SALIVA MAY BE CONSIDERED AS RELIABLE TOOL FOR DIAGNOSIS OF COVID-19 WHEN COMPARED WITH NASOPHARYNX OR THROAT SWABS

Is saliva considered as a reliable tool for COVID-19 diagnosis and monitoring when compared with nasopharynx or throat swabs?

REVIEWERS
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SUMMARY

Selection Criteria

With no date or language restrictions, an electronic search to evaluate the available data regarding the use of saliva as a reliable tool for coronavirus 2019 (COVID-19) diagnosis and monitoring was conducted on July 22, 2020, using the following databases: (1) PubMed, (2) Embase, (3) LILACS, (4) Scopus, and (5) Web of Science, and the references of the related articles were cross-checked. The review included case reports and series, case–control, cross-sectional, and prospective observational studies.
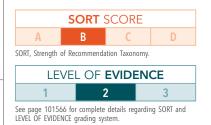
Key Study Factor

The reliability of saliva as a testing sample for the diagnosis of COVID-19 as compared with gold standard samples (nasopharynx and throat swabs) was evaluated in 28 studies conducted in 10 different countries. A total of 2095 patients were included in this review. The most used SARS-CoV-2 detection test in saliva samples was the RT-qPCR. Drooled saliva, coughed-out saliva, oral swabs, glandular secretion, posterior oropharyngeal saliva, and throat saliva were used as specimens.

Main Outcome Measure

Sensitivity and specificity of reverse-transcription quantitative polymerase chain reaction (RT-qPCR) using saliva as samples in detecting the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) were investigated.

Main Results

Twenty-five studies evaluated COVID-19 markers in adults, and three studies assessed the same markers in neonates and pediatric patients. Twenty-eight studies detected the presence of SARS-CoV-2 RNA in saliva. The reported viral

load ranged from 9.9 × 102 to 1.2 × 108 copies/ml. Nine studies compared the sensitivity or specificity of RT-qPCR-analyzed saliva specimens with that of the throat and nasopharyngeal swabs, the gold standard for COVID-19 diagnosis. This varied from 66% to 92%, and from 97% to 100%, respectively. One study analyzed the cost of different testing samples and reported US $8.24 per 100 saliva specimens compared with US $104.87 per 100 for naso-pharyngeal swabs. Two studies reported impact of the times of saliva collection on the test results. The cycle threshold values of posterior oropharyngeal saliva specimens collected at different time points were obtained and analyzed, differences during the day were identified, as were higher viral loads early in the morning versus bedtime. Saliva specimens collected during the day had a lower rate of positive concordance with the nasopharyngeal swab viral load than saliva collected early in the morning.

Conclusions

The detection of SARS-CoV-2 in the saliva of patients with COVID-19 has been confirmed, with diagnostic perfor-mance comparable with the current standards (nasopha-ryngeal and throat swabs); however, there is a lack of understanding of salivary biomolecules that could be used for salivary diagnostics in the context of COVID-19 infection.

COMMENTARY AND ANALYSIS

Because of the exponential growth in the number of COVID-19 cases, the World Health Organization has declared a global public health emergency.[1] Globally, over 98 million cases with close to 2.1 million deaths have been confirmed as of 27th of January 2021. SARS-CoV-2 transmission is mainly dependent on respiratory droplets spontaneously formed by talking and coughing.[2]

The primary method of containing the COVID-19 pandemic relies on testing as many persons as possible to avoid the possibility of other persons and health care providers being infected, particularly by asymptomatic people, who account for about 79% of the contagion.[3]

Although COVID-19 testing is expected to be widely accessible, only part of the population has rapid testing access. Available COVID-19 tests are technically complex and costly, and some have a high proportion of false-negative findings on samples from the upper respiratory tract. In addition, the collection of respiratory samples can irritate patients and pose an increased risk of virus trans-mission to health care workers. Studies have demonstrated the validity of fast and inexpensive preventive salivary testing against other viruses (eg, HIV and Zika) for use in laboratory and home settings. Because the oropharyngeal cavity has high SARS-CoV-2 RNA, saliva can be an excellent diagnostic fluid for COVID-19 monitoring.[4]

The main weakness of this review is that the risk of bias from individual studies was omitted. A critical step in performing a systematic review is the risk of bias assessment, as the overall judgment of the quality of the included studies in-fluences the interpretation of the results and contributes to formulating a well-balanced conclusion. The Cochrane Screening and Diagnostic Tests Methods Group has pub-lished validity guidelines for diagnostic research. Internal validity refers to the research properties that prevent sys-tematic error or bias. External validity provides insight into the study's generalizability and determines whether the test under evaluation was conducted in accordance with the agreed standards. Internal and external validity criteria can be used to assess the overall level of evidence.[5]

The number and methodological quality of the included primary studies, together with the degree of heterogeneity of their diagnostic accuracy estimates, determine whether a meta-analysis can be carried out. Owing to limited infor-mation regarding the diagnostic accuracy and heteroge-neous nature of the included studies, conducting a meta-analysis is not easy. If it is difficult or not advisable to carry out a meta-analysis, the review may be limited to a quali-tative descriptive analysis of the available diagnostic research.[5] This review did not report whether a meta-analysis was possible or not. Moreover, most of the included articles in this review had missed essential data that, in turn, may halt reaching robust conclusions regarding the possible effects of confounding factors on the diag-nostic accuracy of COVID-19 salivary tests.

The use of saliva as a tool to diagnose COVID-19 has several limitations. Coughed-out saliva and saliva collected from the posterior oropharynx may contain respiratory secretions and secretions from the posterior nasopharynx. Therefore, a more standardized sample collection should be carried out in future studies. Sample collection, transportation, pro-cessing, and analysis may also affect the tests' outcomes and should be reported in detail. To increase the completeness and transparency of diagnostic studies, the Standards for the Reporting of Diagnostic Accuracy Studies (STARD) statement was developed. STARD provides a list of essential items that writers, reviewers, and readers may use as a checklist to ensure that the correct information is included in a diagnostic accuracy study report.[6]

In addition to the cost savings and noninvasive nature, the use of saliva serves as an excellent alternative sample in the diagnosis of respiratory virus infections, particularly for extensive population-level screenings. As health pro-fessionals are not required for the collection, it will reduce the risk of hospital transmission to health care workers and other patients. In addition, the use of salivary samples eliminates the waiting time; therefore, the results would be

available in a shorter time, which is essential during a pandemic.

Dental practitioners are at significant risk of transmitting airborne infectious diseases via persistent exposures to aerosols and possible infectious droplets in their environments. Chairside screening for COVID-19 in saliva will serve as a brilliant method to protect them. Following the infection control guidelines and using personal protective equipment is vitally important, and all that can be confidently recommended for dental practitioners and dental health care workers. Additional measures suggested in the dental clinic include effective use of high-volume suction devices, rubber dam isolation, adjunct chemotherapeutic agents mouth rinse with 0.2% povidone-iodine or 0.5%-1% hydrogen peroxide may also be used preoperatively to reduce the viral load in the oral cavity.[7,8]

The range of COVID-19 saliva tests' sensitivity and specificity in this review overlapped with nasopharyngeal swabs, which are the gold standard of COVID-19 diagnostic tests. Further studies are needed to reduce this range and confirm COVID-19 diagnosis accuracy using saliva as a test specimen. These studies are recommended to be conducted at different stages of COVID19 infection and should be reported following the STARD statement and considering the limitations mentioned previously.

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