Covid-19 pandemic: Evaluation of the SARS-CoV-2 Rapid Antigen Test produced by SD Biosensor, distributed by Roche Diagnostics GmbH, in Norway

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1 Summary

Introduction

Reverse transcription polymerase chain reaction (RT-PCR) is the standard laboratory diagnostic tool for detection of SARS-CoV-2 infection. Under certain clinical circumstances, the World Health Organization recommends the use of less sensitive antigen detecting rapid detections tests (Ag-RDTs), which are cheaper and faster. The Norwegian Organization for Quality Improvement of Laboratory Examinations (Noklus) was commissioned by the Norwegian Directorate of Health to perform a limited verification of the diagnostic performance and user-friendliness of the SARS-CoV-2 Ag-RDT produced by SD Biosensor, distributed by Roche Diagnostics GmbH.

Methods

Persons over the age of 16 approaching a dedicated test center for Covid-19, and with known exposure to a confirmed case of SARS-CoV-2 infection, were invited to participate. Parallel testing with RT-PCR and SD Biosensor Ag-RDT was performed for a total of 382 participants. Information on symptoms (yes/no) and symptom duration was collected. End-users filled in a questionnaire to evaluate user-friendliness.

Results

Out of 382 participants, 28 tested positive for SARS-CoV-2 infection by RT-PCR, giving a prevalence of 7.3%. Using RT-PCR as the reference standard, the Ag-RDT had a sensitivity of 89% and a specificity of 99%. Most of the RT-PCR-positive results had low Ct-values, indicating high viral loads in the RT-PCR-positive participants. User-friendliness was considered satisfactory by end-users.

Conclusion

We performed a limited verification of the diagnostic performance and user-friendliness of the SD Biosensor SARS-CoV-2 Ag-RDT. Building on accumulating evidence from other manufacturer independent evaluations, our results confirmed that the diagnostic performance of SD Biosensor SARS-CoV-2 Ag-RDT was not inferior to that of the Abbot Panbio Ag-RDT, which was thoroughly evaluated in Norway during November 2020. Therefore, the SARS-CoV-2 Ag-RDT produced by SD Biosensor, distributed by Roche Diagnostics GmbH, can be used in the clinical situations where the Norwegian Institute of Public Health recommends the use of Ag-RDTs.

2 Introduction

Reverse transcription polymerase chain reaction (RT-PCR) is the gold standard method used to detect SARS-CoV-2, the virus causing Coronavirus disease 2019 (Covid-19). RT-PCR requires advanced laboratory equipment, trained personnel, and a steady supply of reagents, all potentially vulnerable to shortages during a pandemic. The World Health Organization (WHO) recommends the use of less sensitive, but cheaper and faster, antigen detecting rapid detections tests (Ag-RDTs) under certain clinical circumstances, provided the tests fulfill minimum performance criteria (1). The Norwegian Institute of Public Health publishes updated recommendations for clinical use of Ag-RDTs in Norway (2).

To secure national testing capacity, the Norwegian health authorities purchased several million Ag-RDTs for SARS-CoV-2 in 2020. A comprehensive evaluation of Abbot's Panbio™ Covid-19 Ag-RDT, including more than 4800 participants undergoing testing for SARS-CoV-2 infection, was performed by a broad collaborative group during November 2020 (3). Using RT-PCR as the reference standard, the overall sensitivity of the Abbot's Panbio Ag-RDT was 74% (95% confidence interval (CI) 69-79%), and the specificity was 99.9% (99.7-99.9%). In December 2020, the Norwegian Directorate of Health commissioned the Norwegian Organization for Quality Improvement of Laboratory examinations (Noklus) to perform a limited evaluation of the SARS-CoV-2 Ag-RDT produced by SD Biosensor, distributed by Roche Diagnostics GmbH, the second Ag-RDT purchased by Norwegian health authorities.

Emerging evidence published before (4, 5) and during (6) the current evaluation, indicated the diagnostic accuracy of the SD Biosensor Ag-RDT was not inferior to Abbot's Panbio™ Covid-19 Ag-RDT. Our aim was therefore to perform a limited verification of the SD Biosensor SARS-CoV-2 Ag-RDT to confirm its diagnostic performance under Norwegian conditions, and to investigate its user-friendliness.

3 Methods

Noklus collaborated with a dedicated test center for Covid-19 at the Bergen Accident and Emergency Clinic to perform parallel testing with the Ag-RDT and RT-PCR. Our initial aim was to enroll participants until 50 RT-PCR-positive results were obtained, but earlier termination was also considered acceptable, depending on prevalence of infection and preliminary data analyses. During January 15th-February 12th, 2021, subjects above 16 years of age with known exposure to a confirmed case of SARS-CoV-2 infection were invited to participate. During the study period, there was an outbreak of Covid-19 in the nearby rural Ulvik municipality. The Bergen test center assisted Ulvik with testing, also inviting eligible participants for the verification of the Ag-RDT.

For each participant, a nasopharyngeal sample for RT-PCR was obtained first, followed by a second nasopharyngeal swab obtained through the other nostril, for the Ag-RDT. The Ag-RDT was then performed on site, following the manufacturer's instructions. The comparison method was the routine RT-PCR method for SARS-CoV-2 at the Department of Microbiology, Haukeland University Hospital in Bergen, Norway. This laboratory is accredited according to NS-EN ISO/IEC 15189 (2012). In addition to the Ag-RDT and RT-PCR results, the test center collected information on number of days since exposure, whether the participant had experienced symptoms, and if so, the number of days since symptom onset. In cases where the RT-PCR result was positive, the Cycle threshold (Ct)-value was obtained. Anonymous results were then transferred to Noklus for data analyses.

After completion of the study, the personnel at the test station filled in a questionnaire evaluating user-friendliness of the Ag-RDT. The items included assessment of the operation facilities (e.g.,

preparations of test and sample, application of sample, specimen volume, number of steps, test design, reading of test result, and sources of error) and the information in the manual/quick guide (e.g., pre-analytical procedures, specimen collection, measurement procedure, reading of result, description of sources of error, help for troubleshooting). Each item could be rated as satisfactory, intermediate, or unsatisfactory.

Data analysis was performed using Stata version 16.1 (StataCorp LLC). Data were summarized with descriptive statistics. Sensitivity and specificity for the Ag-RDT with 95 % confidence intervals (CI, using the Agresti-Coull method), as well as positive and negative predictive values, were computed using RT-PCR as the reference standard.

4 Results

After recruiting a total of 382 participants, we performed interim data analyses. We were satisfied the results obtained thus far were sufficient to confirm the SD Biosensor SARS-CoV-2 Ag-RDT diagnostic performance under Norwegian conditions, and recruitment therefore was stopped.

112 participants (29%) reported having had symptoms of Covid-19, and 85 had had symptoms for five days or less (Table 1). 28 participants tested positive for SARS-CoV-2 infection by RT-PCR, giving an overall prevalence of 7.3%. Ct-values were available for 27 PRC-results. Median Ct-value was 21 (range 12-37), and only two Ct-values exceeded 30.

Table 1

	Total, N	RT-PCR negative (%)	RT-PCR positive (%)
Symptoms			
No	268	260 (97.0)	8 (3.0)
Yes	112	92 (82.1)	20 (17.9)
Unknown	2	2 (100)	0
Symptom duration			
≤5 days	85	70 (82.4)	15 (17.6)
>5 days	24	19 (79.2)	5 (20.8)
Unknown	3	3 (100)	0

Of the 354 participants with a negative RT-PCR result, 351 tested negative also by the Ag-RDT, yielding a specificity of 99.2% (95% CI 97.4-99.8%). 25 of the 28 RT-PCR positive participants also tested positive by the Ag-RDT (Table 2), yielding a sensitivity of 89% (70-97%). The Ct-values of the three participants with false negative Ag-RDT results were 12,37 and 37, respectively. The point estimates of sensitivity were higher when restricting analyses to participants with Ct-values below 30, and in RT-PCR-positive participants who reported Covid-19 related symptoms (Table 2).

Table 2

	Ag-RDT neg (n)	Ag-RDT pos (n)	Total (n)	Sensitivity % (95% CI)
RT-PCR positive	3	25	28	89 (72-97)
RT-PCR negative	351	3	354	
Ct <30	1	24	25	96 (79-100)
RT-PCR pos and symptoms	0	20	20	100 (81-100)
RT-PCR pos asymptomatic	3	5	8	63 (30-87)

At the observed prevalence of 7.3%, the positive predictive value of the Ag-RDT was 89% and the negative predictive value was 99%.

Overall, user-friendliness of the operation facilities and the quick guide of the SD Biosensor Ag-RDT were rated as satisfactory by five end-users.

5 Discussion

This verification of the diagnostic performance of the SARS-CoV-2 Ag-RDT produced by SD Biosensor, distributed by Roche Diagnostics GmbH, was performed recruiting 382 participants with known exposure to a confirmed case of SARS-CoV-2 infection. The overall prevalence in this population was 7.3%. Using RT-PCR as the reference standard, the Ag-RDT had a sensitivity of 89% and a specificity of 99%. Most of the RT-PCR-positive results had low Ct-values, indicating high viral loads in the RT-PCR-positive participants. User-friendliness was considered satisfactory by end-users.

Our findings are in line with previous reports about the diagnostic performance of SD Biosensor SARS-CoV-2 Ag-RDT. Independent evaluations at three sites, organized by the global non-profit Foundation of Innovative New Diagnostics (FIND), found overall sensitivity between 76% and 89% when using RT-PCR as the reference standard, and 88%-92% when restricting to RT-PCR-results with Ct-values ≤ 33 (4). Specificity was between 97.6% and 99.7%. A Dutch study reported overall sensitivity of 85% and specificity of 99.6% (5). A Danish study including results from 4,800 individuals, found an overall sensitivity of 70% of the SD Biosensor SARS-CoV-2 Ag-RDT, and 81% for RT-PCR-results with Ct-values ≤ 30 (6). Specificity was 99.5%.

Strengths of our study include the recruitment of consecutive participants in real-life situations, both at an urban test center and in an ongoing outbreak in a rural area. The main limitation is the small numbers. Although we found a relatively high sensitivity of the SD Biosensor SARS-CoV-2 Ag-RDT, small numbers yielded a wide confidence interval, which warrants cautious interpretation. Also, the Ct-values for our RT-PCR positive results were generally low, indicating high viral loads. Thus, we were not able to evaluate the diagnostic performance of the SD Biosensor SARS-CoV-2 Ag-RDT when viral loads are lower.

6 Conclusion

We performed a limited verification of the diagnostic performance and user-friendliness of the SARS-CoV-2 Ag-RDT produced by SD Biosensor, distributed by Roche Diagnostics GmbH. Building on accumulating evidence on its performance from other manufacturer independent evaluations, our results confirmed that the diagnostic performance of SD Biosensor SARS-CoV-2 Ag-RDT was not inferior to that of the Abbot Panbio Ag-RDT, which was thoroughly evaluated in Norway during November 2020. Therefore, the SD Biosensor SARS-CoV-2 Ag-RDT can be used in the clinical situations where the Norwegian Institute of Public Health recommends the use of Ag-RDTs.

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