Editorial

Application of saliva in COVID-19 diagnosis: Challenges and opportunities.

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Sir,

Corona virus disease 2019 (COVID-19) is a life threatening severe global pandemic, caused by severe acute respiratory syndrome novel coronavirus-2 (SARS-CoV-2). It was first transmitted from animal (bats) to human and subsequently resulted in human-to-human transmission.[1]

SARS-Cov-2 virus has viral RNA genome enclosed by a shell with crown like projections having spike proteins at its end. Infectivity, pathogenesis and host range is regulated by receptor recognition mechanism of the virus. Angiotensin converting enzyme-2 (ACE-2) receptors in humans are recognized by both SARS-CoV-2 and SARS-CoV. A spike protein of coronavirus surface facilitates its entry into the host cells. The SARS-CoV spike protein have a receptor binding domain (RBD) which recognizes ACE2 as its receptor. SARS-CoV-2 RBD, ACE2-binding ridge has a more compact conformation as compared to RBD of SARS-CoV. SARS-CoV-2 RBD have higher binding affinity for ACE2 and stability at the two virus-binding hotspots of RBD–ACE2 interface due to mutation in several residues in SARS-CoV-2 RBD. SARS-CoV-2 also uses the TMPRSS2, a serine protease for priming of S protein [1,2]. This may probably underpin increased infectivity of SARS-CoV-2 disease.[Figure 1]

SARS-CoV-2 presents as fever, dry cough, nasal congestion, sore throat, head ache with mild symptoms, may quickly deteriorate into pneumonia, acute respiratory distress syndrome (ARDS), septic shock, heart failure and multi organ dysfunction. Besides elderly, patients with co morbidities are more prone to develop the severe variant of disease with increased fatality. The mean incubation period of SARS-COv-2 is 5.1 days [95% CI: 4.5–5.8 days] but can extend upto 14 days, hence early diagnosis is critical.[1]

Nasopharyngeal specimen (NPS) using RT-PCR (Real time-polymerase chain reaction) makes confirmatory diagnosis.[1] NPS collection requires trained staff and logistics support. Also, it is painful, usually requires multiple attempts and may elicit sneeze reflex leading to accidental aerosol release. Moreover,

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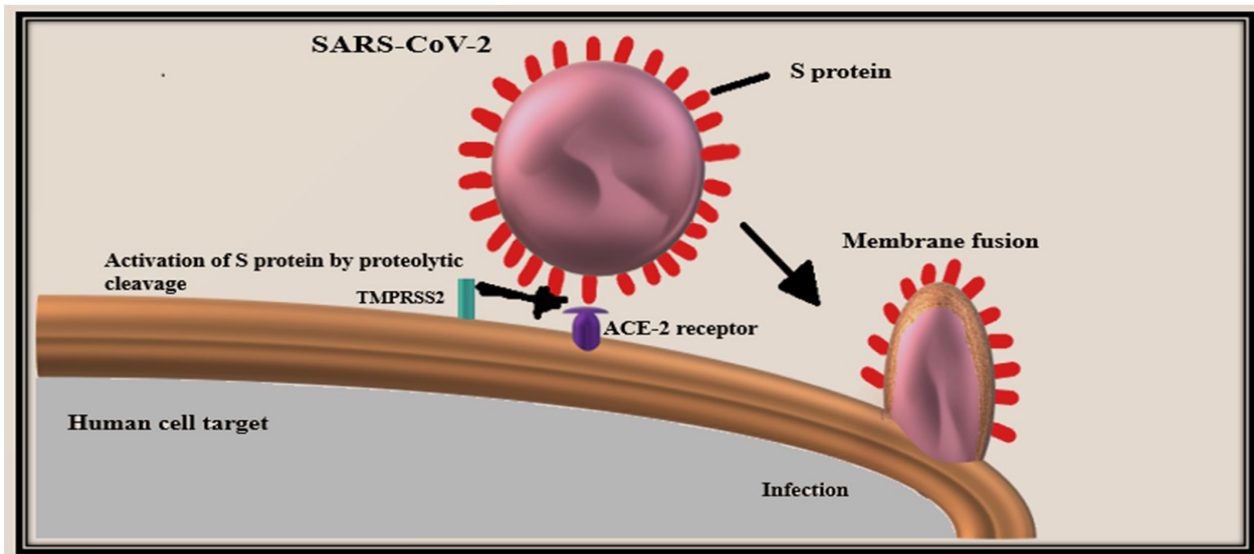
Figure 1: Figure showing the binding of Severe acute respiratory syndrome coronavirus 2 (SARS-cov-2) to angiotensin-converting enzyme 2 (ACE2) receptor after activation of the attachment Spike protein by transmembrane protease serine 2(TMPRSS2) which facilitates entry of virus by endocytosis.

NPS collection in patients with thrombocytopenia is contraindicated as it may cause bleeding.[3]

Saliva is readily available, non-invasive diagnostic fluid . It is pooled by salivary glands and gingival crevicular exudate which is derived from the serum. Moreover, oral cavity communicates with nasopharynx with continuous mixing of nasopharyngeal secretions with saliva leading to a mixed salivary nasopharyngeal milieu.[4]

Notably, saliva has been used in diagnosing coronavirus responsible for severe acute respiratory syndromes (SARS-CoV) and Middle East respiratory syndrome (MERS).[5]

Saliva has SARS-CoV-2 viral pool contributed from oral nasopharyngeal and lower respiratory tract secretions. Also, oral epithelial cells and salivary glands have increased expression of ACE-2 receptors for the virus. Salivary viral load is highest in the first week after clinical manifestation of disease and may extend for more than 3 weeks. Therefore, health care workers who work in close proximity to oral cavity with aerosol and debris generating procedures are increased risk of disease transmission. [6,7]

Interestingly, the sensitivity of saliva test in COVID-19 diagnosis is approximately 91% (95% CI; 80% to 99%) as compared to NPS which is about 98 % (95% CI; 89% to 100%) which is quite similar due to considerable overlap of confidence interval.[7]

Advantages of saliva are easy self collection by the patient at home eliminating chances of viral transmission, decreased risk of hospital infection and reduced health care costs and logistics. Also, Saliva collection is painless, non-invasive and employed in viral load monitoring of patients. Moreover, saliva test may be used as alternative test where NPS is contraindicated or repeat NPS not possible.[7,8]

Nevertheless, saliva test has technical confounding issues like method and time of collection, time lag between specimen collection and RNA isolation and extraction using PCR kits. There is paucity of data required to conclude the sensitivity as well specificity of saliva for diagnosis of COVID-19 infection.[9]

Apart from RT-PCR based technique, serological diagnostic tests employing IgM and IgG antibodies against SARS Cov-2 can be used to diagnose recent as well past infection, as an isolation of anti SARS-CoV antibody in animal models have already been done.[10] This gives impetus for development of saliva based point of care devices for COVID-19 diagnosis. This simple, innovative and non-invasive procedure can easily be emulated at various government hospital set-up where patients load is challenging as an alternative to manage COVID-19 pandemic.[11]

To conclude, saliva can be used as an alternative or adjunct to NPS in COVID -19 diagnoses. However, further robust studies are required to validate its efficacy.

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