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Review Article

Pool Testing: Reliability and Cost Effectiveness is a way out in Coronavirus Pandemic

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ABSTRACT:
The coronavirus disease 2019 (COVID-19) pandemic has revealed the global importance of robust diagnostic testing to differentiate severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) from other routine respiratory infections and guide appropriate clinical management. Given the limited testing capacity available in the all the nations early in the pandemic, individuals with a clinical syndrome consistent with COVID-19, but without travel or exposure history, were not tested. Therefore, it remains uncertain whether there may have been community circulation of SARS-CoV-2 prior to the identification of individuals with positive results through standard public health surveillance. Sample pooling, a strategy used for community monitoring of other infectious diseases
Keywords Coronavirus, sample pooling, community transmission.

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INTRODUCTION

Since the first detection in Wuhan, China in December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen of coronavirus diseases 2019 (COVID-19), has spread worldwide to now be considered a pandemic.[1] Countries are experiencing an acute shortage of certain reagents important for performance of assays for the detection of SARS-CoV-2. They have been forced to stop testing due to lack of test supplies. The ability to rapidly diagnosis COVID-19 is important for evaluating the spread of disease and for tracing the contacts of infected individuals. Polymerase Chain Reaction (PCR) is an important diagnostic tool for detection of coronavirus in public health laboratories.

At the peak of the pandemic, there is a high volume of specimens that requires testing. One possible way to increase testing capacity and conserve reagents is to pool specimens prior to RNA extraction, concentrate the RNA, test the pools, and subsequently retest single specimens from positive pools to identify the positive specimens.[2]

A pooled testing algorithm involves the PCR screening of a specimen pool comprising multiple individual patient specimens, followed by individual testing (pool deconvolution) only if a pool screens positive. As all individual samples in a negative pool are regarded as negative, it results in substantial cost savings when a large proportion of pools tests negative.

Pooling specimens to increase efficiency of testing and cost effectiveness is not unprecedented. Testing specimens in pools has been used to detect infections such as human immunodeficiency virus (HIV) and the hepatitis B and C viruses.[3] Blood banks worldwide are able to screen millions of blood donations by implementing the mini-pool nucleic acid amplification technology (NAT) testing method to detect transfusion-transmissible viruses.[4] The size of the mini-pools differs from country to country, but each sample in a positive pool is retested individually. Pooling of specimens has also been evaluated earlier for the detection of Chlamydia trachomatis and Neisseria gonorrhoeae as a measure to reduce cost and labour while maintaining accuracy.[5]

If resources or capacity are limited, rational approaches should be implemented to prioritise high-yield actions, which include: rational use of confirmatory testing, reducing contact tracing to focus only on high-yield contacts, rational use of PPE and hospitalisation and implementing rational criteria for de-isolation. Testing approaches should prioritise vulnerable populations, protection of social and healthcare institutions, including staff. A strategic approach based on early and rigorous application of these measures will help reduce the burden and pressure on the healthcare system, and in particular on hospitals, and will allow more time for the testing of therapeutics and vaccine development.[6]

National surveillance systems should initially aim at rapidly detecting cases and assessing community transmission. As the epidemic progresses, surveillance should monitor the intensity, geographical spread and the impact of the epidemic on the population and healthcare systems and assess the effectiveness of measures in place. In circumstances with capacity shortages and strict implementation of social distancing measures, surveillance should focus on severe acute respiratory infections, sentinel surveillance in outpatient clinics or collection of data through telephone helplines. [6]

Over the course of the infection, the virus has been identified in respiratory tract specimens 1-2 days before the onset of symptoms and it can persist for 7-12 days in moderate cases and up to 2 weeks in severe cases.[7] In faeces, viral RNA has been detected from day 5 after onset and up to 4 to 5 weeks in moderate cases. The virus has been detected also in whole blood, serum, saliva and urine. Prolonged viral RNA shedding has been reported from nasopharyngeal swabs, up to 37 days among adult patients and in faeces, for more than one month after infection in paediatric patients. Based on Chinese data, the international WHO mission report indicates that up to 75% of initially asymptomatic cases will progress to clinical disease, making the true asymptomatic infection rather rare (estimated at 1-3%).[8]

PROCEDURE FOR POOL TESTING

This assay employs an extraction procedure of viral RNA from specimens collected by nasopharyngeal (NP) swabs (200µl/sample) by pooling 5 samples. It is feasible when the prevalence rates of infection are low. All individual samples in a negative pool to be regarded as negative. The second step in the assay employs reverse transcription and amplification using a real time PCR instrumentation. The assay therefore requires two kits, one for extraction and another for amplification of the target and detection. Positive pools were deconvoluted and individual samples tested for both E and the RNA-dependent RNA polymerase (RdRp) gene for confirmation.[9] Deconvoluted testing is recommended if any of the pool is positive. Pooling of more than 5 samples is not recommended to avoid the effect of dilution leading to false negatives.[10]

DISCUSSION

Group testing of pooled samples has been successfully employed by the blood procurement and infectious disease testing for many years5. The strategy became effective due to the development of highly sensitive molecular based assays and several studies reported on statistical measures to determine appropriate parameters for use.[11]

For laboratories lacking automated extraction instrumentation, manual extraction of genomic material of virus methods validated, can be used to extract and concentrate pools of specimens. However, laboratories should take into consideration that manual extraction methods can be more labour intensive than automated systems. Additional studies need to be performed in order to determine whether manual extraction methods will provide similar results using a pooling protocol and be useful in surge situations.[9]

The decision to implement a pooling protocol should take into consideration the current positivity rate. The benefit of pooling is nullified if every pool yields a positive result, which may occur during periods of high positivity rate, and thus demands subsequent testing to reassess every specimen in the pool individually. One strategy to circumvent this is to alter the size of the pool to account for the prevalence of the situation. For instance, if the positivity rate is near 10%, pools of five specimens may prove more practical than 10 specimens. [9]

RECOMMENDATIONS FOR SAMPLE POOLING

For real-time RT-PCR screening for COVlD-19 are as follows (based on the KGMU study in Lucknow):

1. Use only in areas with low prevalence of COVID-19 (initially using proxy of low positivity of 5% for COVID-19
2. ln areas with positivity of 2-5%, sample pooling for PCR screening may be considered only in community survey or

surveillance among asymptomatic individuals, strictly excluding pooling samples of individuals with known contact with confirmed cases, Health Care Workers (in direct contact with care of COVID-19 patients). Sample from such individuals should be directly tested without pooling

3. Pooling of sample is not recommended in areas or population with positivity rates of >5% for COVID-19

Preferable number of samples to be pooled is five, though more than two samples can be pooled, but considering higher possibility of missing positive samples with low viral load, it strongly discouraged to pool more than 5 samples, except in research mode.[10] During a rapidly changing epidemic, testing strategies will need to adapt to potential increases in the positive test rate. Additionally, studies are needed on the impact of new assays and different extraction methods on the recovery of RNA and overall test sensitivity. Group testing of pooled specimens requires the use of highly sensitive assays to avoid missing low positive samples. Strategies must be employed to closely monitor the use of pooling as the positive rate of test specimens increases in an outbreak of disease.

Key principles for successful application of group testing involve knowledge of the limit-of-detection, sensitivity and specificity of the assay, and the prevalence of disease in the population. The goal of the process is to determine a pool size that provides the greatest conservation of resources while maintaining the reliable performance of testing.[9] As number of COVID-19 cases in lndia is rising exponentially, it is critical to increase the numbers of tests conducted by laboratories. Positivity rate in cases is still low. Hence, it may help to use the pooled samples for screening.[10]

CONCLUSION

Strategies such as pooled screening may facilitate detection of early community transmission of SARS-CoV-2 and enable timely implementation of appropriate infection control measures to reduce spread. But additional data are thus required to validate this approach on a larger scale.

REFERENCES

1. Del Rio C, Malani PN. COVID-19-New Insights on a Rapidly Changing Epidemic. JAMA. 2020 Feb 28. doi: 10.1001/jama.2020.3072.
2. Van et al. PCR Testing for Influenza Viruses Using Pooled Specimens. Journal of Clinical Microbiology 2012;50(3):891–896. doi:10.1128/JCM.05631-11
3. Emmanuel JC, Bassett MT, Smith HJ, Jacobs JA. Pooling of sera for human immunodeficiency virus (HIV) testing: an economical method for use in developing countries. J. Clin. Pathol. 1988;41:582–585.
4. Gallarda JL, Dragon E. Blood screening by nucleic acid amplification technology: current issues, future challenges. Mol. Diagn. 2000;5:11–22.
5. Currie MJ, McNiven M, Yee T, Schiemer U, Bowden FJ. Pooling of clinical specimens prior to testing for Chlamydia trachomatis by PCR is accurate and cost saving. J. Clin. Microbiol. 2004;42:4866–4867.
6. European Centre for Disease Prevention and Control. Novel coronavirus disease 2019 (COVID-19) pandemic: increased transmission in the EU/EEA and the UK – sixth update – 12 March 2020. Stockholm: ECDC; 2020.
7. Woelfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Mueller MA, et al. Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. medR xiv. 2020:2020.03.05.20030502.
8. World Health Organization (WHO). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) 2020 [cited 2020 1 March]. Available from: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf.
9. Van TT, Miller J, Warshauer DM, et al. Pooling nasopharyngeal/throat swab specimens to increase testing capacity for influenza viruses by PCR. J Clin Microbiol.2012;50(3):891-896.
10. Indian Council of Medical Research, Department of Health Research. Advisory on feasibility of using pooled samples for molecular testing of COvID-19.Available on https://www.mohfw.gov.in/pdf/letterregguidance onpoolingsamplesfortesting001.pdf
11. Dwyre DM, Fernando LP, Holland PV. Hepatitis B, hepatitis C and HIV transfusion transmitted infections in the 21st century. Vox Sang. 2011;100(1):92-98.