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LETTER TO THE EDITOR

Clinical status determines the efficacy of salivary and nasopharyngeal samples for detection of SARS-CoV-2

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Recently, salivary samples have been widely investigated for the detection of SARS-CoV-2 RNA with variable success rate [1–9]. The rationale claims that the virus particles possibly come from the respiratory system and infected salivary glands [1]. Proposed advantages are less-invasive, convenience, self-collection, and minimum risk of cross infection [2]. To draw a meaningful conclusion in this regard, the most important study design would be a comparative cross-sectional analysis of salivary and nasopharyngeal samples (NPSs) in the detection of SARS-CoV-2 RNA with a cycle threshold value. Hence, we decided to critically analyze the results of published papers with such a study design.

We searched PubMed, SCOPUS, and Web of Science databases with keywords such as COVID-19, SARS-CoV-2, saliva, and nasopharyngeal swab in various permutations and combinations to retrieve the papers exclusively on the comparative analysis of saliva and NPS for detection of SARS-CoV-2 RNA using RT-PCR. After a thorough literature search, we could able to shortlist a total of nine studies from the literature [1–9]. Data such as sample size, disease status, detection rate, and cycle threshold value were retrieved. (Table 1) All the studies projected saliva as potential sampling material for the detection and diagnosis of SARS-CoV-2 RNA using RT-PCR.

One interesting trend apprehended our attention is the detection rate and cycle threshold values in symptomatic and asymptomatic patients. The categorization and characterization of the symptomatic and asymptomatic status of the patient were available in four [1, 4, 5, 9] and two [2, 7] cases, respectively. In asymptomatic cases, the sensitivity and detection rate was more in salivary samples as compared to NPS [2, 7]. Moreover, the cycle threshold values were comparatively low in salivary samples depicting high viral load in the oral cavity, whereas studies on symptomatic patients showed better results in NPS with high detection rate and low cycle threshold value as compared to salivary samples [1, 4, 5, 9]. This discriminatory result between symptomatic and asymptomatic cases is highly intriguing; however, proper cognizance of this fact has not been taken in the literature.

The majority of the symptomatic SARS-CoV-2 positive cases show respiratory symptoms in the form of coughing, sneezing, and breathlessness, suggesting viral localization in the nasal and respiratory tract [3]. Hence, we envisaged that NPS is the most representative sample in the case of symptomatic cases and thus responsible for high sensitivity and detection rate. On the contrary, in asymptomatic cases, NPS could not be a representative sample (probably due to absent or limited viral localization) for the detection of SARS-CoV-2. This contention is also supported by the lower cycle threshold for asymptomatic patients salivary samples and symptomatic patients NPS samples reported in the present analysis. Although this explanation is highly conceivable and is supported by the data reported in the literature, future studies are warranted in this direction with the appropriate characterization of the study samples into symptomatic and asymptomatic cases. Looking at this discriminative trend, prescription of saliva samples for asymptomatic cases and NPS for

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Table 1 Details of the comparative studies on saliva and nasopharyngeal specimens in detection of SARS-CoV-2 infection

Sr. No.	Author	Sample size	Patient status	Detection rate	Mean Ct value
1.	Procop et al. [1]	216	Symptomatic	NPS, 10.3%; saliva, 5.2%; both, 84.5%	NPS: 20.55 (± 5.36) Saliva: 24.16 (± 4.80)
2.	Rao et al. [2]	217	Asymptomatic	Saliva, 93.1%; NPS, 52.5%	NPS: 33.2 Saliva: 30.6
3.	Jamal et al. [3]	91	Mixed	Saliva, 72%; NPS, 89%	NA
4.	Landry et al. [4]	124	Symptomatic	NPS, 94.3%; saliva, 85.7%	NPS: 33.68 Saliva: 37.62
5.	Vaz et al. [5]	155	Symptomatic	NPS, 45.8%; saliva, 43.22%	NA
6.	Sutjpto et al. [6]	105	Active: 73 Negative: 32	NPS, 85%; saliva, 38–52%	< 7 days: NPS, 24.05; saliva: 32.49 > 7 days: NPS, 32.20; saliva: 30.98
7.	Yokota et al. [7]	1924	Asymptomatic	NPS, 86%; saliva, 92%	NA
8.	Williams et al. [8]	622	NA	NPS: 39/622 (6.3%) Saliva: 33/39 (84.6%)	Significantly lower in NPS than saliva
9.	Iwasaki et al. [9]	76	Symptomatic positive: 10 Suspicious negative: 66	Both: 8 out of 10 patients NPS: 1 out of 10 patients Saliva: 1 out of 10 patients	NPS: 26.5 (± 8.1) Saliva: 30.6 (± 4.6)

NPS nasopharyngeal swab, *Ct* cycle threshold, *NA* not available

symptomatic cases would be a valuable recommendation subject to validation in future randomized prospective studies. This will not only enhance the detection rate but also help in controlling the spread of the virus through the "test, trace and isolate, support" approach.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study, formal consent is not required.

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