Cross-sectional Study

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Comparison of SARS-CoV-2 virus detection using the Xpert Xpress rapid molecular test on Abbott M2000 Real-Time System: a cross-sectional study

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Introduction: Emergency use of molecular rapid test kits approved by the Food and Drug Administration (FDA) includes the Xpert Xpress SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) kit. The rapid molecular test is one of the examinations using the reverse transcription-polymerase chain reaction (RT-PCR) method. Compared to conventional PCR, the examination time is faster, so it is suitable for diagnostic purposes.

Objectives: Determining the diagnostic capabilities of the Xpert Xpress SARS-CoV-2 rapid molecular test in detecting the SARS-CoV-2 virus in the Indonesian population.

Methods: A cross-sectional study was conducted with consecutive sampling, in which participants were diagnosed with coronavirus disease 2019 (COVID-19) infection using the RT-PCR Abbott M2000 SARS-CoV-2 System. A molecular rapid test examination was carried out using the Xpert Xpress SARS-CoV-2 kit. Assessing the correlation between the cycle threshold (CT) value of Xpert Xpress SARS-CoV-2 and the Abbott M2000 SARS-CoV-2 System using the Pearson and Spearmen test with $P < 0.05$.

Results: Molecular rapid test using Xpert Xpress has a compatibility of 100% with RT-PCR using Abbott M2000 SARS-CoV-2 and a sensitivity and specificity value of 100%. The Xpert Xpress SARS-CoV-2 CT value had a significant correlation with the Abbott M2000 SARS-CoV-2 System CT value, with moderate correlation strength for the CT protein E value ($r = 0.444$; $P = 0.007$) and robust correlation for CT value of protein N2 ($r = 0.829$; $P < 0.001$). The negative predictive and positive predictive values were 100% each.

Conclusion: The Xpert Xpress SARS-CoV-2 molecular rapid test has a sensitivity and specificity of 100% and can be recommended for diagnosing COVID-19.

Keywords: COVID-19, infectious disease, rapid molecular test, RT-PCR

Introduction

The coronavirus disease 2019 (COVID-19) has become a global health problem since being declared a pandemic by the World Health Organization (WHO) in early 2020[1]. Based on clinical symptoms and laboratory test results, the severity of COVID-19 patients is classified into mild, moderate, severe, and critical. Around 81% experience mild-moderate symptoms, 14% experience severe symptoms, and 5% experience critical symptoms[2]. Epidemiological studies in East Java, Indonesia, show that based on age group in the adult population, the highest prevalence of IgG SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is found in the age group 40–49 years, and the lowest prevalence is found in the age group 20–29 years[3].

The COVID-19 pandemic has impacted laboratories worldwide since its inception, particularly in the pre-analytical, analytical, and post-analytical phases. In most conditions, the primary examination method for diagnosing COVID-19 is the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) method. Various diagnostic tests have been developed with different SARS-CoV-2 gene targets, including N, E, RdRp, and ORD[4,5].

Various studies related to diagnostic tests for COVID-19 are still being widely researched. A study proved the potential for cross-reactivity between COVID-19 and dengue virus antibodies.

HIGHLIGHTS

- Reverse transcription-polymerase chain reaction (RT-PCR) and Xpert Xpress can be used for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) identification.
- Xpert Xpress is sensitive and specific for SARS-CoV-2 identification.
- Molecular rapid test Xpert Xpress is effective in SARS-CoV-2 identification.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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A rapid diagnostic test with high sensitivity and specificity is needed to distinguish SARS-CoV-2 from other infectious diseases[6]. Emergency use authorization of the Xpert Xpress SARS-CoV-2 inspection tool itself has been approved by the United States (US) Food and Drug Administration (FDA)[7]. The Xpert Xpress SARS-CoV-2 diagnostic tool is a commercially available molecular test that detects the envelope (E) and nucleocapsid (N2) genes of SARS-CoV-2 as specific targets. The Xpert Xpress SARS-CoV-2 diagnostic tool integrates specimen processing, nucleic acid extraction, ribonucleic acid (RNA) amplification using the RT-PCR method, and amplicon detection using a single cartridge. Detection of the SARS-CoV-2 gene with Xpert Xpress requires a relatively fast time, around 45 min[8]. There are only a few studies in Indonesia examining the suitability of the testing of the SARS-CoV-2 molecular rapid test with the current Abbott M2000 SARS-CoV-2 COVID-19 test, namely the RT-PCR examination. This study aimed to examine the suitability of the results of the Xpert Xpress rapid molecular test and RT-PCR examination using the Abbott M2000 SARS-CoV-2.

Methods

This study was a cross-sectional design diagnostic test conducted at a tertiary hospital in Indonesia from October 2020 to July 2021. The population of this study were patients with suspected COVID-19 infection who came to the polyclinic and were inpatients with nasopharyngeal swabs examined. Sixty-one participants were subjected to nasopharyngeal swabs collected in viral transport media (VTM) tubes before being examined using the Abbott M 2000 Real-Time System. Samples were then stored and frozen at – 80°C, and then thawed to be examined with the Xpert Xpress SARS-CoV-2 cartridge kit using the system GeneXpert[9,10]. Sampling was carried out with consecutive sampling. The study report was based on Strengthening the Reporting of Cohort, Cross-sectional and Case-control Studies in Surgery (STROCSS) 2021 guidelines[11].

Molecular rapid test examination used the Xpert Xpress SARS-CoV-2 cartridge, a rapid, real-time RT-PCR examination aiming to detect SARS-CoV-2 nucleic acid in nasopharyngeal swab specimens and/or nasal aspiration/rinse specimens that are collected from patients with suspected/possible COVID-19 with symptoms such as cough, fever, shortness of breath, weakness, malaise, respiratory distress, muscle pain, sore throat, and loss of taste and/or smell[12]. The sample was inserted into the Xpert Xpress SARS-CoV-2 cartridge, which already had primers and probes and internal controls (sample processing control and probe check control) used in RT-PCR for qualitative in-vitro detection of SARS-CoV-2 RNA in specimen's nasopharyngeal swab. The process of isolating the genetic material, mixing reagents, amplification, and detection happened automatically in the cartridge using the GeneXpert system. A positive result was obtained if the GeneXpert system passed the probe check and the N2 and E gene targets were detected. A hypothetical result was when the E gene target was detected, and a negative result was when no probe signal was detected. The CT value was detected if the accumulated fluorescent signal detected was less than or equal to 45 for each gene target. The duration of the examination using the Xpert Xpress SARS-CoV-2 cartridge was 45 min. The Abbott M2000 SARS-CoV-2 examination, which became the reference standard in this study, was the RT-PCR examination using the Abbott M2000 SARS-CoV-2 Real-Time System. Sample extraction was performed automatically using the Abbott sample preparation system magnetic microparticle-based protocol. The PCR stages, namely denaturation, annealing, and extension, were carried out at 96, 55–65, and 72°C. The target genes detected were the (RNA dependent RNA polymerase) RdRp and N genes with a cut-off value of cycle threshold (CT) 31.5, and the inspection process took up to 7 h.

Data analysis used SPSS tool version 22 (IBM Corp., Armonk, New York, USA). The diagnostic value of the TCM Xpert Xpress examination was evaluated by determining the diagnostic sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy using a 2×2 table compared to the results of the Abbott M2000 SARS-CoV-2 System RT-PCR examination as Abbott M2000 SARS-CoV-2. Correlation analysis of the CT value between Xpert Xpress and Abbott M2000 System was performed using the Pearson and Spearman correlation test. A P value less than 0.05 was considered statistically significant.

Results

Characteristics of the participants

The average age of the participants was 43.17 ± 12.42 years with a median of 39.00 (38.96–47.37) years (COVID-19 group) and 37.72 ± 15.73 years with a median of 32 (31.22–44.22) years (non-COVID-19 group; $z = 1.566$; $P = 0.117$). Most participants were male, in the COVID-19 group of 52.8% and the non-COVID-19 group of 52.0% ($P = 0.952$). Most of the participants experienced shortness of breath (55.6%), and most had CT values between 20 and less than 25% (47.2%; Table 1). The average value of participant's CT was 20.05 ± 6.02%, with a median value of 20.49 (18.01–22.09)%.

Comparison of Xpert Xpress and Abbott M 2000 System RT-PCR test results

A comparison of the CT values from the Xpert Xpress examination (protein E and protein N2) with the Abbott M2000 SARS-CoV-2 examination in 36 participants with positive

Table 1

Characteristics of the participants

Characteristic	COVID-19	Non-COVID-19
Gender		
Male	19 (52.8)	13 (52.0)
Female	17 (47.2)	12 (48.0)
Signs		
Breathlessness	20 (55.6)	
Fever	14 (14.9)	
Cough	17 (47.2)	
Weakness	4 (11.1)	
No signs	9 (25.0)	
Cycle threshold		
< 15%	6 (16.7)	
15 to <20%	9 (25.0)	
20 to <25%	17 (47.2)	
25 to <30%	3 (8.3)	
≥ 30%	1 (2.8)	

COVID-19, coronavirus disease 2019.

Table 2

Comparison between Xpert Xpress and Abbott M2000 System RT-PCR in detecting SARS-CoV-2 in the COVID-19-positive population

Participant	Xpert Xpress		
	E	N2	Abbott M2000 SARS-CoV-2 System
01	29.0	31.8	20.16
02	23.9	26.4	22.14
03	29.9	32.9	21.17
04	25.9	28.5	18.23
05	26.9	29.8	18.33
06	32.8	35.9	23.36
07	28.7	31.7	23.88
08	35.4	38.4	24.23
09	26.8	28.3	17.84
10	29.9	32.5	18.77
11	20.4	22.7	10.8
12	29.1	32.6	10.5
13	36.1	39.3	22.65
14	0.0	40.9	18.61
15	16.6	19.2	6.07
16	28.7	32.1	18.95
17	0.0	39.9	25.09
18	32.1	34.8	23.62
19	32.5	36.7	24.4
20	18.5	20.3	7.31
21	0.0	43.0	27.42
22	0.0	42.8	27.89
23	27.5	30.2	15.65
24	29.9	33.1	20.54
25	42.9	41.1	24.34
26	27.2	29.5	16.73
27	24.9	27.1	13.87
28	37.9	39.4	23.41
29	30.7	32.7	20.45
30	30.0	32.3	20.2
31	20.0	22.4	10.81
32	37.2	39.5	26.53
33	34.3	38.3	23.5
34	35.2	36.5	23.24
35	36.4	38.4	35.1
36	26.2	28.2	16.11

Note: Correlation of CT GeneXpert values with Abbott M2000 SARS-CoV-2 System results in Gen E of $r = 0.444$ with $P = 0.007$ and Gen N2 of $r = 0.829$ with $P < 0.001$.

COVID-19, coronavirus disease 2019; RT-PCR, reverse transcription-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 3

GeneXpert diagnostic performance and statistical analysis compared to Abbott M2000 SARS-CoV-2 in detecting SARS-CoV-2 RNA

	COVID-19	
GeneXpert	Positive	Negative
Positive	36	0
Negative	0	25
Sensitivity	36÷(36 + 0) = 100%	
Specificity	25÷(25 + 0) = 100%	
Positive predictive value	36÷(36 + 0) = 100%	
Negative predictive value	25÷(25 + 0) = 100%	

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

COVID-19 is shown in Table 2. Based on the analysis, a significant correlation was found between the CT Xpert Xpress values and Abbott M2000 SARS-CoV-2, where the CT Xpert Xpress value in detecting E and N2 proteins was found to have a moderate ($r = 0.444$; $P = 0.007$) and very strong ($r = 0.829$; $P < 0.001$) correlation with CT values of Abbott M2000 SARS-CoV-2. The Xpert® Xpress assay has 100% compatibility with Abbott M2000 SARS-CoV-2 in this study, with a sensitivity, specificity, positive predictive value and negative predictive value of 100%(Table 3).

Discussion

This prospective study with a cross-sectional design aims to assess the suitability of the GeneXpert rapid molecular test results with RT-PCR in diagnosing SARS-CoV-2 infection. Of the 61 subjects included in this study, 35 subjects (59%) were diagnosed with COVID-19 based on the results of the RT-PCR examination. The GeneXpert TCM assay targets genes in the SARS-CoV-2 genome, specifically nucleocapsid 2 (N2) and envelope proteins. The N1 and N2 targets in the N gene are recommended by the Centers for Disease Control and Prevention (CDC). In contrast, WHO recommends initial screening with the E gene target and confirmation of the RdRp enzyme examination[4,13].

The ideal performance of the SARS-CoV-2 detection test is determined based on its accuracy and examination time. Regarding the impact of the widespread use of a diagnostic tool in society, accurate results from testing for SARS-CoV-2 are more critical than fast testing times. False-negative results can result in serious problems, especially in elderly patients. False-positive results can also have a negative impact, for example, the patient must undergo an unnecessary period of self-isolation[14].

The findings in this study are similar to those of a previous study conducted in eight hospital laboratories in Oman. The study showed that the Xpert Xpress SARS-CoV-2 assay has a sensitivity and specificity of 100% in detecting SARS-CoV-2 infection[15]. The results obtained by this study also comply with previous meta-analysis study, which consisted of eight studies examining the diagnostic value of Xpert Xpress, where the combined sensitivity and specificity (pooled sensitivity and pooled specificity) were obtained, respectively, at 0.99 (95% CI 0.97–0.99) and 0.97 (95% CI 0.95–0.98). The findings in this study indicate that Xpert Xpress meets the requirements of a fast and straightforward SARS-CoV-2 detection test. The combined negative likelihood ratio for Xpert Xpress was 0.01, indicating a 1% probability that a patient infected with SARS-CoV-2 will have a negative Xpert Xpress test result, which is low enough to exclude SARS-CoV-2 infection in the clinical setting[16].

Regarding the type of sample used, WHO recommends a specimen taken from the nasopharynx to diagnose COVID-19. Several previous studies have shown that other samples, such as samples from the posterior oropharynx, sputum, tracheal aspirate, bronchoalveolar washings, and others, still have a significant diagnostic value. Another meta-analysis study showed that the Xpert Xpress test still has excellent diagnostic capabilities in detecting SARS-CoV-2 in non-respiratory samples, such as feces. These results indicate that Xpert Xpress can detect samples from various sources and types[17]. Another meta-analysis study also compared the diagnostic performance of Xpert Xpress with another COVID-19 rapid molecular test, namely ID NOW from Abbott M2000 SARS-CoV-2 System. The study showed that

Xpert Xpress had better performance for screening purposes than ID NOW with a higher sensitivity of Xpert Xpress (99% vs. 77%)[16,18].

The findings of this study and previous studies show that the performance of Xpert Xpress in detecting SARS-CoV-2 is unaffected by the target gene. A study showed that some primers were more sensitive to detect protein N2 or protein E[19]. Examinations that target two different gene targets can increase the sensitivity of the assay tool and prevent the risk of decreasing the sensitivity of an assay due to polymorphic genomic mutations[20].

This article serves as the first study conducted in Indonesia to examine the diagnostic performance of Xpert Xpress in detecting SARS-CoV-2. Nevertheless, several limitations need to be considered when interpreting the results of this study, including the prevalence of COVID-19 in this study, which was much higher than the prevalence of COVID-19 in the population (55.6%), where the prevalence of the disease also affects the diagnostic performance of a patient: examination tools, precisely the PPV and NPV.

The limitation of this study includes the relatively few number of samples from the participants. The performance of this assay with direct nasal swabs requires further evaluation in subsequent studies.

Conclusions

The Xpert Xpress SARS-CoV-2 molecular rapid test examination has excellent diagnostic performance and compatibility with conventional RT-PCR assays. Due to its excellent sensitivity and specificity and faster examination time, this examination can be considered for screening and diagnosing COVID-19.

Ethical approval

We have conducted an ethical approval based on the Declaration of Helsinki with registration study at the Health Research Ethics Committee in Dr Soetomo General Academic Hospital, Surabaya, Indonesia.

Consent

All participants are required to fill out an informed consent.

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We got a grant from Airlangga University, Surabaya, Indonesia.

Author contribution

All authors contributed toward data analysis, drafting and revising the paper, and gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Conflicts of interest disclosure

All authors declare that there are no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: Health Research Ethics Committee in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
2. Unique identifying number or registration ID: 0134/KEPK/IV/2020.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): not applicable.

Guarantor

Aryati is the person in charge of the publication of our manuscript.

Data availability statement

Datasets generated during and/or analyzed during the current study are available upon reasonable request.

Provenance and peer review

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