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Review Article

Feasibility of sputum testing for detection of COVID-19

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ABSTRACT

For the prevention of COVID-19 spread, early and accurate detection is important. Specimens are collected through respiratory mucosal surfaces with nasopharyngeal or oropharyngeal swabs, from infected patients are highly complex. Sputum testing could preferably be a more convenient technique for the detection of COVID-19 as being noninvasive method, which could easily be collected by having a patient cough deeply to produce and expel phlegm which could be in compliance to patient in comparison to Nasopharyngeal swab (NPS). Consequently, broader testing than the current methods of nasal or throat swabs will significantly increase the number of people screening, leading to more effective control of the spread of COVID-19. Nonetheless, a comparison of the saliva-based assay with current swab test is needed to understand what and how we can benefit from this newly developed assay. Therefore, in this review article, we aimed to summarize the feasibility of sputum testing in relation to Covid-19. Any implementation of clinical sampling for diagnosis should take into considerations of the sensitivity of assays, risks to healthcare professionals, and global shortage of equipment.

Keywords: COVID-19, SARS-CoV-2, Sputum sample, Sputum testing

INTRODUCTION

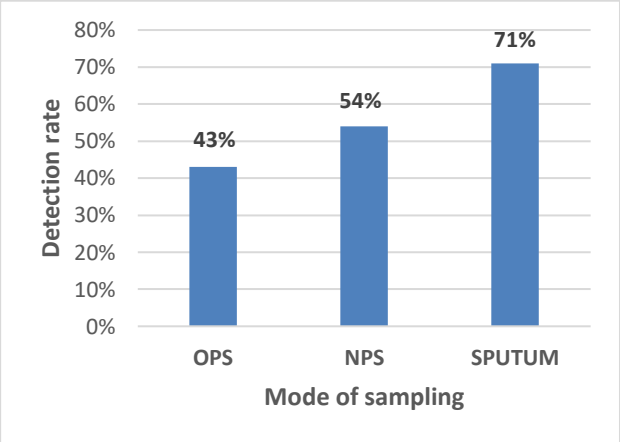
In late December 2019, a cluster of zoonotic pneumonia cases in Wuhan, China, was reported and galloping pace over the world.[1] Since then, the 2019 novel coronavirus was categorized as a public health outbreak of international concern by the World Health Organization on 30 January 2020, and therefore, this was declared as global pandemic on 11 March 2020, and the disease was named COVID-19.[2]

Currently, viral loads are routinely measured to monitor severe viral respiratory tract infections for clinical progression, response to treatment, cure and relapse. To diagnose COVID-19, Nucleic acid testing, most commonly Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), plays a significant role. Specimens are collected through respiratory mucosal surfaces with nasopharyngeal or oropharyngeal swabs, from infected patients, as recommended by the WHO for the detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which eventually require adequate human resources like trained medical staff with their expertise, guards to avoid overcrowding, and appropriate logistics for timely and effective diagnosis. The same guideline also recommended collection of lower respiratory specimens: sputum (if produced) and/or endotracheal aspirate or bronchoalveolar lavage in patients with more severe respiratory disease.[3]

Consideration to use sputum as a diagnostic fluid

COVID-19 pandemic brought diagnostic and technical challenges to testing laboratories, for its ability to provide accurate and rapid test results, as lack of attention on various parameters like, sample collection (i.e., poor-quality collection), specimen collection devices (including swab material and transport media), specimen transport and storage, testing outside the diagnostic window, and non-compliance to the patient as the process

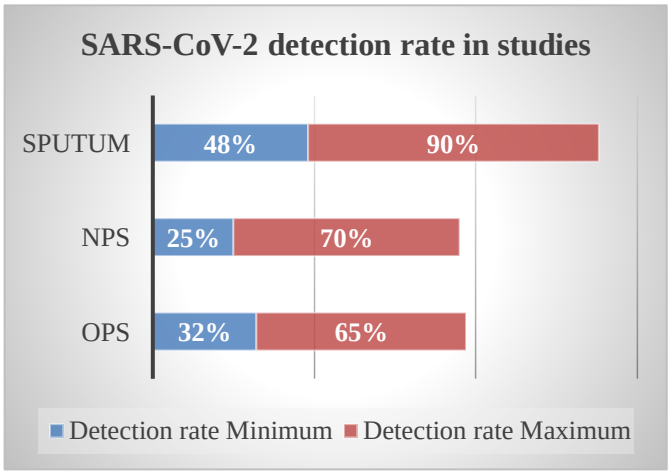
of NPS sampling is painful as well as unaccepted by many in the community. These parameters would highly raise the possibility of false-negative results, which seems to be contagious for the community and also found delayed to mitigate the transmission. So as to overcome these challenges, sputum testing could preferably be more convenient technique for the detection of COVID-19 as being non-invasive method, which could easily be collected by having a patient cough deeply to produce and expel phlegm which could be compliance to patient in comparison to Nasopharyngeal swab (NPS). Secondly, it also provides with less expertise staff, fewer logistics, easy to collect on the patient's home and the site, no aerosol generation, and no transport media required for storage. In NTEP, all peripheral health workers are previously sensitized to the procedure of sample collection and they have already trained regarding the process therefore health care workers, as well as community, are already accustomed with the process of sputum collection. Home collection of samples could be advised for sputum collection of suspects along with integrated TB-COVID laboratory services under NTEP program, which would decrease the burden of medical colleges and district hospitals laboratories.



OPS- Oropharyngeal swabs, NP- Nasopharyngeal swab.

Figure 1: SARS-CoV-2 Detection in different respiratory sites in systematic review and meta-analysis conducted by Mohammadi A et al.

In a systematic review and meta-analysis conducted, concluded that the detection rate of SARS-CoV-2 for oropharyngeal swabs were 43%, for NP swabs 54%; and for sputum, it was maximum i.e.,71%.[4] The SARS-CoV-2 was most reliably detected in sputum samples, which contained the highest viral load, followed by nasal swabs.[5] It revealed that options of sputum test, are more accurate in diagnosing SARS-CoV-2 compared to the NPS, despite of the NPS being the most commonly used test for diagnosis. Various other studies also reported that in COVID-19 diagnosed individuals, the SARS-CoV-2 detection rate ranged about 32% to 65% for oropharyngeal swabs, 25% to 70% of collected nasopharyngeal swabs, and 48% to 90% for sputum.[6-11]



OPS-Oropharyngeal swabs, NP-Nasopharyngeal swabs.

Figure 2: The SARS-CoV-2 detection rate in oropharyngeal swabs, nasopharyngeal swabs and sputum specimens in patients with COVID-19.[6-11]

Hence, it was found that the rate of SARS-CoV-2 detection was significantly higher in sputum than either oropharyngeal swabs or NP swabs.[8,12,13] The higher sensitivity for the detection of COVID-19 in sputum is also supported by previously reported studies on the detection of other non-COVID-19 respiratory viruses.[14-16]

DISCUSSION

As mentioned previously, an accurate identification of respiratory viruses are critically affected by the source of clinical specimens. While several studies on up to 15 common respiratory viruses suggest that the use of nasopharyngeal swabs provides a higher sensitivity than that of nasopharyngeal washings or oropharyngeal swabs, this is not necessarily the case for SARS-CoV-2, as the infectivity and the predilection for transmission may differ significantly between viruses.[17-20] In addition, even if a given type of clinical specimen offers a relatively higher accuracy in diagnosis, it remains an open question whether the technique-demanding test is the most needed during a pandemic with the global shortage of medical supplies as of today.[21] Study done by Chen et al reveals that some patients who develop a productive cough at the later course of the disease may still be positive with SARS-CoV-2 RNA in the sputum despite the NPS became negative.[22] Similarly, Wolfel et al. have demonstrated the presence of infectious viral particles in the lower respiratory tract, the detection of SARS-CoV-2 RNA in sputum, particularly those with low to moderate CT values, likely indicate the possibility of persistent infection.[23] A testing algorithm for sputum may need to be developed with the support of various other branches of medical specialists. Therefore, testing of sputum may be necessary for a certain patient population indicated as below: (i) hospitalized individuals

with endotracheal intubation before the NPS samples could be taken for COVID-19 evaluation (endotracheal with a traumatic fracture to the facial/nasal area or anatomic anomaly; (iii) symptomatic patients who have a productive cough with negative NPS results. One major drawback of sputum collection is the generation of aerosols; therefore, induced sputum is not recommended aspiration may be indicated in this situation); (ii) patients

by the Centre for Disease Control.[24] However, self-collected sputum (with proper instructions) in a defined patient population would provide several advantages over NPS, such as the discomfort associated with NPS sampling.

Table 1: Summary description of studies and reports included, with sample size and key findings.

Authors	Sample size and respondents	Key findings
Mohammadi et al.	11 studies that met inclusion criteria, with SARS-CoV-2 testing results from a total of 3442 respiratory tract specimens.	Compared to NPS sampling, sputum testing resulted in significantly higher rates of SARS-CoV-2 RNA detection while OPS testing had lower rates of viral RNA detection.
Falsey Ann et al.	A total of 532 subjects admitted for 556 respiratory illnesses were enrolled. A total of 189 virus strains were identified by RT-PCR	23% were positive by NTS (Nose throat swab) alone, 33% were positive only with sputum samples.
Jeong et al.	154 adults who were admitted or presented to the clinics of Gil Medical Center with acute respiratory symptoms were recruited from 1 November 2012 to 31 March 2013. 154 specimens of nasopharyngeal swabs and sputum were taken.	The positive rate was 53% (81/154) for nasopharyngeal swabs and 68% (105/154) for sputum ($p<0.001$).
Branche et al.	During the four winters from 2008 to 2012, 965 respiratory illnesses were evaluated. A viral infection was identified in 295 of 965 patients (31%), of which 7 subjects had two different viruses for a total of 302 viruses identified using the in-house uniplex RT-PCR assays.	Of the 302 viral detections, 124 (41%) were positive in both the Nose Throat Swab and sputum samples, 105 (35%) were positive by the sputum sample alone, and 73 (24%) were positive by the NTS alone.
Chenyao Lin et al.	Paired specimens of throat swabs and sputum were obtained from 52 COVID-19 suspected patients. All patients received RT-PCR assays in both throat swabs and sputum specimens at the same time.	The positive rates of SARS-CoV-2 from sputum specimens was 76.9% and for throat swabs 44.2%. The findings showed that the positive rate from sputum specimens was significantly higher than that from throat swabs ($p=0.001$)

CONCLUSION

The current procedures, however, are technically complex, often inconvenient for patients, and require personal protective equipment. Sputum testing, on the other hand, is feasible and requires less expertise staff also has readily accepted in the community. The diagnostic testing is crucial for controlling the COVID-19 pandemic. Any implementation of clinical sampling for diagnosis should take into considerations of the sensitivity of assays, risks to healthcare professionals, and the global shortage of equipment.

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