

## COMMENTARY

# Role of Saliva as a Viable Bio Sample for COVID-19 Detection

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### ABSTRACT

Coronavirus disease 19 (COVID-19) has been promptly spreading to different countries becoming a global pandemic, to the reports of the World Health Organization (WHO). Sufficient immune responses over whelming the virus in the first or second phase without immune over-reaction can be seen in patients with competent immune functions and no obvious risk factors like old age, co-morbidities, etc. There is high sensitivity and specificity of saliva specimens in detecting respiratory viruses by an automated multiplex molecular assay while comparing with those of nasopharyngeal aspirate. The beneficial role of saliva as a quick and non-invasive diagnostic bio sample has been established.

**KEYWORDS:** COVID-19, Saliva, Bio Sample, Diagnosis.

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Coronavirus disease 19 (COVID-19) was first reported and confirmed in Wuhan, China in December 2019 and is thought to be caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).<sup>1</sup> Since then it has been promptly spreading to different countries becoming a global pandemic, to the reports of the World Health Organization (WHO).<sup>2</sup> Two life threatening epidemics have been reported so far; Severe Acute Respiratory Syndrome (SARS) in 2002–2003 in China and Middle East Respiratory Syndrome (MERS) in the Middle Eastern countries approximately after ten years later.<sup>3</sup> SARS-CoV-2 has the genetic sequence similar to 79.6% and 96% to that of SARS-CoV and bat coronavirus respectively.<sup>4</sup> Regardless of its zoonotic nature, clinical features associated with this virus are quite typical including fever, nonproductive cough mostly, malaise, dyspnoea and pneumonia.<sup>5</sup> While sputum production, hemoptysis, headache and gastrointestinal symptoms such as diarrhea, nausea and vomiting are less commonly presented symptoms.<sup>6</sup>

Patients infected with COVID-19 show increased number of leukocytes, higher levels of plasma pro-inflammatory cytokines and abnormal respiratory findings.<sup>7</sup> The main pathogenesis of COVID-19 include three phases; viremia, acute (pneumonia) phase and severe or recovery phase that determine the clinical course of SARS-CoV-2 infection.<sup>8</sup> High level cytokines and chemokines including IL1- $\beta$ , IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFN $\gamma$ , IP10, MCP1, MIP1 $\alpha$ , MIP1 $\beta$ , PDGFB, TNF $\alpha$ , and VEGFA are raised in the blood of patients with COVID-19 infection. While in severe cases, increased levels of pro-inflammatory cytokines including IP10, MCP1, MIP1 $\alpha$ , GCSF, IL2, IL7, IL10 and TNF $\alpha$  are present.<sup>9</sup>

Active and sufficient immune responses over whelming the virus in the first or second phase without immune over-reaction can be seen in patients with competent immune functions and no obvious risk factors like old age, co-morbidities, etc. However, there is a high risk of mortality in patients with immune dysfunction as they cannot cope with the initial phase and become critically ill. Therefore, quick and accurate diagnosis of COVID-19 is crucial in controlling the outbreak in hospitals so that treatment of COVID-19 should be done immediately depending on the stage of patients.<sup>8</sup>

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Swabs from the nasopharynx and oropharynx are the recommended upper respiratory tract specimen types for making diagnosis of COVID-19 but the collection of swab requires close contact between healthcare workers and patients that not only increase the risk of transmission of the virus among healthcare workers but also causes discomfort resulting in bleeding, especially in condition like thrombocytopenia.<sup>5</sup> To overcome this problem, saliva has been found as an alternate source for making the diagnosis. It can be used for detecting respiratory viruses, including Coronaviruses because of high consistency > 90% with nasopharyngeal specimens.<sup>10</sup>

Public Health Laboratory Services Branch for patients in Hong Kong collected saliva of 12 patients (confirmed COVID-19 infection) at a median of two days after hospitalization for detection of COVID-19. Nucleic acid extraction and real-time reverse transcription-quantitative polymerase chain reaction was performed to get the results and it was found positive in the initial saliva specimens of 11 patients (91.7%).<sup>11</sup>

The source of COVID-19 virus in the saliva can be from either the salivary glands through the ducts or from the gingival crevicular fluid or simply from secretions of the lower and upper respiratory tract that combines with the saliva.<sup>12</sup> Salivary gland cells might play a role in the initial entry of virus and its progression as angiotensin-converting enzyme 2 (ACE2) epithelial cells of the salivary glands have been found as an initial target for the SARS-CoV.<sup>13</sup> Also high levels of mRNA and cellular protease, furin, have been found in the salivary glands which vary according to the cell type levels.<sup>14</sup> Transmembrane protease/serine subfamily member 2 (TMPRSS2) expression in the salivary glands has also been reported.<sup>15</sup>

Saliva has been successfully been validated as a possible bio sample source for detecting COVID-19 while comparing to nasopharyngeal or oropharyngeal swabs by the researchers from RUCDR Infinite Biologics at Rutgers University. According to them, saliva can be utilized as a strong source to extract viral RNA that is approved equal to swab-based collection samples in performance. Saliva testing can also compensate the global shortage of swabs for sampling and increase testing of patients. It will also help in reducing health care professionals to collect samples.<sup>16</sup>

There is high sensitivity and specificity of saliva specimens in detecting respiratory viruses by an automated multiplex Clinical Laboratory Improvement Amendments-waived point-of-care molecular assay while comparing with those of nasopharyngeal aspirate. Also, saliva lessens the time and cost associated with specimen collection.<sup>11</sup> Therefore in settings where screening is required for a large number of individuals, saliva would serve as an easy and noninvasive specimen type. It will also reduce the manpower requirements, waiting time and the results would be accessible much quicker. So it is vital in busy and rushy clinical settings where COVID-19 might be transmitted via saliva among patients without coughing or other respiratory symptoms.<sup>17</sup>

Though the beneficial role of saliva as a quick and non-invasive diagnostic bio sample has been established the pathogenesis, presence of any antibodies to the novel COVID-19 virus or prognosis still needs further probing. In addition to this we can also find the ways to develop targeted drug therapies by involving other receptors or cellular proteases.

### CONFLICT OF INTEREST

None to declare.

### FINANCIAL DISCLOSURE

None to disclose.

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