The utility of rapid FIA antigen test to detect SARS-CoV-2 infection – preliminary experiences of the Hospital for Infectious Diseases in Warsaw

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Since the beginning of the SARS-CoV-2 epidemic, several diagnostic techniques have been developed to detect the infection. Real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay is considered the gold standard in confirming the diagnosis of COVID-19 in clinical settings [1]. However RT-PCR technology is considered time consuming, costly and requires significant resources, both in terms of available laboratory equipment and experienced staff. Therefore, using RT-PCR in epidemiological surveillance or in mass testing is difficult and meeting the necessary number of tests to be performed has been shown to be impossible in practical terms. On the contrary, antigen tests can be used as point-of-care diagnostics with a rapid turnaround time and could play a critical role in implementation of infection prevention and control strategies. The Centres of Disease Control and Prevention (CDC) provides interim guidance to support effective use of antigen tests for different testing situations as they become available on the market and are therefore bought by physicians [2]. The World Health Organisation (WHO) does not provide a specific recommendation on the basis of which, before these tests can be recommended, they must be further validated in given populations and settings [3–5]. In fact there is a lack of reliable research regarding the usefulness of these tests in the laboratory diagnosis of infections caused by SARS-CoV-2 [6]. Therefore, we performed comparative testing for the antigen test available from the Ministry of Health resources to all public health services using RT-PCR test as the gold standard.

PCL COVID-19 Ag Rapid FIA (Ag Rapid FIA) is an *in vitro* diagnostic medical device using sandwich fluorescent immunoassay to qualitatively detect SARS-CoV-2 antigen in human nasopharyngeal and sputum specimens [7]. We have performed analyses of 266 nasopharyngeal samples collected from patients hospitalized in the Hospital for Infectious Diseases in Warsaw. SARS-Cov-2 infection was confirmed in 40 samples by real time RT-PCR (SARS-CoV-2 Genesig Real-Time PCR Assay, Vitassay). Sixteen of these samples were positive in PCL COVID-19 (Ag Rapid FIA) test (Serial no. COV05-2003N405 and COV05-2003N401) and five of 226 SARS-CoV-2 negative samples were positive in Ag Rapid FIA. Basing on these results, sensitivity was calculated as 40% (16 of 40) and specificity as 98% (221 of 226).

In addition, we recalculated sensitivity of Ag Rapid FIA for different RT-PCR cycle threshold (CT) ranges. The CT is defined as the number of cycles required for the fluorescent signal used in the RT-PCR assay to cross the background threshold and is inversely proportional to the amount of target nucleic acid in the sample [8]. Briefly, CT < 29 is strong positive reactions indicative of a large amount of nucleic acid in the sample, CT of 30–37 indicates moderate amounts of target nucleic acid and CT of 38–40 indicates a weak reaction and minimal amounts of nucleic acid.

All positive results obtained in Ag Rapid FIA were for samples with CT of 17-28 and false negative Ag Rapid FIA in CT of 26-39. We observed that sensitivity of Ag Rapid FIA depended on the CT value of RT PCR for SARS-CoV-2 positive samples (Table 1).

It has been noted by laboratory technicians that using two drops of assay buffer was not always sufficient to complete the test with the result stated as "no sample or insufficient sample volume". In the subset of tests, the results were read according to the instructions after 10 min and after a further 10 min, extending the incubation. It did not change the negative results.

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Table 1. Ag Rapid FIA test results stratified by the cycle threshold (CT) value in SARS-CoV-2 RT-PCR

CT value in RT-PCR test	*N*	Positive Ag Rapid FIA	Negative Ag Rapid FIA	Sensitivity of Ag Rapid FIA (%)
≤ 22	20	16	4	80
23–32	62	32	30	52
33–40	79	21	58	27
≤ 40	161	69	92	42
≤ 32	82	48	34	58

In concordance with other studies, we found that point-of-care antigen tests have a lower sensitivity and similar specificity for detecting SARS-CoV-2 compared to RT-PCR tests. A recent literature review found that antigen test sensitivity varied from 0% to 94% across published studies with the average sensitivity of 56.2% (95% CI: 29.5–79.8%) and average specificity of 99.5% (95% CI: 98.1–99.9%) [9]. In our study the overall sensitivity for the tested Ag Rapid FIA test was 40%, thus not acceptable for its routine use for laboratory diagnosis of the SARS-CoV-2 infection. At the same time our results suggest that this test could be utilized in the group of patients with the highest titre of the SARS-CoV-2 virus in the upper respiratory tract, therefore with the higher infectivity [10]. Taking into account its current availability and short time to receive the result it is possible to use this test for immediate identification and isolation of the most infectious patients in specific settings e.g. at emergency departments, schools or nursing home facilities. We advise to interpret a positive Ag Rapid FIA as a potential SARS-CoV-2 infection requiring further confirmation with RT-PCR. On the contrary, a negative Ag Rapid FIA should be interpreted as inconclusive.

Conflict of interest

The authors declare no conflict of interest.

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