What is the sensitivity of SARS-CoV-2 RT-PCR done on different clinical specimens?

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This rapid review summarizes the available evidence on the sensitivity of SARS-CoV-2 RT-PCR across different clinical specimens. This may change as new evidence emerges.

KEY FINDINGS

The pooled sensitivity of non-respiratory tract specimens of confirmed COVID-19 patients were as follows: Saliva 77%, stool/ rectal swab 22%, blood/serum 2% and urine 22%.

- Human-to-human transmission of COVID-19 is via direct or indirect contact and inhalation of respiratory droplets.
- Viral replication begins in the upper respiratory tract and a myriad of symptoms such as high fever, sore throat, myalgia and fatigue may set in. Infected individuals may be asymptomatic for 5.2 to 12.5 days. Viral replication in the upper respiratory tract peaks at day 5 of infection and is mediated by cleavage of S1 and S2 regions of the viral protein.
- In the lower respiratory tract, ACE II receptors binds to viral capsid antigen which facilitates viral entry into the epithelial cells lining the alveoli. Viral particles in lower respiratory secretions are expelled by coughing, sneezing or talking.[1]
- The presence of viral particles in respiratory secretions is the basis for using respiratory tract specimen for the diagnosis of the disease using RT-PCR or viral load detection.
- According to the WHO laboratory testing for COVID-19 in suspected human cases published on March 19,2020, the decision to test an individual should be based on clinical and epidemiological factors and linked to an assessment of the likelihood of infection. Specimens should be collected from upper respiratory tract: nasopharyngeal (NPS) and oropharyngeal swab (OPS) or wash in ambulatory patients and/or lower respiratory tract: sputum (if applicable) and/or endotracheal aspirate (ETA) or bronchoalveolar lavage (BAL) in patients with more severe respiratory disease, and sent for real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) to confirm the diagnosis of COVID-19.[2]
- A meta-analysis by Mohammadi et al demonstrated the pooled sensitivity of OPS, NPS and sputum which are 43% (95% CI 34-52%), 54% (95% CI 14-67%), and 71% (95% CI 61-80%), respectively.[3]
- Only 27% of patients diagnosed to have COVID-19 have sputum production.[4]
- NPS and OPS swabs causes discomfort and may cause bleeding especially in patients with thrombocytopenia.[5]

RESULTS

Characteristics of Included Studies

The search keywords: COVID-19, nasopharyngeal, oropharyngeal, swabs, and respiratory sample were used. A total of 130 search results were obtained from PubMed MEDLINE, Cochrane Library and MedRixv on May 21, 2020. 19 articles remained after review of title and abstract. Eight articles remained after full paper review.

All studies included are prospective or retrospective cohort studies. Among these, five are prospective and three are retrospective. One study was done in the United States, one in Japan, one in Italy, and five were done in China, between the months of January to March 2020.

The studies investigated the following specimen types for viral RNA detection through RT-PCR: saliva, blood/serum/plasma, urine, and stool/rectal swab/anal swab.

The characteristics of included studies is summarized in Appendix 1.

Outcomes

The pooled estimate of sensitivity of the different non-respiratory tract specimens are as follows:

1. saliva at 77% (95%CI 71-83%, n=4),
2. stool/rectal swab at 22% (95%CI 22-37%, n=5),
3. blood at 2% (95%CI 1-3%, n=4) and
4. urine at 22% (95%CI 18-25%, n=5).

There was significant heterogeneity in all the comparisons for the different specimen sites.

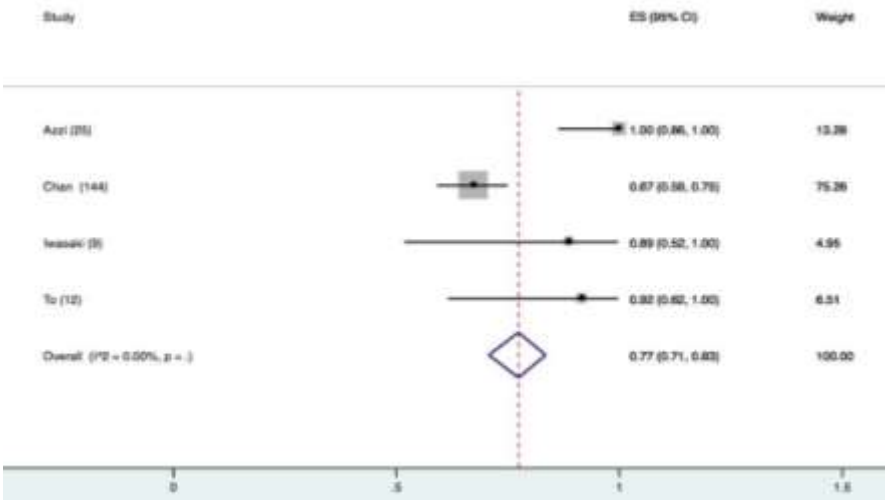

Figure 1: Pooled estimate of the sensitivity of saliva

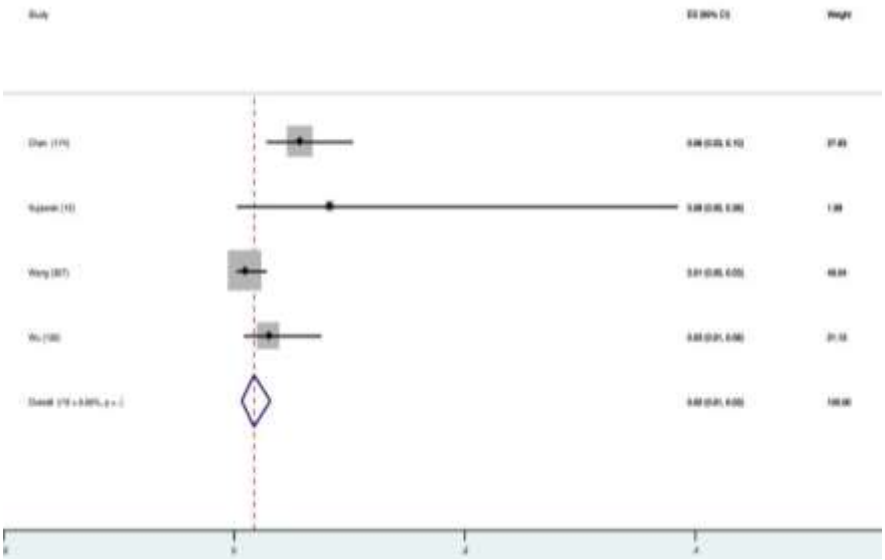

Figure 2: Pooled estimate of the sensitivity of blood/serum

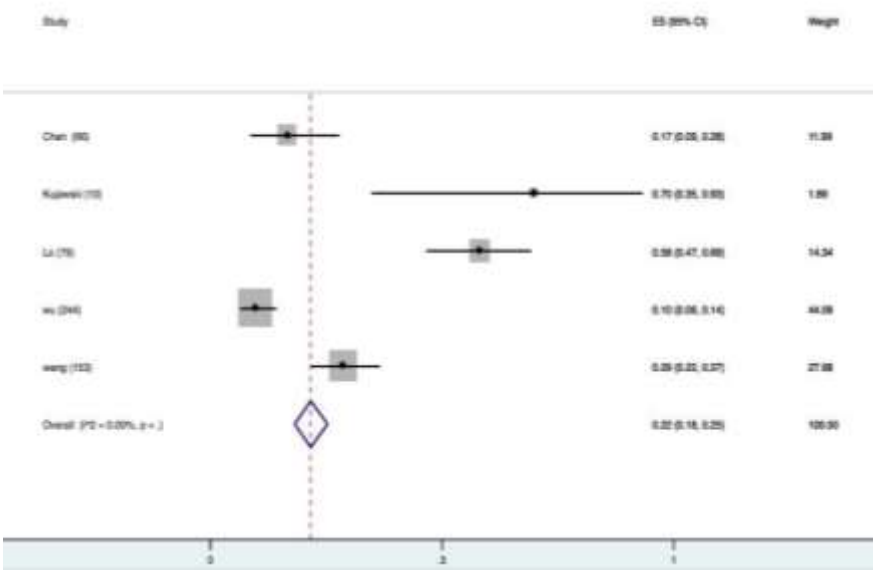

Figure 3: Pooled estimate of the sensitivity of stool/rectal swab

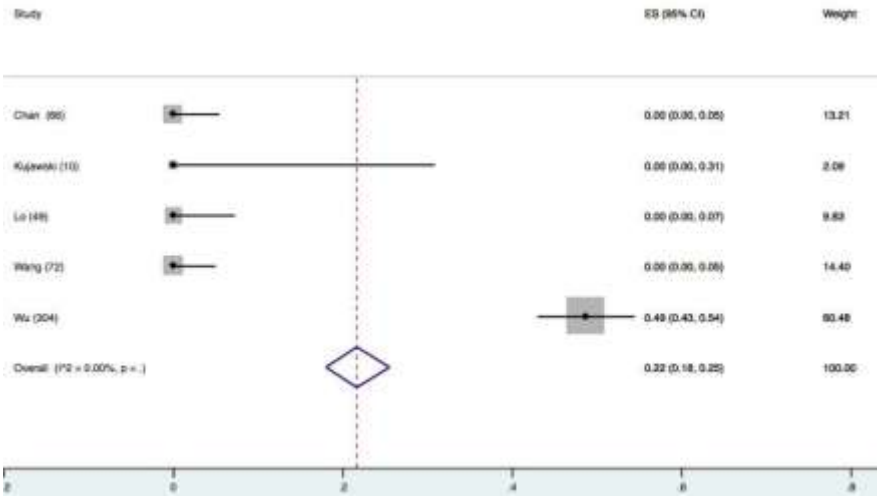

Figure 4: Pooled estimate of the sensitivity of urine specimen

Table 1: Summary of results of individual studies

Author	Saliva	Stool/Rectal swab	Blood/Serum	Urine
Azzi	25/25			
Chan	97/144	11/66	10/174	0/66
Iwasaki	8/9			
Kujawski		7/10	1/12	0/10
Lo		46/79		0/49
To	11/12			
Wang		44/153	3/307	0/72
Wu		24/244	4/132	148/304

Recommendation from Other Guidelines

The recommendation from the Center for Disease Control and Prevention as of July 8, 2020 for collection and testing of specimens for SARS-CoV-2 include the following: (1) Nasopharyngeal specimen collected by a health care provider, (2) Oropharyngeal specimen collected by a health care provider, (3) Nasal mid-turbinate swab collected by a healthcare provider or a supervised onsite self-collection (using a flocked tapered swab) (4) Anterior nares (nasal swab) specimen collected by a healthcare provider or by onsite or home self-collection (using a flocked or spun polyester swab) (5) Nasopharyngeal wash/aspirate or nasal wash/ aspirate specimen collected by a health care provider.

CONCLUSION

The pooled sensitivity of detecting SARS-CoV-2 nucleic acid in non-respiratory tract specimens of patients was highest for saliva 77% (95%CI 71-83%). However, the pooled sensitivity was unacceptably low for stool/ rectal swab 22% (95% CI 22-37%), blood/serum 2% (95% CI 1-3%), and urine 22% (95% CI 18-25%).

Declaration of Conflict of Interest

No conflict of interest.

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Appendix 1

Characteristics of Included Studies

First author Article Title Month-Year Country	Study Design	Sample Population	Intervention	Outcome Measured	Population Characteristics	Study Results
Azzi, Lorenzo Saliva is a reliable tool to detect SARS-CoV-2 Apr-20 Italy	Prospective observational study	25 SARS-CoV-2 infected patients who underwent hospital admission after the diagnosis of COVID-19 provided by rRT-PCR on NPS	Saliva collected through the drooling or pipetting technique, analyzed by rRT-PCR.	Prevalence of positivity in saliva and association between clinical data and the cycle threshold as a semiquantitative indicator of viral load were considered	Male: female ratio 2.1:1; age range of 39-85 years (mean 61.5 years +/- 11.2 years); all were admitted in the ICU; included severe and very severe disease	Positive rate for saliva 25/25 (100%), Ct values (range 18.12–32.23, mean value 27.16 + / − 3.07); no differences in the Ct values with regards to the period elapsed after the onset of symptoms; inverse correlation between the LDH values recorded and the Ct values (p=0.04); no significant correlation between usRCT and the Ct values (p=0.07); Ct values were not influenced by the patient's age (p=0.34), sex (p=0.31) or comorbidities; Eight patients underwent a second salivary swab after 4 days and results were consistent with the initial analysis.
Chan, Jasper Fuk-Woo Improved Molecular Diagnosis of COVID-19 by the Novel, Highly Sensitive and Specific COVID-19-RdRp/Hel Real-Time Reverse Transcription-PCR Assay Validated In Vitro and with Clinical Specimens	Prospective observational cohort study	15 patients with laboratory-confirmed COVID-19 in Hong Kong whose NPA/NPS/TS, and/or sputum specimens tested positive for SARS-CoV-2 RNA by the RdRp2 assay	120 respiratory tract (NPA/NPS, TS, saliva, and sputum) and 153 non-respiratory tract specimens (plasma, urine, feces/rectal swabs) were collected and sent for COVID-19-RdRp/Hel and RdRp-P2 assays	Comparison between the COVID-19-RdRp/Hel and RdRp-P2 real-time RT-PCR assays for the detection of SARS-CoV-2 RNA in different types of clinical specimens	Male: female ratio of 1:1.4; age range of 37-75 years (median 63 years); all had clinical features of acute community-acquired atypical pneumonia and radiological evidence of ground-glass lung opacities; 11 were in stable condition, 3 in critical condition, 1 expired	Among 273 specimens collected from these 15 patients, 77 (77/273, 28.2%) were positive by the RdRp-P2 assay; COVID-19-RdRp/Hel assay were positive for all these 77 patients, in addition to 42 other specimens including 29/120 (24.2%) respiratory tract specimens, and 13/153 (8.5%) non-respiratory tract specimens that were negative in the RdRp-P2 assay (119/273, 43.6%) ($p < 0.001$)

May-20 China						
Iwasaki, Sumio Comparison of SARS-CoV-2 detection in nasopharyngeal swab and saliva May-20 Japan	Prospective observational cohort study	9 COVID-19 patients diagnosed by a positive NPS SARS-CoV-2 RT-PCR	Paired nasopharyngeal swab and saliva samples were taken and sent for RT-qPCR when symptoms were relieved to determine the timing of discharge	Comparison of the efficacy of PCR detection of SARS-CoV-2 between paired NPS and saliva samples	Median age 70.5years (range 30-97 years); most had mild to moderate disease; all patients received favipiravir	Specimens were sampled within 10 days (range, 7-19 days) after symptom onset. SARS-CoV-2 was detected in all 9 patients in nasopharyngeal samples and in 8/9 (89%) patients in saliva samples. The mean ± SD of the CT values were 24.2 ± 4.4 and 30.4 ± 4.9 in nasopharyngeal and saliva samples, respectively, and significantly higher in saliva samples (P=0.018). The CT values were equivalent between the two samples at earlier time points but higher in saliva at later time points; All 11 samples taken within 2 weeks from the onset of symptoms were positive in both NPS and saliva. After 2 weeks, some samples tested negative.
Kujawski, Stephanie A First 12 patients with coronavirus disease 2019 (COVID-19) in the United States Mar-20 USA	Prospective observational study	12 patients diagnosed with COVID-19 who were confirmed by CDC during Jan 20- Feb 5,2020 by a positive SARS-CoV-2 rRT-PCR in >/= 1 respiratory tract specimen (NP, OP or sputum)	Respiratory, stool, serum, and urine specimens were submitted for SARS-CoV-2 rRT-PCR testing every 2-3 days for the first 17 days of illness for SARS-CoV-2 virologic testing	Report the epidemiology, clinical course, clinical management and virologic characteristics of the first 12 patients with COVID-19 diagnosed in the US	5 patients received only out-patient care and were isolated at home, 7 were hospitalized; male: female ratio of 1.5:1; median age 53 years (range 21-68 years); 4/5 patients with >/= 1 underlying medical conditions were hospitalized; 10 patients travelled to mainland China 2 weeks before onset of illness, 2 other patients reported	398 specimens were collected and tested from the 12 patients throughout the course of illness. All 12 patients had SARS-CoV-2 RNA detected in at least one NP swab, 11/12 in an OP swab, 6/6 in sputum, 1/12 in serum, 7/10 in stool, and 0/10 in urine (Figure 3). Among 98 pairs of simultaneous NP and OP specimens, 58 (59%) had concordant results. Among 27 discordant pairs with one positive specimen, the NP specimen was positive in 70%; the remaining 13 discordant pairs had one negative and one inconclusive specimen. Two patients provided sputum specimens when NP and/or OP specimens tested

					exposure with a previously infected patient with COVID-19; Over the course of illness, patients reported cough (n=12), subjective or measured fever (n=9), diarrhea (n=3), and vomiting (n=2). Three patients who did not report fever were never hospitalized and remained on home isolation.	negative, and sputum continued to be positive in both patients. In Patient 7, viral RNA was detected in sputum 17 days after the last positive OP specimen and ≥2 weeks after reported symptom resolution. In seven patients who had SARS-CoV-2 RNA detected in stool, most detections occurred when viral RNA was still detectable in the respiratory tract. Among three patients who reported diarrhea, all had viral RNA detected in stool. Mean Ct values in positive specimens were 17.0–39.0 for NP, 22.1–39.7 for OP, and 24.1–39.4 for stool. Ct values were lower in the first week of illness than the second in most patients; in some patients, low Ct values continued into the 2nd and 3rd week of illness. There was no apparent relationship between Ct values in the upper respiratory tract and disease progression. SARS-CoV-2 rRT-PCR results turned positive in serum of Patient 9 in the second week of illness at the time of rapid clinical deterioration; Serial testing to determine duration of RNA detection and viral shedding. SARS-CoV-2 RNA has been detected at a maximum of day 26 in NP specimens, day 26 in OP, day 29 in sputum, and day 25 in stool. The duration of viral RNA detection did not differ by hospitalization status or supplemental oxygen requirement.
Lo, Iek Long Evaluation of SARS-CoV-2 RNA	Retrospecti ve observation al study	Ten COVID-19 patients enrolled in the Centro	Serial qRT-PCR for SARS-CoV-2 were performed for different specimens,	Evaluation of SARS-CoV-2 RNA shedding in	Male: female ratio 1: 2.3; median age 54 years (range 27-64 years); 5 patients had	There were positive SARS-CoV-2 RNA signals in all patients' NPS (100%) and stool specimens (100%) but negative in all urine specimens (0%). The

shedding in clinical specimens and clinical characteristics of 10 patients with COVID-19 in Macau Feb-20 China		Hospitalar Conde de São Januário (CHCSJ) between Jan 21-Feb 16, 20, who were diagnosed through detected RNA signals in NPS and sputum specimen	including NPS, urine, and stool	clinical specimens and clinical characteristics	comorbid medical conditions; 2 had mild disease, 4 had moderate and another 4 had severe disease; all patients received treatment with lopinavir and ritonavir	average viral RNA conversion time in both NPS and feces were 18.2 days (SD:4.6) and 19.3 days (SD:3.4), respectively.
To, Kelvin Kai-Wang Consistent Detection of 2019 Novel Coronavirus in Saliva Feb-20 China	Prospective observational study	12 patients with laboratory-confirmed 2019-nCoV infection by a positive NPS or sputum SARS-CoV-2 RT-PCR, in Hong Kong	Saliva were collected for SARS-CoV-2 RT-PCR	Detection of SARS-CoV-2 nucleic acid in saliva	Male: female ratio of 1.4:1; median age of 62.5 years (range 37-75 years); all were hospitalized	Saliva specimens were collected at a median of 2 days after hospitalization (range 0-7 days); SARS-CoV-2 nucleic acid was detected in the initial saliva specimens of 11 patients (91.7%)

Wang, Wenling Detection of SARS-CoV-2 in Different Types of Clinical Specimens Mar-20 China	Retrospective observational study	205 patients with OCIVD-19 diagnosed based on symptoms and radiology and confirmed by SARS-CoV-2 detection in NPS	Pharyngeal swabs were collected from most patients 1 -3 days after hospital admission. Blood, sputum, feces, urine, and nasal samples were collected throughout the illness. Bronchoalveolar lavage fluid and fibro bronchoscope brush biopsy were sampled from patients with severe illness or undergoing mechanical ventilation. Specimens were sent for SARS-CoV-2 RT-PCR	Detection of SARS-CoV-2 in different types of clinical specimens	68% were male; mean age 44 years (range 5-67 years); 19% had severe illness	Bronchoalveolar lavage fluid specimens showed the highest positive rates (14 of 15;93%), followed by sputum(72 of 104; 72%), nasal swabs (5 of 8; 63%), fibro bronchoscope brush biopsy (6 of 13; 46%), pharyngeal swabs (126 of 398; 32%), feces (44 of 153; 29%), and blood (3 of 307; 1%). None of the 72 urine specimens tested positive
Wu, Jianguo Detection and analysis of nucleic acid in various biological samples of COVID-19 patients Apr-20 China	Retrospective observational cohort study	132 patients diagnosed with COVID-19 in East Section of Renmin Hospital of Wuhan University from Jan 31-Feb 29, 20, in accordance with relevant epidemiological and clinical manifestations and a positive SARS-CoV-2 RT-PCR	Nasopharyngeal swabs, sputum, blood, feces and anal swabs were sent for 2019-nCoV nucleic acid detection	Detection and analysis of nucleic acid in various biological samples of COVID-19 patients	Male: female ratio of 1.2:1; mean age of 66.7 years +/- 9.1 years; 33% had severe disease, 6% had were critical cases	Positive rate of 2019-nCoV nucleic acid test of oropharyngeal swab is 38.13% (180/472 times), the positive rate of 2019-nCoV nucleic acid test of sputum is 48.68% (148/304 times), the positive rate of blood 2019-nCoV nucleic acid test is 3.03% (4/132 times), and the positive rate of 2019-nCoV nucleic acid test of feces is 0.83% (24/244 times) The positive rate of 2019-nCoV nucleic acid detection in anal swabs is 10.00%（12/120 times) Positive rates of 2019-nCoV nucleic acid test were determined from all specimen types