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Oxygen Saturation Diagnostic Accuracy Against COVID-19 in Rural Areas of Indonesia

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Abstract

As a country with a high proportion of rural areas, Indonesia continues to struggle with a rapid and accurate diagnosis of COVID-19, necessitating the development of a diagnostic tool or parameter that is less expensive, easier to obtain, and produces rapid results. This retrospective study aimed to explore the diagnostic accuracy of oxygen saturation in detecting COVID-19 in rural areas of Indonesia. Data were collected consecutively from medical records of adult patient (30–90 years old) suspected of having COVID-19 based on the WHO criteria and underwent RT-PCR swab test in three (3) hospitals in one of the regions of Indonesia during the timeframe of May 1, 2020 to September 31, 2021. Analysis was conducted using the cross-table analysis with sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve (AUC) as the variables with their respective confidence interval. Results indicated that 548 of 700 patients included in the analysis were confirmed positive for COVID-19 based on the RT-PCR test results. The sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve (AUC) value of oxygen saturation for detecting COVID-19 were 33% (CI 95% 29–37%), 78% (CI 95% 72–85%), 84% (CI 95% 80–89%), 24% (CI 95% 21–28%), and 56% (CI 95% 51–61%), respectively. Thus, the oxygen saturation level alone does not have adequate diagnostic accuracy for the diagnosis of COVID-19 and, therefore, is not recommended to be used for diagnosing COVID-19.

Keywords: COVID-19, Indonesia, oxygen saturation

Introduction

China reported a case of pneumonia caused by infection with a novel coronavirus on December 31, 2019. The *World Health Organization* (WHO) named the new virus as a *Severe Acute Respiratory Syndrome Coronavirus 2* (SARS-CoV2) and the disease *Coronavirus Disease* 2019 (COVID-19) on February 11, 2020. WHO declared COVID-19 as a pandemic on March 11, 2020.[1] WHO reported 228,807,361 confirmed cases of COVID-19 worldwide until the end of September 2021, with a death toll of 4,697,099 cases, and this number was still growing at the time this research was conducted.[2] In addition to the increase in mortality and morbidity, the COVID-19 pandemic has significantly impacted almost every country's public health and social aspects.[3]

Until now, WHO still recommends the use of molecular detection methods/Nucleid Acid Amplification Test (NAAT) such as the Real Time Polymerase Chain Reaction (RT-PCR) examination or the SARS-CoV2 Rapid Antigen Diagnostic Test (RDT) as a tool to establish the diagnosis of COVID 19.[4] Several results from the systematic review and meta-analysis that have been carried out also show fairly good diagnostic accuracy of the two tests.[5,6] Despite their high diagnostic accuracy, both tests have limitations. The RT-PCR test is a costly, labor intensive, and difficult examination to provide in rural areas. Therefore, the RDT antigen test has a lower sensitivity and is not recommended for use after day 7 of symptom onset or in individuals with low viral loads.[7] While a complete blood count has a relative weakness in terms of diagnostic accuracy, a chest X-ray has a significant subjectivity.

Indonesia, an archipelagic country with a significant disparity in resources and the quality of health services between the city center and its

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regions, continues to face difficulties in making a rapid and accurate diagnosis of COVID-19, particularly in underdeveloped areas that are remote from the city center and generally lack health services.[8] As a result, a diagnostic tool or parameter is required that is less expensive, does not require special skills, produces rapid results, and is easily accessible even in the least developed areas. Oxygen saturation is one of them. Until this research was conducted, the researchers found that oxygen saturation can predict the mortality and need for a mechanical ventilation procedure (invasive or non-invasive) in COVID-19 patients in the hospital.[9,10] But, research still needs to be done to determine its diagnostic accuracy in COVID-19. Because of those reasons, the researchers want to know the diagnostic accuracy of this index.

The diagnostic research design to be carried out uses a single-test approach, which is not the best hierarchical diagnostic research design. This is because a research design like this needs to follow everyday practice. Therefore, the appropriate approach is multivariable.[11] However, the design of this study was still carried out because first, the researcher wanted to conduct a more in-depth study of oxygen saturation alone, without paying attention to information from other indices, which, in the researcher's opinion, have relative weaknesses in diagnosing COVID-19. Second, this study is an initial study where researchers want to know whether oxygen saturation has the potential to be developed as a diagnostic tool. The research can be continued with a more ideal research design if it has potential.

The study's primary objective was to ascertain the diagnostic accuracy of oxygen saturation in the detection of COVID-19 (in the form of sensitivity, specificity, predictive value, and area under the curve). Additionally, the diagnostic accuracy of oxygen saturation in detecting COVID-19 at an onset of more than 7 days and during a COVID-19 case outbreak in Indonesia is being determined. The researchers hypothesize that oxygen saturation also has a high diagnostic accuracy for COVID-19 detection and thus has the potential to be used in COVID-19 diagnosis.

Methods

The study was conducted from October to November 2021 by collecting patient data from the medical records of patients suspected of having COVID-19 and agreeing to carry out RT-PCR examinations at three hospitals carrying out COVID-19 treatment in North Luwu Regency, South Sulawesi Province, Indonesia, from May 1, 2020, to September 31, 2021. The research was approved by the Health Research Ethics Committee, Faculty of Medicine and Health Sciences, University of Muhammadiyah Makassar, Indonesia, with the number 001/UM.PKE/X/43/2021.

Patients who met the inclusion criteria were adults (30–90 years) suspected of having COVID-19 based on WHO criteria[5] and agreed to carry out a diagnostic test using RT-PCR. The specific age range was chosen due to their increased susceptibility to low oxygen saturation levels during COVID-19 infection. Researchers excluded patients confirmed positive for COVID-19 by the RT-PCR method within three months before coming to the hospital.

All patients who met the inclusion criteria based on the screening and evaluation results of medical records by the first investigator (M.A.M) and the fourth investigator (A.S.) were consecutively included in this study. Oxygen saturation levels are measured by placing a pulse oximeter that has been through internal calibration on one of the patient's fingers for a few seconds. For RT PCR, the examination is carried out using the nasopharyngeal and oropharyngeal swab method based on the Ministry of Health of the Republic of Indonesia guidelines. Both the oxygen saturation and RT-PCR results were taken from the medical records.

The researcher used RT-PCR as the gold standard test, with positive or negative results,[4] and the oxygen saturation threshold of 90% to determine whether the patient was hypoxemic. An oxygen saturation of 95–100% is considered normal, while values under 90% are significantly associated with progressive deterioration, followed by increased mortality risk for those with saturation below 70%. Symptoms of deterioration include increased respiratory rate, pulse rate, and low blood pressure, commonly considered hallmark symptoms of hypoxemia.[12] The nasopharyngeal and oropharyngeal swab samples were sent to the Central Health Laboratory in Makassar (approximately 8-10 hours by car from the research site), one of the largest reference laboratories appointed by the Indonesian government to assess the RT-PCR examination results. The assessment is conducted by a trained and certified microbiologist unaware of the patient's oxygen saturation examination results.

The researcher obtains the patient's oxygen

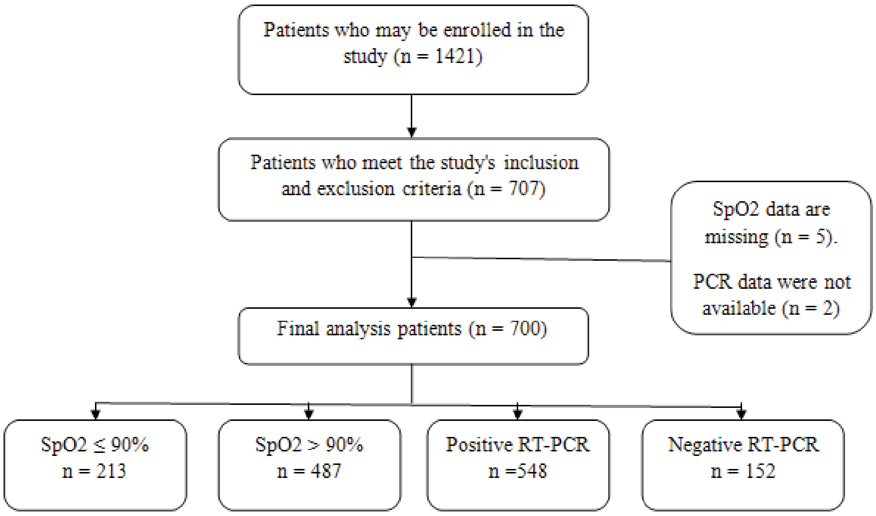

Figure 1 Research Flowchart

saturation data from the oxygen saturation data obtained the first time the patient arrives at the health facility without using oxygen (room air); if the oxygen saturation data obtained in all medical records is oxygen saturation with the assistance of oxygen therapy, the researcher elects to obtain the lowest oxygen saturation level of the patient. Suppose no patient oxygen saturation data is available before the RT-PCR swab. In that case, the researcher obtains oxygen saturation data following the RT-PCR swab with the closest time interval.

Additionally, researchers collected data on the subject's characteristics, including age, gender, comorbidities, and the severity of the patient's disease. Additionally, the researchers examined the diagnostic accuracy of oxygen saturation at disease onset after the seventh day and during an outbreak in Indonesia. The data was analyzed using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp.) in the form of a cross-table analysis with research outcomes in the form of sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve (AUC). Each has a confidence interval associated with it.

With an expected sensitivity of 85%, a generalization error of 5%, a precision of 3%, and a prevalence of COVID-19 of 73 percent in patients suspected of having COVID-19 based on literature, to determine the sensitivity of oxygen saturation, 745 patients with suspected COVID-19 are required. According to the literature, the prevalence of non-COVID-19 in patients with suspected COVID-19 is 27%. With an expected specificity of 85%, a generalization error of 5%, and a precision of 5%, 726 patients with suspected COVID-19 are required. Additionally, researchers are interested in the area under the curve (AUC) of oxygen saturation to diagnose COVID-19. According to the literature, COVID-19 is present in 73% of patients with suspected COVID-19. With an expected AUC of 80%, a precision of 10%, and an alpha of 5%, this study required 118 patients with suspected COVID-19 infection, with an expected composition of 32 positive and 86 negative patients.

Results

The RT-PCR swab results were not indeterminate. This study had five missing data points for oxygen saturation results and two for RT-PCR results. The researcher chose to omit specific data from the missing data set. Due to the scarcity of missing data discovered, namely 7 out of 700 samples (0.01 percent), data exclusion did not result in bias, though it did reduce research power. The patient characteristics are listed in Table 1.

Between oxygen saturation examination and RT-PCR swab sampling, the median time was 1 day (range, 0–4 days). The diagnostic accuracy of oxygen saturation in diagnosing COVID-19 is shown in Table 2. The RT-PCR examination

Table 1 Characteristics of Patients (n=700)

Variables	Description
Age (years) *	55 (30–89)##
Gender**	
Male	320 (45.7%)
Female	380 (54.3%)
Comorbid#	
Hypertension	136 (19.4%)
Diabetes mellitus	134 (19.1%)
Stroke	5 (0.7%)
Coronary artery disease	13 (1.9%)
Congestive heart failure	12 (1.7%)
COPD	0 (0.0%)
Asthma	11 (1.6%)
Pulmonary tuberculosis	14 (2.0%)
Additional diseases	34 (4.9%)
The severity of the disease	
Severe	216 (30.9%)
Mild	484 (69.1%)

*Numeric variables with abnormal data distribution are presented in the medium (minimum–maximum); **Categorical variables are expressed as n (percent); #Comorbidity type indicates only patients who have comorbidities in the form of n (percent); ##There are three (0.4%) missing values for the patient's age

identified 548 confirmed COVID-19 patients. The sensitivity and specificity of oxygen saturation for detecting COVID-19 were 33% (CI 95% 29–37%) and 78% (CI 95% 72–85%), respectively, with 84% positive predictive values (CI 95% 80–89%), and 24% negative predictive value (CI 95% 21–28%). Apart from mild discomfort, there were no serious adverse effects associated with the RT-PCR examination performed on the patient.

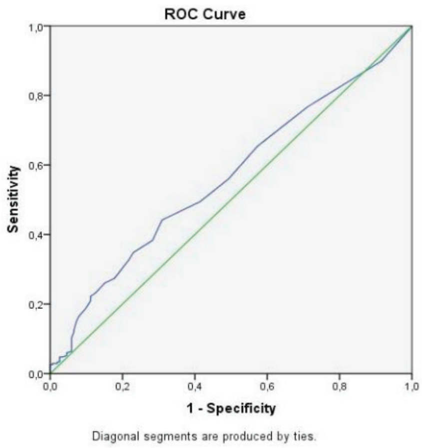

Figure 2 Oxygen Saturation ROC Curve for the Diagnosis of COVID-19

The *Receiver Operating Characteristic* (ROC) curve for oxygen saturation for the diagnosis of COVID-19 is shown in Figure 2, with an AUC value of 56% (CI 95% 51–61%) for oxygen saturation.

The sensitivity and specificity of oxygen saturation values for diagnosing COVID-19 are calculated in Table 3 using a variety of alternative intersection points. At 90.50, oxygen saturation has a sensitivity of 32% and a specificity of 21%,

Table 2 Cross Tabulation of Diagnostic Accuracy of Oxygen Saturation in COVID-19

		RT PCR		
		Positive (n=548)	Negative (n=152)	Total (n=700)
Oxygen Saturation	Hypoxemia	180	33	213
	Non-Hypoxemia	368	119	487

Table 3 Oxygen Saturation Sensitivity and Specificity Values For COVID-19 Diagnosis Using Various Cut-Off Points

Cut-Off Points	Sensitivity	-1 Specificity	Specificity
≤98.50	0.89	0.91	0.09
≤97.50	0.76	0.71	0.29
≤95.50	0.56	0.49	0.51
≤92.50	0.38	0.28	0.72
≤90.50	0.32	0.21	0.79
≤85.50	0.21	0.11	0.89
≤80.50	0.12	0.06	0.94
≤70.50	0.06	0.04	0.96
≤60.50	0.03	0.02	0.98
≤51.50	0.02	0.007	0.993

Table 4 Cross Tabulation of Diagnostic Accuracy of Oxygen Saturation For COVID-19 With Onset Greater Than 7 days

		RT PCR		Total (n=57)
		Positive (n=42)	Negative (n=15)	
Oxygen Saturation	Hypoxemia	15	1	16
	Non-Hypoxemia	27	14	41

Sensitivity (95% CI)=36% (21–50%); Specificity (95% CI)=93% (81–106%); Positive predictive value (95% CI)=94% (82–106%); Negative predictive value (95% CI)=34% (20–49%)

while at 80.50, it has a sensitivity of 12% and a specificity of 94%.

The diagnostic accuracy of oxygen saturation is determined in Tables 4 and 5 for the diagnosis of COVID-19 with an onset date greater than the seventh day and during a case outbreak in Indonesia, respectively.

Discussion

The results of data analysis in Table 1 indicate that oxygen saturation as a single test for COVID-19 has a low diagnostic accuracy. Thus, while oxygen saturation level is generally not recommended as a screening tool for COVID-19, it may be used to assist clinicians in the final stages of diagnosis due to their relatively high specificity.

While the diagnostic accuracy is low, the researchers discovered in Table 2 that the lower the oxygen saturation level, the lower the sensitivity, but the higher the specificity, for diagnosing COVID-19. Additionally, a sufficient oxygen saturation PPV (84 percent) can assist a clinician in initiating or performing emergency mitigation of patients suspected of having COVID-19 in certain circumstances, such as when the results of the reference examination take a long time to confirm the diagnosis, or when the clinician has a strong suspicion that the patient has COVID-19 but other index tests cannot detect it (onset after day 7, lack of viral load, technical error of sampling). Of course, this benefits clinicians or health workers working in rural areas of Indonesia with limited resources, especially where the speed and accuracy of diagnosis could be better.

We also examined the diagnostic accuracy of oxygen saturation at the onset above day 7 in diagnosing COVID-19 as a secondary outcome. This is based on observations made in the research area that patients suspected of COVID-19 may delay hospitalization for a variety of reasons. Some were admitted to the hospital with an onset date greater than the seventh day, and some with an onset date greater than the fourteenth day. In these instances, the majority of rapid tests for SARS-CoV-2 antigen were negative. This could be due to the rapid antigen test's decreased sensitivity on day 7 of onset. Interestingly, the investigators discovered that the oxygen saturation specificity was 93 percent and the PPV was 94 percent at onset after day 7. See Table 4.

Although these results are based on a small sample size and are not primary outcomes, they can serve as a starting point for further research into whether oxygen saturation can be used as a good diagnostic tool to diagnose COVID-19 after the 7th day of onset in several cases where the rapid antigen test results are negative and the RT-PCR examination results are unavailable due to a variety of factors. Additionally, in areas with limited access to rapid diagnostic testing, oxygen saturation can be used to assist clinicians

Table 5 Cross tabulation of Diagnostic Accuracy Of Oxygen Saturation for COVID-19 during a Spike in COVID-19 Cases

		RT PCR		Total (n=535)
		Positive (n=396)	Negative (n=139)	
Oxygen Saturation	Hypoxemia	125	31	156
	Non-Hypoxemia	271	108	379

Sensitivity (95% CI)=32% (27–36%); Specificity (95% CI)=78% (71–85%); Positive predictive value (95% CI)=80% (74–86%); Negative predictive value (95% CI)=28% (24–33%)

and other health care providers in mitigating risks, such as the placement of treatment rooms in hospitals, administering therapy to high-risk groups, and contact tracing), and burial protocols for suspected COVID-19 patients.

Additionally, we analyzed the diagnostic accuracy of oxygen saturation for the first and second spikes in cases in Indonesia (1 December 2020–28 February 2021) and 1 June–30 September 2021, respectively. This is based on clinicians' reservations about using oxygen saturation levels in Indonesia, where the number of cases is quite low. The sloping number of cases suggests a low transmission rate and the possibility of detecting COVID-19 cases. The researchers conducted this analysis to avoid overtreatment or undertreatment. According to Table 4, the diagnostic accuracy of oxygen saturation during the peak of cases in Indonesia is lower and comparable to the diagnostic accuracy of the cumulative oxygen saturation.

The study's limitations include the fact that the reference examination was not conducted according to standard procedures, and that the RT-PCR sampling, which should be performed twice within a 24-hour interval, was performed only once due to resource constraints in the area where the study was conducted. Thus, if the first RT-PCR swab yields a negative result, the second swab cannot be confirmed. This increases the likelihood of false negatives. Then, in some samples, oxygen saturation was determined while the patient was receiving oxygen therapy, resulting in an oxygen saturation level that did not reflect reality. Additionally, diagnostic research should ideally employ a multivariable test approach, rather than with a single test method. Diagnostic modalities such as lymphocyte count, neutrophile lymphocyte ratio (NLR), chest X-ray, and chest CT could be considered in addition to oxygen saturation in diagnosing COVID-19. This is also why the diagnostic accuracy of the index studied may be suboptimal.

The advantages are that this study employs a cross-sectional design, which is the optimal design for diagnostic research; the oxygen saturation index used in this study is a non-invasive medical device that is inexpensive, easy to access and use; and thus, further research is simple to conduct and apply to health services in the underdeveloped area.

As far as researchers are aware, there has been no published research on the diagnostic accuracy of oxygen saturation for COVID-19 in Indonesia or elsewhere until now, so the researchers hope that the findings of this study can serve as input and a foundation for future research.

In conclusion, due to the low diagnostic accuracy of oxygen saturation levels as a single test, they are not recommended for the diagnosis of COVID-19. Further research should be conducted to determine the diagnostic accuracy of oxygen saturation using a multivariable test approach and a larger sample size in a larger health center.

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