Editorial Commentary

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) screening in the general population: specimen collection method is an issue

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has spread globally in communities and hospitals since December 2019. Due to the long latent period and high prevalence, patients with coronavirus disease 2019 (COVID-19) can unknowingly infect other people (1). The accurate and timely identification of SARS-CoV-2-infected individuals is crucial for the initiation of treatment and preventing further transmission for COVID-19. At present, many countries and health organizations are struggling to control the COVID-19 epidemic with various approaches, including isolation of positive or suspected cases, screening in the general population, and close contact tracing (2). The current gold-standard test for detecting SARS-CoV-2 is the real-time reverse transcription-polymerase chain reaction (RT-PCR), which can detect viral load in upper respiratory tract samples. Nasopharyngeal swabs (NP) collected by a healthcare professional using a specialized mini-tip swab are widely used and recommended by the U.S. Food and Drug Administration (FDA) (3). However, this testing method has many drawbacks that limit its clinical application, such as the need for specially trained healthcare workers and discomfort during specimen collection. The World Health Organization (WHO) recommends performing combined oropharyngeal (throat) swabs (OP) and NP simultaneously (OP/NS) (4). The U.S. Centers for Disease Control and Prevention (CDC) recommends upper respiratory specimens, including NP, OP, nasal mid-turbinate, anterior nasal, and nasopharyngeal wash or aspirate, nasal wash or aspirate, or saliva (5). Taken together, the specimen collection method in SARS-CoV-2 testing remains an issue.

The incidence of COVID-19 is low in the mainland of China. To present, the total number of COVID-19 patients is less than 120,000. Many measures have been taken to prevent the spread of SARS-CoV-2 in China. One effective measure is screening COVID-19 in the general population in the area where COVID-19 has emerged. To the best of our knowledge, NP is usually used as a specimen for SARS-CoV-2 screening. Since NP can cause discomfort, a large portion of citizens who received COVID-19 screening wish to receive alternative specimen collection methods, such as OP or saliva. Therefore, it is essential to determine whether the alternative methods can be used for COVID-19 screening.

Two meta-analyses have investigated the effects of different specimen collection methods on the diagnostic accuracy of RT-PCR. Lee and colleagues investigated the diagnosis performance of saliva, OP, nasal swabs (NS), and NP swabs-based testing (6). They searched 1,253 original publications and included 25 studies (25 saliva, 11 NS, 6 OP, and 4 OP/NS) into the meta-analysis. The sensitivities of saliva, OP and NS were 0.88, 0.84 and 0.82, respectively, and combined OP/NS matched the sensitivity of NP (0.97). They concluded that while saliva, OP swab, NS, and OP/NS specimens are promising, NP swabs should be preferred for diagnosing SARS-CoV-2. However, this meta-analysis only analyzed the sensitivities while the specificities of different specimen collection methods were not analyzed. Another meta-analysis (7) included 23 comparative studies. With NP swabs as the gold standard, the authors compared

the diagnostic accuracy of throat swab, saliva and NS. They found that the specificities of these specimen collection methods were near 1.00, while their sensitivities ranged from 0.68 to 0.97. OP was not be recommended because of its low sensitivity (0.68). However, this meta-analysis used NP swabs as the gold standard. If the NP swab was negative, other specimens with positive SARS-CoV-2 RT-PCR testing were categorized as false positives. This study design may overestimate the sensitivity of NP and underestimate the sensitivities of other specimen collection methods.

Although both meta-analyses suggest that NP swabs provide the best diagnostic performance, they only included symptomatic or suspected COVID-19 infected patients. Whether NP is optimal in asymptomatic populations is unknown. For example, in Lee's study, the positive rate of saliva (0.87) is higher than that of NP swabs (0.73) in asymptomatic populations (6), indicating that NP swab is not optimal for asymptomatic individuals. Additionally, one study found that asymptomatic COVID-19 persons may be missed by tests with NP specimens (8). In that study, nine of thirteen asymptomatic COVID-19 patients were collected with NP swabs, and two of them were negative for NP specimens. These thirteen health care workers were all with positive saliva specimens and confirmed by later NP samples (8). This study indicates that the reliability of the specimen collection methods may vary with the stage of the disease.

Since the outbreak of COVID-19, the Chinese government adopted a series of prevention and control measures to screen asymptomatic infected cases in the general population with RT-PCR (9,10). Undoubtedly, the general population is the target population of such a large-scale screening, and the prevalence of COVID-19 in this population is extremely low. The clinical characteristics of the general population and suspected COVID-19 cases are different. Therefore, the conclusions derived from the suspected COVID-19 patients may not be applicable to the general population. If NP swabs are dogmatically deemed to be the optimal specimen collection method, many individuals may be reluctant to receive this uncomfortable specimen collection method. This dilemma may have a negative effect on preventing COVID-19 transmission. In addition, suspected COVID-19 patients may have symptoms of dry cough, sputum, and nasal mucus (11). These symptoms may increase the virus load in the nasopharynx and thus, lead to a higher sensitivity of NP swabs.

Taken together, comparative studies should be carried out to ascertain which specimen collection method is optimal for RT-PCR in asymptomatic people.

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