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Correlation of Fluorescent Immunoassays Biosensor Antigen with RdRp and Envelope Genes RT-PCR of SARS-CoV-2

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RT-PCR, RdRp, Envelope, Fluorescent immunoassay, Antigen.

ABSTRACT

Reverse transcription polymerase chain reaction (RT-PCR) was the gold standard confirmatory test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which requires special facilities, and other reliable tests. The fluorescent immunoassay (FIA) biosensor antigen detects nucleoprotein SARS-CoV-2 viral in the early phase of acute infection, providing a cut-off index (COI) as a measure of the fluorescent signal. Both RNA dependent RNA polymerase (RdRp) and envelope (E) were specific markers for SARS-CoV-2. This research was a cross-sectional study design. The SD biosensor standard antigen F2400 analyzer was correlated with the target of RT-PCR WizDx™ CrystalMix RdRp and E SARS-CoV-2 genes. Secondary data collection from the FIA biosensor antigen and RT-PCR of the RdRp and E genes in January-July 2021 was carried out in February-March 2022. The correlation test of Fisher exact, contingency coefficient, and Spearman's rho used IBM SPSS Statistics 26 version. 100% Positive predictive RT-PCR was obtained at COI >10. The contingency coefficient of COI with RdRp and E genes were 0.560 and 0.533 (strong); the correlation coefficient with Ct values were -0.410 (moderate) and -0.398 (weak). There was a strong correlation between FIA biosensor antigen COI values with RT-PCR RdRp and E genes, but Ct values had a moderate and weak correlation.

1. Introduction

The SARS-CoV-2 caused the Coronavirus disease 2019 (COVID-19) outbreak. it is transmitted through droplets and the highest risk of transmission is obtained in the first days of illness due to the high concentration of virus in secretions. Every new case must be identified, reported, and analyzed in less than 24 hours [1].

The SARS-CoV-2 genome consists of one-third of viral RNA encoding structural proteins, and two-thirds encoding non-structural proteins (NSP) [2]. Structural proteins consist of S, E, M, and N proteins [3], [4].

NSP has 16 types which are encoded by ORF1a and ORF1b through PP1a and PP1b [5]. All of these proteins play a specific role in viral replication [6], each gene has different sensitivity and specificity, and a combination of 2 or 3 genes can be used for the detection of SARS-CoV-2 by the RT-PCR method [7]. Non-structural genes have encoded proteins for viral RNA replication, interferon response, assembly, secretion of viral particles, induce invagination of the endoplasmic reticulum membrane, induce immunomodulators, and adding caps to the 5' end of RNA [8]. NSP SARS-CoV-2 ORF1ab and RdRp genes are targets of RT-PCR.

WizDx™ CrystalMix RT-PCR is a double-labeled hydrolysis probe targeting the RdRp and E genes of SARS-CoV-2 in one step. They have been identified as highly specific markers for SARS-CoV-2 [9]. RdRp does not show cross-reactivity in vitro with other common respiratory pathogens [10]. Detected E gene target RT-PCR was expressed as "suspect positive" [11]. Nevertheless, it kept reported positive to avoid the risk of transmission. Viral ribonucleic acid (RNA) was measured by the cycle threshold (Ct), the number of replication cycles required to occasion a fluorescent signal.

RT-PCR as the gold standard for the diagnosis of SARS-CoV-2 has limited test results and requires biosafety laboratory level 2 (BSL-2) then another type of inspection is needed that is faster and more reliable. FIA examination is expected to be able to detect SARS-CoV-2 virus nucleoprotein quickly, easily, and more affordable [12], [13]. The standard F2400 biosensor provides a COI value as a measure of the detected fluorescent signal for the presence of viral nucleoproteins. This test is considered to have good specificity for detecting SARS-CoV-2 in the early stages of acute SARS-CoV-2 infection [14].

The numerical value of COI can be grouped into 5 categories: very low (1.00-4.99); low (5.00-9.99); moderate (10.00-14.99); high (15.00-1999); and very high (>20). The numerical value of COI in this patient report creates a different understanding for patients and doctors. WHO regulates the standard for confirming COVID-19 with positive or negative RT-PCR, but patients and doctors require the RT-PCR CT value to be included in laboratory results reports. The author is interested in proving the correlation between the COI antigen of the FIA biosensor and RT-PCR of the SARS-CoV-2 RdRp and E genes.

1.1 Materials and Methods

This research is an analytical observational cross-sectional study design of FIA biosensor antigen F2400 analyzer (SD Biosensor, South Korea), correlated with RT-PCR results (WizDx™ F-150, South Korea). FIA biosensor antigen test can measure the number of nucleoproteins (proteins whose structure is bound to viral RNA in the form of index values. Fluorescent-antigen-antibody bonds formed when an antigen is detected in the specimen cannot be observed visually but must use the F200 analyzer biosensor to read it. The fluorescent intensity read by the biosensor F2400 analyzer is proportional to the concentration of the target molecule in the specimen.

Secondary data collection of FIA biosensor COI antigen values, both RdRp and E genes of RT-PCR for the period January-July 2021, was carried out in February-March 2022. The sample of this study is an affordable population, of official personnel (military, civil serva,nts and their families) serving at the Navy Headquarters Jakarta, who converge the inclusion criteria: positive FIA biosensor antigen, symptomatic and asymptomatic, male and female, age 2-65 years; and exclusion criteria: using the nasal spray. The sampling method uses a consecutive sampling technique, and each specimen converges the inclusion and exclusion criteria will be analyzed.

The sample size was calculated according to the cross-sectional research design for the correlation test, and

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the minimum number of samples for each group needed in this study was 18 samples. The collection and examination of specimens at the Navy Headquarters Jakarta is routine screening before entering the office area as an effort to prevent and control the COVID-19 pandemic in the Navy Headquarters Jakarta.

2. RESULTS

Based on registration records for handling Covid-19 at the Navy Headquarters clinic of Jakarta, 24,583 people have been tested for antigen swabs: 8,860 people using two FIA biosensor antigen units and 15,723 using visual antigens (manual). The FIA biosensor used is the SD Biosensor Standard type F2400 code FA24A02AA0222 and FA24C01AA0665. The selection of positive results for the FIA biosensor antigen was carried out and 542 people were found to be positive for the FIA biosensor antigen, subsequently tracing the results of the RT-PCR for both RdRp and E genes.

Elimination of outlier data is done to avoid bias in the results of the study. Identification of outliers in multivariate data is an important task in statistics because these data can affect the results of statistical tests [15]. There are several different ways to detect outliers. Boxplot visualization is a simple way to detect the presence of outliers in data [16]. Based on the boxplot visualization of this research data, there are 16 outliers: 5 outliers data from FIA biosensor antigen COI value, 4 outliers data from the value of Ct RT-PCR RdRp gene, and 7 outliers data from the value of Ct RT-PCR E gene.

The antigen test conducted on 526 people who were positive for FIA biosensor antigen showed results (Table 1): there were more male adults because tracking was carried out in military office areas where most of the personnel were male and of production age. The isolation place is determined based on the symptoms of the disease, morbidities, and the availability of the isolation room.

Table 1. Characteristics of Research Objects

Category		Frequency	
		Sum	%
Gender	Male	359	68.3
	Female	167	31.7
Age	Children (2-10 Years)		
	Juvenile (11-19 Years Old)	25	4.7
	Adult (20-60 Years Old)	30	5.7
	Elderly (>60 Years)	469	89.2
		2	0.4
Isolation Place			0.2
	Gatot Subroto Hospital	1	26.6
	Mintoharjo Hospital	140	45.1
	Wisma Atlet Hospital	237	16.9
	Nagrak Flats	89	11.2
	Self Isolation	59	

2.1 COI Value of FIA Biosensor Antigen

Antigen tests performed on 526 people who were positive for the FIA biosensor antigen showed: 47.7% (251 people) very high COI; 24% (126 people) high COI; 14.8% (78 people) very low COI; 7.4% (39 people) Low COI; and 6.1% (32 people) moderate COI (Table 2).

Table 2. COI Value of FIA Antigent Biosensor

COI Classification of	N	COI of FIA Biosensor Antigen

FIA Biosensor Antigen		Mean±SD	Median (min-max)
Very low	78	2.56±1.160	2.38 (1.01 – 4.91)
Low	39	7.16±1.326	7.25 (5.05 – 9.78)
Moderate	32	12.72±1.468	12.80 (10.09 – 14.96)
High	126	18.07±1,259	18.49 (15.08 – 19.88)
Very high	251	23.51±0.778	23.78 (20.02 – 25.73)

2.2 RT-PCR of the RdRp Gene

This study shows that the higher the COI of the FIA biosensor antigen, the higher PPV of the FIA biosensor antigen when confirmed by RT-PCR of the RdRp gene. The higher the COI antigen biosensor, the higher the chance of being infected with COVID-19. Positive predictions of 100% were obtained at moderate, high, and very high COI. If the FIA biosensor antigen test results in a COI >10 then the RT-PCR of the RdRp gene is predicted to be positive (Table 3).

Table 3. RT-PCR of the RdRp Gene

COI Classification of FIA Biosensor Antigen	RT-PCR of the RdRp Gene			Ct RT-PCR of the RdRp Gene	
	Pos	Neg	PPV (%)	Rerata±SD	Median (min-max)
Very low	35	43	44.9	33.74±6.812*	37.55 (18.82-43.37)
Low	34	5	87.2	26.29±6.860*	24.69 (15.02-41.50)
Moderate	32	0	100	24.40±3.959	24.70 (18.41-32.22)
High	126	0	100	25.02±4.972	24.93 (15.29-35.93)
Very high	251	0	100	22.99±3.542*	22.81 (15.42-32.67)

PPV: Positive predictive value; * shows the data distribution is not normal

The mean and median Ct RT-PCR of the RdRp gene did not always decrease at higher COI antigen biosensors. The mean Ct RT-PCR of the RdRp gene in the moderate COI group showed lower than the Ct RT-PCR mean of the RdRp gene in the high COI group. The median Ct RT-PCR of the RdRp gene in the low COI and moderate COI groups showed lower than the mean Ct RT-PCR of the RdRp gene in the high COI group. It shows that the Ct RT-PCR value of the RdRp gene cannot always be predicted based on the COI value of the FIA biosensor antigen (Table 3).

2.3 RT-PCR of the E Gene

This research shows that the higher the FIA biosensor COI antigen value, the higher the positive prediction of FIA biosensor antigen confirmed by RT-PCR gene E. The higher the biosensor COI antigen value, the higher the possibility of being infected with COVID-19. A positive prediction of 100% was obtained at moderate COI, high COI, and very high COI, indicating that if the FIA biosensor antigen examination results in COI >10, the RT-PCR for gene E is predicted to be positive (Table 4).

Table 4. RT-PCR of the E Gene

COI Classification of FIA Biosensor Antigen	RT-PCR of the E Gene			Ct RT-PCR of the E Gene	
	Pos	Neg	PPV (%)	Mean±SD	Median (min-max)
Very low	42	36	53.8	32.24±7.717*	36.57 (15.28-41.82)
Low	37	2	94.9	24.54±7.033*	24.17 (15.70-38.44)
Moderate	32	0	100	21.42±4.130*	20.64 (16.25-31.23)
High	126	0	100	23.27±5.401*	22.63 (13.11-35.25)
Very high	251	0	100	20.65±3.324*	20.31 (12.15-29.45)

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PPV: Positive predictive value; * shows the data distribution is not normal

The mean and median Ct RT-PCR gene E did not always decrease at higher COI antigen biosensors. The mean and median Ct RT-PCR of gene E in the medium COI group showed lower than the mean Ct RT-PCR of gene E in the high COI group. It shows that the Ct RT-PCR value of gene E cannot be predicted based on the COI value of the FIA biosensor antigen (Table 4).

2.4 Correlation FIA Biosensor Antigen with RT-PCR

The number of cells with an expected frequency of less than 5 >20%, then the alternative to the Chi-square test with a 5x2 table is the Fisher exact test. Fisher's exact test and contingency coefficient test (Table 5) showed that the COI category FIA biosensor antigen with RT-PCR had a strong significant correlation.

Table 5. Fisher exact and contingency coefficient test results

		RT-PCR	
		RdRp gene	**E gene**
COI Classification of FIA Biosensor Antigen	c	0.560	0.533
	p	0.000*	0.000*

c = contingency coefficient
p = value of significance
* = significance (p≤0,05)

2.5 Correlation COI Value of FIA Biosensor Antigen with CT Value of RT-PCR

Spearman's rho correlation test (Table 6) shows: the COI value of the FIA biosensor antigen with the Ct RT-PCR value of the RdRp gene has a significant correlation (p<0.05) with a correlation coefficient value of -0.410 (medium) and a negative correlation direction (converse). The COI value of the biosensor antigen with the Ct RT-PCR value of gene E had a significant correlation (p<0.05) with a correlation coefficient value of -0.398 (weak) and a negative correlation direction (converse).

Table 6. Spearman's rho Correlation Test Results

		CT RT-PCR	
		RdRp gene	**E gene**
COI Classification of FIA Biosensor Antigen	r	- 0.410	- 0.398
	p	0.000*	0.000*
	n	526	526

r = correlation coefficient
p = value of significance
* = significance (p≤0,05)
n = number of samples

3. DISCUSSION

SARS-CoV-2 is transmitted from person to person mainly through respiratory droplets and airborne transmission [17], the average incubation period is about 5.8 days [18], and the transmission period begins about 1-3 days before the onset of symptoms, then early to decrease the transmission period 7-10 days after the onset of symptoms [19], [20]. Estimates of the risk of gender and age, or comorbidities with the risk of being infected with COVID-19 are not widely known, but in this study, adult males dominated the research object. Previous studies have revealed that there is no significant difference in the distribution of Ct RT-PCR values by sex [7], and mean Ct RT-PCR scores by age group [21]. Other studies have shown that patients who are male, aged 50 years, or have comorbidities are significantly associated with an increased

risk of death with COVID-19 [22].

The COVID-19 antigen test detects proteins in the SARS-CoV-2 virus rapidly, identifying disease during the infection phase, whereas the RT-PCR test detects the genome before the infection phase but also reacts to remnants of the viral genome, even weeks after the virus has died [23]. Previous studies have shown that biosensor antigens can be relied upon to test close patient contacts before symptoms develop until the fifth day after infection with the SARS-CoV-2 virus [24]. The sensitivity of this test increases with an increase in upper respiratory tract viral load, which is known to peak on day 5 after infection [25], [26]. The viral load at any given time after diagnosis or detection tends to be similar between asymptomatic and symptomatic cases [27]. Antigen tests showed a higher positive predictive value (90%) than RT-PCR (70%) when compared with positive results of SARS-CoV-2 virus culture [28].

This research shows that 526 persons were positive for the FIA biosensor antigen: 90.9% positive for COVID-19 when confirmed with RdRp gene RT-PCR and 92.8% positive for COVID-19 when confirmed with E gene RT-PCR. The positive prediction of RT-PCR for gene E was 2.8% higher than RT-PCR for the RdRp gene, the mean and median Ct RT-PCR values for the RdRp gene were higher than the mean and median Ct RT-PCR values for gene E. It is similar to the study Previously by [29] who observed at each stage of infection, the median Ct RT-PCR value of the RdRp gene was higher than the Ct RT-PCR value of the E gene. Another study from [30] showed that asymptomatic and symptomatic SARS-CoV-2 patients had no difference in the mean Ct RT-PCR values of the RdRp and E genes.

The SARS-CoV-2 viral variant poses a challenge in controlling the COVID-19 pandemic [19]. Mutations in the spike (S) glycoprotein increase the ability to bind to the ACE-2 receptor leading to increased disease transmission [31], [32]. The SARS-CoV-2 virus has been noted to have undergone a series of genetic mutations since its emergence, and these genetic mutations can affect the performance of the RT-PCR test [33], [34]. The use of multiple primers can help overcome the problem of false positive results due to other Coronaviruses that may share a specific genome sequence [35], [35]. The Omicron variant is known to cause S-gene target failure (SGTF), rapidly displacing Delta as the dominant variant and driving the fourth wave of infection [36]. Detection of suspected Omicron cases using SGTF has a lower probability of hospitalization compared to non-SGTF infections [37]. Other studies have shown that the Omicron variant causes milder symptoms than the Delta variant of SARS-CoV-2 [38], [39].

The RdRp gene is involved in the process of replicating the RNA genome and encoding several proteins important for building living viruses [40]. RdRp target delay is the difference in the Ct RT-PCR value of the RdRp gene target minus the target gene of not more than 3.5 in the Seegene AllplexTM 2019-nCoV RT-PCR test, the concept is similar to SGTF. RdRp target delay has a sensitivity of 93.6% and specificity of 89.7% in detecting the Delta variant when compared with whole genome sequencing (WGS) [41] and succeeded in assessing the relationship between Delta variance and mortality in the third wave [42].

The value of contingency coefficient (c) ranges from 0–1 and it is categorized as follows: 0.00-0.099 (no closeness); 0.10-0.199 (weak); 0.20-0.299 (medium); and >3 (strong) [43]. The interpretation of the Spearman's rho correlation coefficient is categorized as follows: 0.00-0.199 (very weak); 0.20-0.399 (weak); 0.40-0.599 (medium); 0.60-0.799 (strong); and 0.80-1,000 (very strong) [44], [45].

The increase in the COI value of the biosensor antigen in this study was not always followed by a decrease in the Ct RT-PCR value of the RdRp and E genes in each group. The mean and median Ct RT-PCR values in the moderate COI group were lower than in the high COI group. It shows that an increase in the COI

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value of the biosensor antigen does not always follow in a decrease in the Ct RT-PCR value of the both RdRp and E genes.

Previous studies have shown that FIA biosensor antigens are strongly correlated with the ORF1ab gene (r 0.62), a numerical value of COI >20 indicates a 100% positive result with RT-PCR of SARS-CoV-2 target gene ORF1ab [46], and CLEIA method antigen levels were strongly correlated with viral load (r 0.768) [47]. This study showed that the FIA biosensor antigen had a strong significant correlation with the RT-PCR of the RdRp (c 0.560) and E (c 0.533) genes. positive prediction of RT-PCR for SARS-CoV-2 target genes RdRp and E. The target genes used to affect the results and value of Ct RT-PCR. The correlation of the COI value of the biosensor antigen in each group with the SARS-CoV-2 viral load and other genes requires further research.

Gene E encodes a structural envelope protein, is associated with the assembly and release of the SARS-CoV-2 virus, and has ion channel activity required for pathogenesis [48]. Mutations of the gene encoding protein E affect the structure and activity of the ion channel of the protein E [49], weaker viral infectivity [50], and ultimately apoptosis [51]. [52] concluded that the target gene E was more stable for detecting Coronavirus, while the RdRp gene was mostly targeted to confirm the results. Double-labeled RT-PCR can keep give a positive result if one target fails to amplify [53].

The COI value of the FIA biosensor antigen had a positive prediction when confirmed by RT-PCR of the RdRp and E genes. The higher the COI value of the FIA biosensor antigen, the higher the probability of a positive RT-PCR, but not with the Ct RT-PCR value. A COI value ≥10 indicates a 100% positive prediction, but the Ct RT-PCR value cannot be predicted from the FIA biosensor antigen COI value. The COI value is a numerical representation of the measured fluorescence signal, the value depends on the number of virus particles present in the oropharyngeal/nasopharyngeal swab sample [46]. The more SARS-CoV-2 virus particles, the stronger the fluorescent signal and the higher the COI value [54]. The Ct RT-PCR value is not a determinant of viral load or viral exposure in the body of COVID-19 patients, but in several journals, it is stated that the Ct RT-PCR value is used to predict the risk of transmission of COVID-19 disease [55]. The Ct RT-PCR value of gene E is appropriated to predict the ability of viral infection because Coronavirus cannot be cultured from patient samples with a Ct value ≥34 [56]. WHO has regulated the standard for confirmation of COVID-19 with positive or negative RT-PCR, there is no standardization of Ct RT-PCR values. Ct RT-PCR values should not be used as quantitative values for therapeutic or diagnostic [57]. The FIA biosensor antigen can depend for the examination of COVID-19, especially with COI values ≥10.

Research Limitations

The RT-PCR test of the RdRp and E genes in this research was not performed if the FIA biosensor COI antigen value was <1 and the sample size in each FIA biosensor COI antigen group was not the same (not homogeneous).

4. CONCLUSION

The conclusions of this research are (i) there is a strong correlation (c= 0.560) COI antigen biosensor FIA with RT-PCR SARS-CoV-2 gene RdRp; (ii) There is a strong correlation (c = 0.533) FIA biosensor COI antigen with SARS-CoV-2 gene E RT-PCR (iii) There is a moderate correlation (r = - 0.410) the COI value of the FIA biosensor antigen with the Ct RT-PCR value of the SARS-CoV-2 gene RdRp; (iv) There is a weak correlation (r = - 0.398) the COI value of the FIA biosensor antigen with the Ct RT-PCR value of SARS-CoV-2 gene E.

5. STATISTIC ANALYSIS

Collected data were analyzed with IBM SPSS Statistics for Windows, Version 26.0 Armonk, NY: IBM Corp.

6. RESEARCH QUALITY AND ETHICAL CLEARANCE

This research has received approval from the Research Ethics Committee of Telogorejo Hospital Semarang Number: 1789/TU.710/KEPK/K/2022.

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8. REFERENCES

[1] Alanagreh, L. A., Alzoughool, F., & Atoum, M. (2020). The human coronavirus disease covid-19: Its origin, characteristics, and insights into potential drugs and its mechanisms. Pathogens, 9(5). https://doi.org/10.3390/pathogens9050331.

[2] Kim, D., Lee, J. Y., Yang, J. S., Kim, J. W., Kim, V. N., & Chang, H. (2020). The Architecture of SARS-CoV-2 Transcriptome. Cell, 181(4), 914–921. https://doi.org/10.1016/j.cell.2020.04.011.

[3] Bianchi, M., Benvenuto, D., Giovanetti, M., Angeletti, S., Ciccozzi, M., & Pascarella, S. (2020). Sars-CoV-2 Envelope and Membrane Proteins: Structural Differences Linked to Virus Characteristics? BioMed Research International, Published 2020 May 30. https://doi.org/10.1155/2020/4389089.

[4] Robert, K., & Arkadiusz, D. (2020). Molecular and Serological Test for COVID-19. A Comparative Review of SARS-CoV-2 Coronavirus Laboratory and Point-of-Care Diagnostics. Diagnostics, 10(6). https://doi.org/10.3390/diagnostics10060434.

[5] Minggu, R. B., Rumbajan, J. M., & Turalaki, G. L. A. (2021). Struktur Genom Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Jurnal Biomedik : Jbm, 13(2), 233–240. https://doi.org/10.35790/jbm.13.2.2021.31996.

[6] Dhama, K., Khan, S., Tiwari, R., Sircar, S., Bhat, S., & Malik, Y. S. (2020). Coronavirus Disease 2019–COVID-19. Clinical Microbiology Reviews, 33(4), 1–48. https://doi.org/10.1128/CMR.00028-20.

[7] Abbasi, H., Tabaraei, A., Hosseini, S. M., Khosravi, A., & Nikoo, H. R. (2021). Real-time PCR Ct value in SARS-CoV-2 detection: RdRp or N gene? Infection, 0123456789, 1–4. https://doi.org/10.1007/s15010-021-01674-x.

[8] Pangerapan, M. C., & Kolondam, B. J. (2015). Peran Gen Struktural, Gen Non-Struktural, dan Untranslated Region dalam Perakitan Virus Dengue. Jurnal Biomedik (Jbm), 7(2), 71–78. https://doi.org/10.35790/jbm.7.2.2015.9322.

[9] Corman, V., Landt, O., Kaiser, M., Molenkamp, R., Meijer, A., & Chu, D. K. (2020). Detection of 2019-nCoV by RT-PCR. Euro Surveill, 25(3), 1–8. https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045.

ISSN: 0005-2523
Volume 62, Issue 09, November, 2022

[10] Chan, J. F. W., Yip, C. C. Y., To, K. K. W., Tang, T. H. C., Wong, S. C. Y., & Leung, K. H. (2020). Improved Molecular Diagnosis of COVID-19 by the Novel, Highly Sensitive and Specific COVID-19-RdRp/Hel Real-Time Reverse Transcription-PCR Assay Validated In Vitro and with Clinical Specimens. Journal of Cinical Microbiology, 1–10. https://doi.org/10.1128/JCM .00310-20.

[11] Khoshchehreh, M., Dickler, N. W., Holtom, P., & Wu, S. M. B. (2020). A needle in the haystack? Assessing the significance of envelope (E) gene-negative, nucleocapsid (N2) gene-positive SARS-CoV-2 detection by the Cepheid Xpert Xpress SARS-COV-2 assay. Journal of Clinical Virology, 133(October), 104683. https://doi.org/10.1016/j.jcv.2020.104683.

[12] Chaimayo, C., Kaewnaphan, B., Tanlieng, N., Athipanyasilp, N., Sirijatuphat, R., & Chayakulkeeree, M. (2020). Rapid SARS-CoV-2 antigen detection assay in comparison with real-time RT-PCR assay for laboratory diagnosis of COVID-19 in Thailand. Virology Journal, 17(1), 1–7. https://doi.org/10.1186/s12985-020-01452-5.

[13] Diao, B., Wen, K., Zhang, J., Chen, J., Han, C., & Chen, Y. (2021). Accuracy of a nucleocapsid protein antigen rapid test in the diagnosis of SARS-CoV-2 infection. Clinical Microbiology and Infection, 27(2), 289.e1-289.e4. https://doi.org/10.1016/j.cmi.2020.09.057.

[14] Liotti, F. M., Menchinelli, G., Lalle, E., Palucci, I., Marchetti, S., & Colavita, F. (2021). Performance of a novel diagnostic assay for rapid SARS-CoV-2 antigen detection in nasopharynx samples. Clinical Microbiology and Infection, 27(3), 487–488. https://doi.org/10.1016/j.cmi.2020.09.030.

[15] Tarr, G., Muller, S., & Weber, N. C. (2016). Robust estimation of precision matrices under cellwise contamination. Computational Statistics and Data Analysis, 93, 404–420. https://doi.org/10.1016/j.csda.2015.02.005.

[16] Dai, W., Mrkvicka, T., Sun, Y., & Genton, M. G. (2020). Functional outlier detection and taxonomy by sequential transformations. Computational Statistics and Data Analysis, 149(11901573), 106960. https://doi.org/10.1016/j.csda.2020.106960.

[17] Morawska, L., & Cao, J. (2020). Airborne transmission of SARS-CoV-2: The world should face the reality. Environment International, 139(April), 105730. https://doi.org/10.1016/j.envint.2020.105730.

[18] Griffin, J., Casey, M., Collins, A., Hunt, K., McEvoy, D., & Byrne, A. (2020). Rapid review of available evidence on the serial interval and generation time of COVID-19. BMJ Open, 10(11), 1–9. https://doi.org/10.1136/bmjopen-2020-040263.

[19] He, X., Lau, E. H. Y., Wu, P., Deng, X., Wang, J., & Hao, X. (2020). Temporal dynamics in viral shedding and transmissibility of COVID-19. Nature Medicine, 26(5), 672–675. https://doi.org/10.1038/s41591-020-0869-5.

[20] Arons, M. M., Hatfield, K. M., Reddy, S. C., Kimball, A., James, A., & Jacobs, J. R. (2020). Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. New England Journal of Medicine, 382(22), 2081–2090. https://doi.org/10.1056/nejmoa2008457.

[21] Buchan, B. W., Hoff, J. S., Gmehlin, C. G., Perez, A., Faron, M. L., & Price, L. S. M. (2020).

Distribution of SARS-CoV-2 PCR cycle threshold values provide practical insight into overall and target-Specific sensitivity among symptomatic patients. American Journal of Clinical Pathology, 154(4), 479–485. https://doi.org/10.1093/AJCP/AQAA133.

[22] Biswas, M., Rahaman, S., Biswas, T. K., Haque, Z., & Ibrahim, B. (2021). Association of Sex, Age, and Comorbidities with Mortality in COVID-19 Patients: A Systematic Review and Meta-Analysis. Intervirology, 64(1), 36–47. https://doi.org/10.1159/000512592.

[23] Polechova, J., Johnson, K. D., Payne, P., Crozier, A., Beiglbock, M., & Plevka, P. (2022). SARS-CoV-2 rapid antigen tests provide benefits for epidemic control – observations from Austrian schools. Journal of Clinical Epidemiology, 145, 14–19. https://doi.org/10.1016/j.jclinepi.2022.01.002.

[24] Schuit, E., Veldhuijzen, I. K., Venekamp, R. P., Bijllaardt, W. V. D., Pas, S. D., & Lodder, E. B. (2021). Diagnostic accuracy of rapid antigen tests in asymptomatic and presymptomatic close contacts of individuals with confirmed SARS-CoV-2 infection: Cross sectional study. The BMJ, 374. https://doi.org/10.1136/bmj.n1676.

[25] Kucirka, L. M., Lauer, S. A., Laeyendecker, O., Boon, D., & Lessler, J. (2020). Variation in false-negative rate of reverse transcriptase polymerase chain reaction–based SARS-CoV-2 tests by time since exposure. Annals of Internal Medicine, 173(4), 262–268. https://doi.org/10.7326/M20-1495.

[26] Lauer, S. A., Grantz, K. H., Bi, Q., Jones, F. K., Zheng, Q., & Meredith, H. R. (2020). The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. Annals of Internal Medicine, 172(9), 577–582. https://doi.org/10.7326/M20-0504.

[27] Challenger, J. D., Foo, C. Y., Wu, Y., Yan, A. W. C., Marjaneh, M. M., & Liew, F. (2022). Modelling upper respiratory viral load dynamics of SARS-CoV-2. BMC Medicine, 20(1). https://doi.org/10.1186/s12916-021-02220-0.

[28] Pekosz, A., Parvu, V., Li, M., Andrews, J. C., Manabe, Y. C., & Kodsi, S. (2021). Antigen-Based Testing but Not Real-Time Polymerase Chain Reaction Correlates with Severe Acute Respiratory Syndrome Coronavirus 2 Viral Culture. Clinical Infectious Diseases, 73(9), E2861–E2866. https://doi.org/10.1093/cid/ciaa1706.

[29] Colton, H., Ankcorn, M., Yavuz, M., Tovey, L., Cope, A., & Raza, M. (2021). Improved sensitivity using a dual target, E and RdRp assay for the diagnosis of SARS-CoV-2 infection: Experience at a large NHS Foundation Trust in the UK. Journal of Infection, 82(1), 159–198. https://doi.org/10.1016/j.jinf.2020.05.061.

[30] Zuin, M., Gentili, V., Cervellati, C., Rizzo, R., & Zuliani, G. (2021). Viral load difference between symptomatic and asymptomatic COVID-19 patients: Systematic review and meta-analysis. Infectious Disease Reports, 13(3), 645–653. https://doi.org/10.3390/IDR13030061.

[31] Lupala, C. S., Ye, Y., Chen, H., Su, X. D., & Liu, H. (2022). Mutations on RBD of SARS-CoV-2 Omicron variant result in stronger binding to human ACE2 receptor. Biochemical and Biophysical Research Communications, 590, 34–41. https://doi.org/10.1016/j.bbrc.2021.12.079.

ISSN: 0005-2523
Volume 62, Issue 09, November, 2022

[32] Harvey, W. T., Carabelli, A. M., Jackson, B., Gupta, R. K., Thomson, E. C., & Harrison, E. M. (2021). SARS-CoV-2 variants, spike mutations and immune escape. Nature Reviews Microbiology, 19(7), 409–424. https://doi.org/10.1038/s41579-021-00573-0.

[33] Wang, R., Hozumi, Y., Yin, C., & Wei, G. W. (2020). Mutations on COVID-19 diagnostic targets. Genomics, 112(6), 5204–5213. https://doi.org/10.1016/j.ygeno.2020.09.028.

[34] Nalla, A. K., Casto, A. M., Casto, A. M., Huang, M. L. W., Perchetti, G. A., & Sampoleo, R. (2020). Comparative performance of SARS-CoV-2 detection assays using seven different primer-probe sets and one assay kit. Journal of Clinical Microbiology, 58(6). https://doi.org/10.1128/JCM.00557-20.

[35] Romero, C. A. P., Tonda, A., Maldonado, L. M., MacSharry, J., Szafran, J., & Claassen, E. (2022). SARS-CoV-2 Omicron Variant AI-based Primers. BioRxiv, 13–17. https://doi.org/10.1101/2022.01.21.475953.

[36] Scott, L., Hsiao, N., Moyo, S., Singh, L., Tegally, H., & Dor, G. (2021). Track Omicron's spread with molecular data account for gender bias. Science, 374(6574), 1454–1455. https://doi.org/10.1126/SCIENCE.ABN4543.

[37] Wolter, N., Jassat, W., Walaza, S., Welch, R., Moultrie, H., & Groome, M. (2022). Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study. The Lancet, 399(10323), 437–446. https://doi.org/10.1016/S0140-6736(22)00017-4.

[38] Abdullah, F., Myers, J., Basu, D., Tintinger, G., Ueckermann, V., & Mathebula, M. (2022). Decreased severity of disease during the first global omicron variant covid-19 outbreak in a large hospital in tshwane, south africa. International Journal of Infectious Diseases, 116, 38–42. https://doi.org/10.1016/j.ijid.2021.12.357.

[39] Jassat, W., Karim, S. A., Mudara, C., Welch, R., Ozougwu, L., & Groome, M. (2021). Clinical Severity of COVID-19 Patients Admitted to Hospitals in Gauteng, South Africa During the Omicron-Dominant Fourth Wave. SSRN Electronic Journal. https://doi.org/10.2139/ssrn.3996320.

[40] Poltronieri, P., Sun, B., & Mallardo, M. (2015). RNA Viruses: RNA Roles in Pathogenesis, Coreplication and Viral Load. Current Genomics, 16(5), 327–335. https://doi.org/10.2174/1389202916666150707160613.

[41] Omar, V. Z., Marais, G., Iranzadeh, A., Naidoo, M., Korsman, S., & Maponga, T. (2022). Reduced amplification efficiency of the RNA-dependent-RNA-polymerase target enables tracking of the Delta SARS-CoV-2 variant using routine diagnostic tests. Journal of Virological Methods, 302(January), 114471. https://doi.org/10.1016/j.jviromet.2022.114471.

[42] Hussey, H., Davies, M. A., Heekes, A., Williamson, C., Omar, V. Z., & Hardie, D. (2021). Higher mortality associated with the SARS-CoV-2 Delta variant in the Western Cape, South Africa, using RdRp target delay as a proxy. MedRxiv, 13(July), 2021.10.23.21265412. https://www.medrxiv.org/content/10.1101/2021.10.23.21265412v1%0Ahttps://www.medrxiv.org/content/10.1101/2021.10.23.21265412v1.abstract.

[43] Schubert, P., & Leimstoll, U. (2007). Importance and Use of Information Technology in Small and Medium-Sized Companies. Electronic Markets, 17(1), 38–55. https://doi.org/10.1080/10196780601136799.

[44] Napitupulu, D., Rahim, R., Abdullah, D., Setiawan, M. I., Abdillah, L. A., & Ahmar, A. S. (2018). Analysis of Student Satisfaction Toward Quality of Service Facility. Journal of Physics: Conference Series, 954(1). https://doi.org/10.1088/1742-6596/954/1/012019.

[45] Prion, S., & Haerling, K. (2014). Making sense of methods and measurement: Spearman-Rho ranked-ordered coe_cient. Clinical Simulation in Nursing, 10(10), 535–536. https://doi.org/10.1016/j.ecns.2014.07.005.

[46] Colavita, F., Vairo, F., Meschi, S., Valli, M. B., Lalle, E., & Castilletti, C. (2021). Covid-19 rapid antigen test as screening strategy at points of entry: Experience in lazio region, central italy, august–october 2020. Biomolecules, 11(3), 1–8. https://doi.org/10.3390/biom11030425.

[47] Hirotsu, Y., Maejima, M., Shibusawa, M., Nagakubo, Y., Hosaka, K., & Amemiya, K. (2020). Comparison of automated SARS-CoV-2 antigen test for COVID-19 infection with quantitative RT-PCR using 313 nasopharyngeal swabs, including from seven serially followed patients. International Journal of Infectious Diseases, 99, 397–402. https://doi.org/10.1016/j.ijid.2020.08.029.

[48] Cao, Y., Yang, R., Lee, I., Zhang, W., Sun, J., & Wang, W. (2021). Characterization of the SARS-CoV-2 E Protein: Sequence, Structure, Viroporin, and Inhibitors. Protein Science, 30(6), 1114–1130. https://doi.org/10.1002/pro.4075.

[49] Zhu, Y., Alvarez, F., Wolff, N., Mechaly, A., Brule, S., & Neitthoffer, B. (2022). Interactions of Severe Acute Respiratory Syndrome Coronavirus 2 Protein E With Cell Junctions and Polarity PSD-95/Dlg/ZO-1-Containing Proteins. Frontiers in Microbiology, 13(February), 1–14. https://doi.org/10.3389/fmicb.2022.829094.

[50] Hassan, S. S., Choudhury, P. P., & Roy, B. (2020). Molecular phylogeny and missense mutations at envelope proteins across coronaviruses. Genomics, 112(6), 4993–5004. https://doi.org/10.1016/j.ygeno.2020.09.014.

[51] Boson, B., Legros, V., Zhou, B., Siret, E., Mathieu, C., & Cosset, F. L. (2021). The SARS-CoV-2 envelope and membrane proteins modulate maturation and retention of the spike protein, allowing assembly of virus-like particles. Journal of Biological Chemistry, 296(14), 100111. https://doi.org/10.1074/jbc.RA120.016175.

[52] Li, D., Zhang, J., & Li, J. (2020). Primer design for quantitative real-time PCR for the emerging Coronavirus SARS-CoV-2. Theranostics, 10(16), 7150–7162. https://doi.org/10.7150/thno.47649.

[53] Tahan, S., Parikh, B. A., Droit, L., Wallace, M. A., Burnham, C. A. D., & Wang, D. (2021). SARS-CoV-2 E Gene Variant Alters Analytical Sensitivity. Journal of Cinical Microbiology, 59(7). https://doi.org/10.1128/JCM.00075-21.

[54] Kiro, V., Gupta, A., Singh, P., Sharad, N., Khurana, S., & Prakash, S. (2021). Evaluation of COVID-19 antigen fluorescence immunoassay test for rapid detection of SARS-CoV-2. Journal of Global

ISSN: 0005-2523
Volume 62, Issue 09, November, 2022

Infectious Diseases, 13(2), 91. https://doi.org/10.4103/jgid.jgid_316_20.

[55] Kashyap, B., Goyal, N., & Prakash, A. (2020). COVID diagnostics: Do we have sufficient armamentarium for the present and the unforeseen? Indian Journal of Medical Specialities, 11(3), 117. https://doi.org/10.4103/injms.injms_92_20.

[56] Scola, B., Bideau, M., Andreani, J., Hoang, V. T., Grimaldier, C., & Colson, P. (2020). Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. European Journal of Clinical Microbiology and Infectious Diseases, 39(6), 1059–1061. https://doi.org/10.1007/s10096-020-03913-9.

[57] Markewitz, R., Torge, A., Wandinger, K. P., Pauli, D., Dargvainiene, J., & Franke, A. (2021). Analysis of SARS-CoV-2 reverse transcription-quantitative polymerase chain reaction cycle threshold values vis-à-vis anti-SARS-CoV-2 antibodies from a high incidence region. International Journal of Infectious Diseases, 110, 114–122. https://doi.org/10.1016/j.ijid.2021.07.014.

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