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Head-to-head validation of six immunoassays for SARS-CoV-2 in hospitalized patients

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ARTICLE INFO

Keywords:
SARS-CoV-2
COVID-19
Serology
Immunoassay
ELISA

ABSTRACT

Background: Detecting SARS-CoV-2 antibodies may help to diagnose COVID-19. Head-to-head validation of different types of immunoassays in well-characterized cohorts of hospitalized patients remains needed.

Methods: We validated three chemiluminescence immunoassays (CLIA) (Liaison, Elecsys, and Abbott) and one single molecule array assay (SIMOA) (Quanterix) for automated analyzers, one rapid immunoassay RIA (Biozek), and one ELISA (Wantai) in parallel in first samples from 126 PCR confirmed COVID-19 hospitalized patients and 158 pre-COVID-19 patients. Specificity of the Biozek was also tested in 106 patients with confirmed parasitic and dengue virus infections. Specificity of the Wantai assay was not tested due to limitations in sample volumes.

Results: Overall sensitivity in first samples was 70.6 % for the Liaison, 71.4 % for the Elecsys, 75.4 % for the Abbott, 70.6 % for the Quanterix, 77.8 % for the Biozek, and 88.9 % for the Wantai assay, respectively. Sensitivity was between 77.4 % (Liaison) and 94.0 % (Wantai) after 10 dpso. No false positive results were observed for the Elecsys and Abbott assays. Specificity was 91.1 % for the Quanterix, 96.2 % for the Liaison, and 98.1 % for the Biozek assay, respectively.

Conclusion: We conclude that low sensitivity of all immunoassays limits their use early after onset of illness in diagnosing COVID-19 in hospitalized patients. After 10 dpso, the Wantai ELISA has a relatively high sensitivity, followed by the point-of-care Biozek RIA that compares favorably with automated analyzer immunoassays.

1. Introduction

SARS-CoV-2 is a novel coronavirus causing the current pandemic of the acute respiratory disease termed COVID-19 [1]. During the acute stage of infection, detection of viral RNA in respiratory specimens by reverse transcriptase polymerase chain reaction (RT-PCR) is the diagnostic method of choice. However, RT-PCR results may be false negative, especially in hospitalized patients who usually present relatively late in the course of infection when viral loads are declining [2–4]. Detecting SARS-CoV-2 antibodies with reliable immunoassays can be of crucial added diagnostic value in these cases [5].

Several SARS-CoV-2 antibody tests are currently commercially available. This study was conducted to validate six different immunoassays for the detection of SARS-CoV-2 antibodies in first samples from PCR confirmed COVID-19 patients and pre-COVID-19 patients.

Abbreviations: RIA, rapid immunoassay; CLIA, chemiluminescence immunoassay; CMIA, chemiluminescence microparticle immunoassay; ECLIA, electrochemiluminescence immunoassay; SIMOA, single molecule array assay.


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https://doi.org/10.1016/j.jcv.2021.104821
Received 7 January 2021; Received in revised form 29 March 2021; Accepted 6 April 2021
Available online 18 April 2021
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available or in development and measure either total antibodies or specific immunoglobulin subclasses binding to the viral nucleocapsid (N) and/or spike (S), including the S1 and S2 subunits and receptor binding domain (RBD), protein. Diagnostic performance of these assays is likely dependent on antigen and technique used and type of antibody subclass detected [6–20].

Earlier studies reported the clinical applicability of different types of immunoassays for diagnosis of COVID-19 when added to regular PCR testing. However, validation studies in hospitalized patients were often hampered by small sample sizes, risk of bias, limited specificity testing and lack of parallel evaluation of different relevant assays [6–20]. In the current study, samples from a well-characterized cohort of hospitalized patients with PCR-Confirmed COVID-19 were used for parallel validation of six assays for detection of SARS-CoV-2 antibodies, including chemiluminescence-, ELISA- or single molecule array-based assays for high-throughput laboratory testing and a lateral flow-based rapid immunoassay (RIA) for point-of-care diagnostics. Specificity was evaluated using a comprehensive set of samples from pre-COVID-19 patients with documented relevant infectious and non-infectious conditions. This head-to-head validation may help to determine specific clinical applications of each immunoassay during the ongoing pandemic.

2. Materials and methods

2.1. Subjects and samples

The sensitivity panel of samples consisted of plasma and serum samples stored at the Amsterdam University Medical Centre (Amsterdam UMC) COVID-19 Biobank. These samples were first samples from patients with PCR-confirmed COVID-19 admitted to the COVID-19 ward or Intensive Care Unit (ICU) of the Amsterdam UMC during the first SARS-CoV-2 wave in the Netherlands in March and April 2020. Patient characteristics (age, sex, immune status, days post symptom onset (dpso), hospitalization location (i.e., COVID-19 ward or ICU) and PCR results were collected from electronic patient charts and the laboratory information management system. Hospitalization location was defined as the location where the patient resided when the first Biobank specimen was obtained. Immunocompromised status was defined as asplenia or splenic dysfunction, presence of a hematologic malignancy, a history of a bone marrow or solid organ transplantation, Human Immunodeficiency Virus (HIV) infection, and/or chronic steroid use (≥7.5 mg prednisone equivalent per day). In addition, nine hospitalized patients with PCR-confirmed COVID-19 were used for parallel validation, because their respective analyzers are widely used globally. Second, a lateral flow-based RIA, the Biozok COVID-19-IgG/IgM Rapid Test (Inzek International Trading BV, Apeldoorn, The Netherlands; N-protein based), was included that could accommodate SARS-CoV-2 diagnostics in areas with no or limited laboratory infrastructure. Last, the ELISA-based Wantai SARS-CoV-2 total antibody assay (Wantai Biological Pharmacy, Beijing, China; S protein RBD-based) was included for favourable performance in earlier studies that deserved further study [14,15,20]. Due to limited volumes only the sensitivity panel was tested on the Wantai ELISA. All immunoassays were performed according to the manufacturers’ instructions. Results in the equivocal range as indicated by the manufacturer (Liaison CLIA and Wantai ELISA) were considered negative. Results of the Biozok RIA were considered positive if either the IgM band, IgG band, or both were reactive.

2.2. Procedures

Upper respiratory tract (i.e., nasopharyngeal and oropharyngeal swabs) and/or lower respiratory tract (i.e., sputum and bronchoalveolar lavage) specimens were obtained as part of routine clinical practice in the COVID-19 work up. Nasopharyngeal and oropharyngeal swabs were collected in E-swab or UTM viral transport medium (COPAN Diagnostics, Murrieta, CA, USA). SARS-CoV-2 RNA was extracted using the MagNA Pure 96 system (Roche, Penzberg, Germany). SARS-CoV-2 PCR targeted at the E-gene was performed according to a previously published protocol [22].

Four immunoassays for automated analyzers were validated, namely the Liaison SARS-CoV-2 S1/S2 IgG chemiluminescence immunoassay (CLIA) on the Liaison XL analyzer (DiaSorin, Saluggia, Italy; S protein S1 and S2 subunit-based), the Elecsys Anti-SARS-CoV-2 total antibody electrochemiluminescence immunoassay (ECLIA) on the Cobas e601 analyzer (Roche Diagnostics, Rotkreuz, Switzerland; N protein-based), the SARS-CoV-2 IgG chemiluminescence microparticle immunoassay (CMIA) on the Architect iSR2000 analyzer (Abbott, Chicago, USA; N protein-based), and a pilot pre-commercial version of a total antibody SARS-CoV-2 single molecule array assay (SIMOA) on the HD-X platform (Quanterix Corp., Lexington, USA; S protein RBD and S1 subunit, and N protein-based). These immunoassays were included in the parallel validation, because their respective analyzers are widely used globally.

Overall sensitivity was calculated with first samples of each COVID-19 patient. Stratified sensitivity was calculated for 0–10 dpso and >10 dpso time intervals of first sample collection, and for hospitalization location (i.e., COVID-19 ward or ICU). Continuous variables were expressed as median and interquartile range (IQR) and categorical variables as absolute numbers with proportions. Differences in median dpso between patients on the COVID-19 ward and ICU were analyzed with a Mann Whitney U test. Positive predictive value (PPV) and negative predictive value (NPV) were calculated with sensitivity and specificity in first samples for 10 % community seroprevalence. P < 0.05 was considered statistically significant. Analyses were performed using GraphPad Prism Version 8 (GraphPad, San Diego, CA, USA) and graphs were created using Adobe Illustrator (Adobe Corp. San Jose, CA, USA).

2.4. Ethics statement

Informed consent was obtained before storage and usage of residual materials from COVID-19 patients in accordance with the Amsterdam UMC COVID-19 Biobank protocol approved by the local institutional review boards. Ethical review was waived for anonymized use of stored diagnostic specimens for specificity testing in accordance with Dutch law.

3. Results

3.1. Patients and samples

A total of 126 patients with PCR-confirmed COVID-19 were included for sensitivity testing. Of these patients, 73 (58 %) were admitted to the COVID-19 ward and 53 (42 %) to the ICU (Table 1). Median dpso was not different between both groups of patients (13 (IQR 8) versus 12 (IQR 6) dpso, respectively (P = 0.49)). Median dpso was 8 (IQR 4) for first samples obtained between 0–10 dpso, and 15 (IQR 6) for first samples obtained after 10 dpso. Specificity was assessed using 158 stored samples, of which 116 were from patients with confirmed bacterial, viral, or fungal infections, and
Table 1
Characteristics of patients with RT-PCR confirmed COVID-19.

|                        | Total (n = 126) | COVID-19 ward (n = 73) | ICU (n = 53) |
|------------------------|----------------|------------------------|-------------|
| Female sex, n (%)      | 30 (29)        | 20 (27)                | 10 (19)     |
| Median age, years (IQR)| 64 (15)        | 65 (15)                | 62 (16)     |
| Immunocompromised, n (%)| 9 (7)          | 6 (8)                  | 3 (6)       |
| First positive RT-PCR  |                |                        |             |
| URT, n (%)             | 76 (60)        | 55 (75)                | 21 (40)     |
| LRT, n (%)             | 50 (40)        | 18 (25)                | 22 (41)     |
| Days post symptom onset>10, n (%) | 42 (33) | 25 (34)                | 17 (32)     |

RT-PCR = reverse transcriptase polymerase chain reaction; URT = upper airway tract; LRT = lower airway tract; NA = not applicable; ICU = intensive care unit. 

42 from dialysis patients or individuals visiting the fertility outpatient clinic. An additional 106 samples from patients with confirmed parasitic and dengue virus infection were tested with the RIA.

3.2. Performance of the immunoassays

Overall sensitivity in first samples was 70.6 % for the Liaison CLIA, 71.4 % for the Elecsys ECLIA, 75.4 % for the Abbott CMIA, 70.6 % for the Quanterix SIMOA, 77.8 % for the Biozek RIA, and 88.9 % for the Wantai ELISA (Fig. 1A; Table 2). Between 0–10 dpso, sensitivity was between 57.1 % (Liaison CLIA) and 78.6 % (Wantai ELISA), which increased to sensitivities between 77.4 % (Liaison CLIA) and 94.0 % (Wantai ELISA) in samples collected after 10 dpso (Fig. 1B and C; Table 2). Sensitivity was higher in ICU patients compared to patients admitted to COVID-19 wards (Table 2). Separate sensitivities for the Biozek RIA IgM versus IgG are given in Supplemental Table 1. Ten patients tested negative in all assays (Supplemental Table 2), of whom three were immunocompromised and for six patients samples were collected before 10 dpso. Of nine patients with high clinical and radiological suspicion, six (66.7 %) tested positive in the Liaison CLIA and seven (77.8 %) in the other immunoassays.

No false positive results were observed for the Abbott CMIA and the Elecsys ECLIA (Table 2). Specificity was 91.1 % for the Quanterix SIMOA, 96.2 % for the Liaison CLIA, and 98.1 % for the Biozek RIA. Wantai ELISA specificity was not tested. Detailed specificity data with all different conditions listed are shown in Supplemental Table 3a. Specificity for the Biozek RIA was 94.3 % in parasitic and dengue virus infection, with four false positive IgM (i.e., specificity 96.2 %) and two false positive IgG results (i.e., specificity 98.1 %), respectively (Supplemental Table 3b).

At 10 % community seroprevalence, PPV was 67.4 % for the Liaison CLIA, 100 % for the Elecsys ECLIA, 100 % for the Abbott CMIA, 47.0 % for the Quanterix SIMOA, 82.0 % for the Biozek RIA (Table 2). NPV was over 95 % for these immunoassays (Table 2).

4. Conclusions

In this validation study, six immunoassays for detection of SARS-CoV-2 antibodies were validated head-to-head in identical sample sets from PCR-Confirmed COVID-19 patients and pre-COVID-19 patients. Sensitivity was limited in specimens obtained between 0–10 dpso for all immunoassays, ranging from 45.2 % to 78.6 % increasing to between 77.4 % and 94.0 % after 10 dpso. Specificity ranged from 91.1 % to 100 %, whereby relatively low specificities were noted for the Liaison CLIA, the pilot version of the Quanterix SIMOA and IgM detection of the Biozek RIA. Importantly, the relatively simple lateral flow-based Biozek RIA showed similar or better overall performance compared to the automated immunoassays evaluated.

The diagnostic performance of the Wantai total antibody ELISA is currently unparalleled by other immunoassays [14,15,20]. Literature shows that IgG antibodies directed against N protein precede those against S protein during the course of infection in hospitalized patients [23,24]. Interestingly, the Wantai ELISA is developed with a double sandwich-, or total antibody bridging design that combines detection of IgM, IgA, and IgG antibodies directed against the S protein RBD. A recent report showed higher sensitivity and specificity of an S protein RBD-targeted total antibody bridging assay compared to its N protein equivalent, also in patients with mild disease [25]. Early detection of IgM and IgA directed against S protein RBD most like determined this difference and may also explain the relatively high performance of the Wantai ELISA. Observed sensitivities for the Abbott CMIA, Elecsys ECLIA, and Biozek RIA were similar to those reported earlier, indicating robust performance in different cohorts, especially at increasing dpso [7–10,15–18,26–28]. Similar to our observations, earlier studies of the Abbott CMIA and Biozek RIA reported detection of SARS-CoV-2 antibodies in up to 90 % of clinically suspected, but PCR-negative patients [17,18]. Overall, these findings support the notion that these immunoassays may be helpful in diagnosing COVID-19 in the absence of PCR confirmation, especially later during the course of infection when viral loads are declining whilst antibodies emerge. As absence of detectable antibodies in early illness does not rule out infection, follow-up samples...
should obviously be collected in case of negative results. Caution is warranted in immunocompromised patients, since our results suggest lower sensitivity in these patients.

Specificities of the Liaison CLIA and Quanterix SIMOA were low compared to the other immunoenzymat assays, but similar to those reported in earlier studies [7,8,28]. In one of these studies, low Liaison CLIA specificity was due to cross-reactivity with two samples from the 2003 SARS-CoV outbreak, which also affected specificity of the Architect MIA and Elecsys ECLIA [7]. The Quanterix SIMOA we evaluated is a pilot version of a total antibody assay targeted at both RBD and S1 gene, EIP Pharma, Esai, Janssen prevention center, Roche, Toyama, and AxonNeurosciences, Biogen, Boehringer, Brainstorm Therapeutics, Celgene, EIP Pharma, Esai, Janssen prevention center, Roche, Toyama, and Vivoryon.

Declarations of Competing Interest

Dr. Teunissen has a collaboration contract with ADx Neurosciences and Quanterix and performed contract research or received grants from AxonNeurosciences, Biogen, Boehringer, Brainstorm Therapeutics, Celgene, EIP Pharma, Esai, Janssen prevention center, Roche, Toyama, and Vivoryon.

Dr. de Jong reports personal fees from Roche, personal fees from Cidara, personal fees from Vertex, personal fees from Janssen, and personal fees from GSK, outside the submitted work.

Dr. de Bree reports grants and other from Gilead Sciences, outside the submitted work.

Acknowledgments

The authors acknowledge all members of the clinical departments and laboratories of Amsterdam UMC that assisted in any way with sample collection and analysis.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jcv.2021.104821.

References

[1] COVID-19: the worst may be yet to come. (Editorial), Lancet 396 (71) (2020)
[2] R. Höppel, V.M. Cormor, W. Guggemos, M. Seilmaier, S. Zange, M.A. Müller, D. Niemeyer, T.C. Jones, P. Vollmar, C. Rothe, M. Hoelzcher, T. Biecker, S. Brünink, J. Schneider, R. Ehmann, K. Zwieglmaier, C. Drosten, C. Wendtner, Virological assessment of hospitalized patients with COVID-19, Nature 581 (2020) 465–469.
[3] Y. Li, L. Yao, J. Li, L. Chen, Y. Song, Z. Cai, C. Yang, Stability issues of RT-PCR testing of SARS-CoV-2 for hospitalized patients clinically diagnosed with COVID-19, J. Med. Virol. 92 (7) (2020) 903–908.
[4] L. Liu, W. Liu, Y. Zheng, X. Jiang, G. Kou, J. Ding, Q. Wang, Q. Huang, Y. Ding, W. Ni, W. Wu, S. Tang, L. Tan, Z. Hu, W. Xu, Y. Zhang, B. Zhang, Z. Tang, X. Zhang, H. Li, Z. Rao, H. Jiang, X. Ren, S. Wang, S. Zheng, A preliminary study on serological assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 238 admitted hospital patients, Microbes Infect. 22 (4) (2020) 206–211.
[5] A. Petherick, Developing antibody tests for SARS-CoV-2, Lancet 395 (2020) 1101–1102.
[6] A. Krüttgen, C.G. Cornelissen, M. Dreher, M. Hornef, M. Imohl, M. Kleinés, Comparison of four new commercial serologic assays for determination of SARS-CoV-2 IgG, J. Clin. Virol. 128 (2020), 104394.
[7] N. Kohmer, S. Westhaus, C. Rühl, S. Ciesek, H.F. Rabenau, Brief clinical evaluation of six high-throughput SARS-CoV-2 IgG antibody assays, J. Clin. Virol. 129 (2020), 104480.

[8] A.J. Jaaskelainen, S. Kuivanen, E. Ekelainen, M.J. Ahava, R. Logino, H. Kallio-Kokko, O. Vapahtila, H. Jarva, S. Kurkela, M. Lappalainen, Performance of six SARS-CoV-2 immunoassays in comparison with microneutralisation, J. Clin. Virol. 129 (2020), 104512.

[9] L. Weidner, S. Gänssfelder, S. Unterweger, L. Weseclidmeyer, C. Drexl, M. Faretz, V. Witt, E. Schistal, P. Schlenke, T.R. Kreil, C. Jungbauer, Quantification of SARS-CoV-2 antibodies with eight commercially available immunoassays, J. Clin. Virol. 129 (2020), 104546.

[10] J.L. Wu, W.P. Tseng, C.H. Lin, T.F. Lee, M.Y. Chuang, C.H. Huang, S.Y. Chen, P. R. Hseuh, S.C. Chen, Four point-of-care lateral flow immunoassays for diagnosis of COVID-19 and for assessing dynamics of antibody responses to SARS-CoV-2, J. Infect. 81 (3) (2020) 435–442. 10.1016/j.jinf.2020.03.040.3047.

[11] M. Lisboa Bastos, G. Tavaziva, S.K. Abidi, J.R. Campbell, L.P. Harazov, J. C. Johnston, Z. Lan, S. Law, E. MacLean, A. Traitman, D. Menzies, A. Benedetti, F. Ahmad Khan, Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis, BMJ 370 (2020) m2516.

[12] J.J. Deeks, J. Dinnes, Y. Takwoingi, A. Ducancelle, F. Lunel-Fabiani, H. Le Guillou-Guillemette, Assessment of SARS-CoV-2 serological tests for the diagnosis of COVID-19 through the evaluation of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study, Lancet Infect. Dis. 20 (5) (2020) 565–574.

[13] P.D. Burbelo, F.X. Riedlo, C. Morishima, S. Rawlings, D. Smith, S. Das, J.R. Strich, D.S. Chertow, R.T. Davey, J.I. Cohen, Sensitivity in detection of antibodies to nucleocapsid and spike proteins of severe acute respiratory syndrome coronavirus 2 in patients with coronavirus disease 2019, J. Infect. Dis. 222 (2) (2020) 206–213.

[14] E.H. Vogelzang, C.F. Loef, N.L.L. Derksen, S. Kruthof, P. Ojeejavvar-de Heer, G. van Mierlo, F. Linty, J.Y. Mok, W. van Esch, S. de Bruin, A.P.J. Vlaz, Amsterdam University Medical Center COVID-19 Biobank Study Group, B. Seppen, M. Leeuw, A.J.G. van Oldenheusen, A.M. Buiting, K.K. Jim, H. Vrielink, F. Swanveld, V. Gadirasar, C.E. van der Schoot, B.J. Bosch, G.J. Wolbink, T. Rispens, Development of a SARS-CoV-2 total antibody assay and the dynamics of antibody response over time in hospitalized and nonhospitalized patients with COVID-19, J. Infect. Dis. 205 (12) (2020) 3491–3499.

[15] A. Bryan, G. Pepper, M.H. Wener, S.L. Fink, C. Morishima, C. Audaibhary, K. Jerome, P.C. Mathias, A.L. Greninger, Performance characteristics of the Abbott architect SARS-CoV-2 IgG assay and seroreversion in Boise, Idaho, J. Clin. Microbiol. 58 (8) (2020) e00941–20.

[16] M.M. Serrano, D.N. Rodríguez, N.T. Palop, R.O. Arenas, M.M. C. Peral, J. Casado, A. Adriano, S. Beese, J. Dretzke, L. Ferrante di Ruffano, I.M. Harris, M.J. Price, D. Emperador, L. Hooft, M.M. Leeflang, A. Van den Bruel, Cochrane COVID-19 Diagnostic Test Accuracy Group, Antibody tests for identification of current and past infection with SARS-CoV-2, Cochrane Database Syst. Rev. 6 (2020), CD013652.

[17] K.K. To, O.T. Tsang, W.S. Leung, A.R. Tam, T.C. Wu, D.C. Lung, C.C. Yip, J.P. Cai, J. Man, T.S. Chik, D.P. Lau, C.Y. Choi, L.L. Chen, W.M. Chan, K.H. Chan, J.D. Ip, A.C.C. Ng, R.W. Poon, C.T. Luo, V.C. Cheng, J.F. Chan, I.F. Hung, Z. Chen, H. Chen, K.Y. Yuen, Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study, Lancet Infect. Dis. 20 (12) (2020) 1390–1400.

[18] L.S. Pfrieger, J.H. Bannasch, T.T. Brehm, S. Pfefferle, A. Hoffmann, D. Nötz, M. van der Meirens, S. Kluge, M. Haddad, S. Pischke, H. Müller, M.M. Addo, A.W. Lobse, J. Schulde Zur Wiesch, S. Peine, M. Aepfelbacher, M. Lütgehetmann, Clinical evaluation of five different automated SARS-CoV-2 serology assays in a cohort of hospitalized COVID-19 patients, J. Clin. Virol. 130 (2020), 104549.

[19] D.A. Korevaar, R.S. Koette, L.P. Smith, J.G. van den Aardwieg, P.J. Bonta, J. Schinkel, R.M. Vigeonno, I.A.H. van den Berk, M.J. Meerbeek, B.A. Lemkes, A. Goorhuis, L.P.M. Beenten, J.T. Ammema, Amsterdam UMC location AMC COVID-19 group, Added value of chest computed tomography in suspected COVID-19: an analysis of 239 patients, Eur. Respir. J. 56 (2) (2020) 2001771, 20.

[20] V.M. Corman, O. Landt, M. Kaiser, R. Molenkamp, A. Meijer, D.K. Chu, T. Bleicker, S. Brunsink, J. Schneider, M.L. Schmidt, D.G. Mulders, B.L. Haagmans, R. van der Veer, S. van den Brink, L. Wijman, G. Goverski, J.L. Romette, J. Ellis, M. Zambon, M. Peiris, H. Goosenn, C. Reusken, M.P. Koopmans, C. Drosten, Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR, Euro Surveill. 25 (3) (2020), 2000045.

[21] F. Ahmad Khan, Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis, BMJ 370 (2020) m2516.

[22] E.H. Criquet, J. Rhode, P. Tillekeratne, O. Moch, D.A. Korevaar, D. Lapa, A. Amendola, F. Vairo, G. Ippolito, M.R. Capobianchi, C. Castilletti, INMICovid-19 laboratory team, Performance evaluation of Abbott ARCHITECT SARS-CoV-2 IgG immunoassay in comparison with indirect immunofluorescence and virus microneutralization test, J. Clin. Virol. 129 (2020), 104539.

[23] National SARS-CoV-2 Serology Assay Evaluation Group, Performance characteristics of five immunoassays for SARS-CoV-2: a head-to-head benchmark comparison, Lancet Infect. Dis. 20 (12) (2020) 1390–1400. S1473-3099(20)30634-4.

[24] C.H. Geurts van Kessel, N.M.A. Okba, Z. Igloi, S. Bogers, C.W.E. Embregts, B.M. Henry, Y.B. Said, A.J. Jobst, N. Kohmer, S. Westhaus, C. Rühl, S. Ciesek, H.F. Rabenau, Brief clinical evaluation of six high-throughput SARS-CoV-2 IgG antibody assays, J. Clin. Virol. 129 (2020), 104480.