Oman Medical Journal [2022], Vol. 37, No. 3: e390

Interpretation of Antigen-detection Rapid Diagnostic Tests (Ag-RDTs) Should Take into Account the Pre-test Probability of COVID-19 Infection

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ARTICLE INFO

Article history:

Received: 7 November 2021

Accepted: 15 November 2021

ONLINE:

DOI 10.5001/omj.2022.58

Dear Editor,

Antigen-detection rapid diagnostic tests (Ag-RDTs) are single-use, lateral flow tests that can be performed outside healthcare settings to diagnose COVID-19 infections. These tests offer direct visual results on small portable devices within 15 minutes. Thus, Ag-RDTs offer significant promise in rapidly identifying COVID-19 infection and facilitating isolation and treatment.

When Al-Alawi et al,[1] evaluated four rapid antigen tests, they found moderate sensitivity (64.0% to 69.8%) and high specificity (94.1% to 100%) compared to reverse transcriptase–polymerase chain reaction (RT-PCR). Nevertheless, they recommended that negative results may need repeat testing or RT-PCR to reduce the possibility of false negatives. A similar study by Bruzzone et al,[2] comparing the performance of seven Ag-RDTs against RT-PCR also found a wide range of sensitivity (66.0 to 93.8%), which was maximal at a cycle threshold (Ct) cut-off value of 29. Although the sensitivity appeared dependent on a viral load, there was still significant variability in the diagnostic performance of Ag-RDTs. Subsequently, a systematic review and meta-analysis which included 17 171 suspected COVID-19 patients found a pooled sensitivity and specificity of 68.4% and 99.4%, respectively.[3] When subgroup analyses were performed, sensitivity was better with nasopharyngeal specimens, symptomatic patients, low Ct values, and European or American settings.

In addition to considering RT-PCR to identify false negatives, what else can be done to improve the sensitivity of Ag-RDTs? A novel study by Nikolai et al,[4] showed no differences in yield between anterior nasal or nasal mid-turbinate sampling using Ag-RDTs. Furthermore, when mid-turbinate self-testing was compared with nasopharyngeal sampling by a healthcare professional, the sensitivity and specificity of Ag-RDTs compared to RT-PCR were similar. This implies that nasal self-testing is simple enough that users can reliably carry out sampling themselves.

Thus, if technical sampling is already optimized, clinicians must decide how to interpret these tests. This goes back to the basic principle of pre-test probability. After the acute phase (more than five days), a low viral load may lead to false-negative Ag-RDTs, thus, molecular or antibody tests are more appropriate. When there is a low probability of COVID-19 cases (for example, asymptomatic people in low prevalence settings such as workplaces or schools), Ag-RDTs with a high negative predictive value are useful to rule out infections. In this situation, as there is a high false-positive rate, RT-PCRs may be required to confirm positive results. There is an intermediate risk for healthcare workers or close contacts of confirmed cases compared to the general population. A two-step testing algorithm should be considered using a high sensitivity Ag-RDT for initial screening of asymptomatic COVID-19 infections, followed by confirmatory tests for positive results. The World Health Organization recommends a 97% minimum specificity, which offers a 63–83% positive predictive value. Provided the likelihood of

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positive tests is 5–10%, this is more likely to lead to false-positive than false-negative results.[5]

In conclusion, Ag-RDT is a useful tool for the diagnosis of COVID-19 infections. However, clinicians need to consider the pre-test probability to determine how to interpret results appropriately.

REFERENCES

1. Al-Alawi S, Al-Hinai H, Al-Kindi N, Al-Rashidi M, Al-Kindi H, Al-Shukri I, et al. Evaluation of four rapid antigen tests for detection of SARS-CoV-2 virus. Oman Med J 2021 Sep;36(5):e297.
2. Bruzzone B, De Pace V, Caligiuri P, Ricucci V, Guarona G, Pennati BM, et al. Comparative diagnostic performance of rapid antigen detection tests for COVID-19 in a hospital setting. Int J Infect Dis 2021 Jun;107:215-218.
3. Khandker SS, Nik Hashim NH, Deris ZZ, Shueb RH, Islam MA. Diagnostic accuracy of rapid antigen test kits for detecting SARS-CoV-2: a systematic review and meta-analysis of 17,171 suspected COVID-19 patients. J Clin Med 2021 Aug;10(16):3493.
4. Nikolai O, Rohardt C, Tobian F, Junge A, Corman VM, Jones TC, et al. Anterior nasal versus nasal mid-turbinate sampling for a SARS-CoV-2 antigen-detecting rapid test: does localisation or professional collection matter? Infect Dis (Lond) 2021 Nov-Dec;53(12):947-952.
5. Peeling RW, Olliaro PL, Boeras DI, Fongwen N. Scaling up COVID-19 rapid antigen tests: promises and challenges. Lancet Infect Dis 2021 Sep;21(9):e290-e295.