC device integrated with a mobile phone app for infectious disease creates a road map towards operative epidemiologic surveillance and public health intervention in the form of active or passive immunization or post exposure rehabilitation such as in the case of COVID-19.

Future recommendations

A highly reliable, accurate diagnostic PoC testing device with high sensitivity specificity, positive predictive and negative predictive values is required in order to combat different infectious diseases in the future and in the current situation of the COVID-19 Pandemic in both developed and underdeveloped countries around the globe. Mobile phone integration with the testing device eliminates the transportation requisite, economic burden, and mitigates the spread of infection. Stakeholders should take the initiative of installing the project on large scale validity and reliability of a PoC testing device with disposable kits for diagnosis of various infectious diseases having the capacity to deal with an extensive spectrum of clinical samples.

Conflict of interest

The authors have no conflict of interest to declare.

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References

1. WHO Coronavirus Disease (COVID-19) Dashboard [Internet]. [cited 2020 May 29]. Available from: https://covid19.who.int/?gclid=CjwKCAjw5cL2BRASEiwAENqAPgF7M77Us6e7FSrlid4UeHmzyS_RlDxdPTYqjSCVXc-GcGuSW2suiRoC_yAQAvD_BwE.

2. COVID-19 Health Advisory Platform by Ministry of National Health Services Regulations and Coordination [Internet]. [cited 2020 May 29]. Available from: http://covid.gov.pk/stats/pakistan.

3. Countries where Coronavirus has spread - Worldometer [Internet]. [cited 2020 May 29]. Available from: https://www.worldometers.info/coronavirus/countries-where-coronavirus-has-spread/.

4. CDC updates COVID-19 transmission webpage to clarify information about types of spread | CDC Online Newsroom | CDC [Internet]. [cited 2020 May 29]. Available from: https://www.cdc.gov/media/releases/2020/s0522-cdc-updates-covid-transmission.html.

5. Q&A on coronaviruses (COVID-19) [Internet]. [cited 2020 May 29]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/q-a-coronaviruses.

6. Yang T, Wang Y, Shen C. Point-of-Care RNA-Based Diagnostic Device for COVID-19; 2020. p. 9–11 (Lcv).

7. Nguyen T, Bang DD, Wol A. 2019 Novel Coronavirus Disease (COVID-19): Paving the Road for Rapid Detection and Point-of-Care Diagnostics; 2020. p. 1–7 (March).

8. Bendavid E, Mulaney B, Sood N, Shah S, Ling E, et al. COVID-19 Antibody Seroprevalence in Santa Clara County, California. MedRxiv; 2020.

9. Mechanics A. A Single and Two-Stage, Closed-Tube, Molecular Test for the 2019 Novel Coronavirus (COVID-19) at Home, Clinic, and Points of Entry Mohamed El-Tholoth; 2019.

10. Lo S-J, Yang S-C, Yao D-J, Chen J-H, Tu W-C, Cheng C-M. Molecular-level dengue fever diagnostic devices made out of paper. Lab Chip. 2013;13(14):2686–92.

11. Paper O, Lippi G, Plebani M. The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks; 2020. p. 39–45, 2019.

12. Lippi G, Plebani M. The novel coronavirus (2019-nCoV) outbreak: think the unthinkable and be prepared to face the challenge. Diagnosis. 2020;7(2):79–81.

13. Reijn E, Swaan CM, Kretzschmar MEE, Van Steenbergen JE. Analysis of timeliness of infectious disease reporting in the Netherlands; 2011.