

Lesson from Indonesia: Covid-19 Testing Strategy In Obstetric Emergency Cases At Low-Resource Health Care Setting

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ABSTRACT

Background: COVID-19 identification in obstetric emergency cases with limited resources is problematic, particularly in asymptomatic cases.

Aim: To examine the screening strategies of COVID-19 obstetric emergency cases in low-resource health care settings.

Method: A retrospective cohort design was carried out on patients with COVID-19 positive screening results. It was assessed based on symptoms, contact history, lymphocytopenia, chest X-rays, and rapid antibody tests compared to RT-PCR results SARS-COV-2.

Result: Out of the 190 cases that came to the delivery room, the staff suspected 69 COVID-19 cases (36.3%) through the first screening protocol. Positive SARS-COV-2 RT-PCR was found in 23 cases with a majority asymptomatic (52.2%). The percentages of sensitivity and specificity from the parameters as follow: 48% and 74% in COVID-19 symptoms (febris or respiratory symptoms); 9% and 100% in contact history; 22% and 83% in lymphocytopenia; 52% and 48% in chest x-ray; 78% and 30% in rapid antibody test. Rapid antibody tests have the highest sensitivity to increase the identification of 12 asymptomatic cases.

Conclusion: Other screening beyond symptoms and contact history such as lymphocytopenia, chest x-ray, and rapid antibody test can improve the identification, especially for asymptomatic cases in areas with the limited testing ability and high Covid-19 transmission

Keywords: Covid-19, Screening, Obstetric Emergency, Low-resource health care

INTRODUCTION

The condition of the COVID-19 pandemic in Indonesia remains to increase exponentially. Surabaya, the second-largest city in Indonesia, is one of the COVID-19 centers for local transmission, and it was handling almost 10% of total COVID-19 cases in Indonesia¹. Cases finding, detecting, and tracing are the main approaches to mitigate COVID-19 transmission in communities and hospitals. Identifying COVID-19 in obstetric emergencies has an essential role since it will affect managing appropriate patient care, allocating isolation rooms, implementing neonatal care management, and preventing transmission to other patients and health workers.

A study from Vintzileos (2020) showed that many COVID-19 patients were asymptomatic in the delivery room². Another study by Sutton (2020) also found almost 88% of pregnant women with COVID-19 who admitted to the hospital were asymptomatic³. According to these reports, universal COVID-19 testing in pregnant women is recommended to detect an asymptomatic patient population. However, this condition will cause other obstacles, mainly in areas with limited testing capacity.

Generally, Indonesia's testing capacity is reported to be 2,378 tests/1 million population. While the testing capacity in developed countries, such as the US, is up to 37 times with a nearly comparable population⁴. Therefore, it is crucial to modify the COVID-19 screening strategy to identify symptomatic cases and be used to identify patients who come to the hospital for obstetric emergencies. Based on the above evidence, it is vital to find a COVID-19 testing

strategy for obstetric emergency cases, primarily in large local transmissions areas with inadequate testing capacity.

METHOD

The study applied a retrospective cohort design using COVID-19 screening protocols at the Department of Obstetrics and Gynecology, Soetomo General Hospital in Surabaya. Since 20th April 2020, we have developed the testing criteria. From testing only based on COVID-19 symptomatic and contact history, we examined several other parameters. The COVID-19 screening protocol includes evaluating the signs and symptoms, COVID-19 history, fever ($\geq 37.8^{\circ}\text{C}$), and respiratory problems (cough and shortness of breath) within 14 days. The presence of any or all of the symptoms was inserted as symptomatic cases. Evaluation of patient contact with the suspect or confirmed COVID-19 patients, COVID-19 laboratory results, and lymphocytopenia (lymphocyte count $< 1 \times 10^9/\text{L}$). Based on Huang's study⁵, we also took a radiological examination through the chest X-Ray and assessed the results as COVID-19 suspected or not based on Jacobi's pictorial review⁶. Subsequently, we arranged a rapid test of COVID-19 antibodies (Wondfo One Step COVID-19; Severe Acute Respiratory Syndrome, Coronavirus 2 / SARS-CoV-2 Antibody Test) based on immunochromatographic assay with lateral flow method in detecting qualitative SARS-CoV-2 IgG/IgM antibody from serum samples.

If any of the first screening tests were positive, the patient would proceed with a diagnostic examination using

Real-Time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) SARS-COV-2 for confirmation. The SARS-COV-2 diagnostic test was performed by taking a swab in the nasopharyngeal and putting it in a viral transport medium. The Abbott m2000 with Abbott Real-time SARS-COV-2 assay was used for the qualitative detection of nucleic acids from SARS-COV-2. Results were reported as positive if RdRp or N-gene examined positive. All processes were carried out in the hospital laboratory.

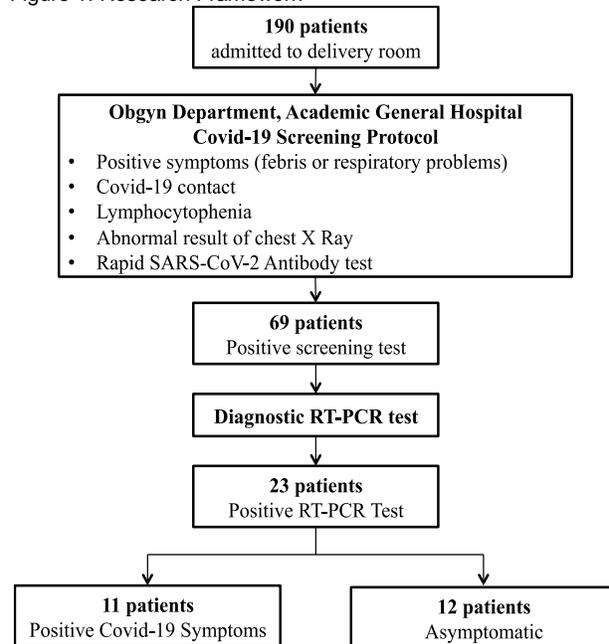
The study was conducted from 20th April 2020 to 10th June 2020, and the COVID-19 risk screening was carried out in all patients coming to the delivery room. If a positive screening result is received, the patient will be included in the study, and a swab test will be performed as confirmation and analyzed. This research has been approved by the ethics committee of Soetomo General Hospital Surabaya.

Categorical variables were shown as numbers (percentage), and continuous variables were represented as means (Standard Deviation / SD) or medians (interquartile ranges /IQRs). SPSS version 24.0 software for Windows (IBM Corp., Armonk. NY, USA) was used for statistical analysis. Chi-Square and Fisher Exact Test as an alternative was applied to compare the difference in the categorical variables, Independent T-Test and Mann-Whitney Test as an alternative was utilized to compare the continuous variables between groups. The value of $p < 0.05$ was considered significant. The accuracy of screening is performed by calculating the sensitivity, specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV).

RESULT

During the study, a total of 190 patients came to the delivery room. Sixty-nine patients (36.3%) were involved in the study, with suspected COVID-19 based on the COVID-19 screening protocol, and RT-PCR diagnostic tests were performed. Twenty-three patients (33%) with positive initial screening (12.1% of all 190 patients came to the delivery room) had positive RT-PCR results. This research framework can be observed in Figure 1.

Figure 1. Research Framework



Sixty-nine patient characteristics with a positive screening test were divided into positive and negative RT-PCR tests (table 1). The majority of COVID-19 positive patients were found to have asymptomatic cases (52.2%). Significant contact history of COVID-19 was only detected in 2 cases. Lymphocytopenia was observed in 21.7% of cases and abnormal chest X-rays in 52.2%. The majority of RT-PCR COVID-19 (+) cases had positive rapid antibody tests (78.3%). There were no significant differences in the characteristics and examination parameters between positive and negative RT-PCR results.

Based on the result, the calculation of several parameters' screening ability is shown in the following table (Table 2). The highest sensitivity was found in the antibody test, while the highest specificity and PPV were obtained from COVID-19 contact history.

The specific findings of the complete examination in the positive RT-PCR case are presented in figure 2. It will comprehend what tests were positive from the screening protocol in each case.

Table 1. Distribution of Patient Characteristics

Variable	COVID-19 PCR (+) COVID-19 PCR (-)		p
	cases (%) N=23	cases (%) N=46	
Maternal Age (mean±SD)	29±5.34	30.85±5.99	0.216
< 20 y.o	0 (0%)	1 (2.2%)	0.634
20-35 y.o	18 (78.3%)	32 (69.6%)	
> 35 y.o	5 (21.7%)	13 (28.3%)	
Gestational Age			0.447
< 20 weeks	2 (8.7%)	2 (4.3%)	
20 - 37 weeks	5 (21.7%)	12 (26.1%)	
> 37 weeks postpartum	15 (62.5%) 1 (4.3%)	32 (69.6%) 0	
Pregnancy Planning			0.282
Conservative Delivery / Pregnancy Termination	9 (39.1%) 14 (60.9%)	12 (26.1%) 34 (73.9%)	
Parity			0.267
Primiparity Multiparity	9 (39.1%) 14 (60.9%)	12 (26.1%) 34 (73.9%)	
Positive Symptoms	11 (47.8%)	12 (26.1%)	0.071
Febris	7 (30.4%)	6 (13%)	0.107
Cough	9 (39.1%)	8 (17.4%)	0.058
Dyspnea	5 (21.7%)	6 (13%)	0.352
Contact History	2 (8.7%)	0	0.108
Obstetric Complication			
Obesity	4 (17.4%)	14 (30.4%)	0.245
Diabetes	2 (8.7%)	1 (2.2%)	0.256
Chronic Hypertension	2 (8.7%)	2 (4.3%)	0.596
Preeclampsia	3 (13%)	11 (23.9%)	0.29
White Blood Count x10⁹/L (median[IQR])	10.19 (5.54)	11.49 (4.69)	0.093
Lymphocytopenia	5 (21.7%)	8 (17.4%)	0.663
Abnormal Chest X-Ray	12 (52.2%)	24 (52.2%)	1
Positive Rapid Antibody Test	18 (78.3%)	32 (69.6%)	0.446

Table 2. COVID-19 Screening Test Performance

Variable	COVID-19 PCR (+) COVID-19 PCR (-)		Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)
	cases (%) N=23	cases (%) N=46				
Positive Symptom	11 (47.8%)	12 (26.1%)	47.83% (26.82%-69.41%)	73.91% (58.97%-85.73%)	47.83% (32.43%-63.65%)	73.91% (64.89%-81.29%)
Febris	7 (30.4%)	6 (13%)	30.43% (13.21%-52.92%)	86.96% (73.74%-95.06%)	53.85% (30.69%-75.45%)	71.43% (65.11%-77.01%)
Cough	9 (39.1%)	8 (17.4%)	39.13% (19.71%-61.46%)	82.61% (68.58%-92.18%)	52.94% (33.35%-71.67%)	73.08% (65.59%-79.45%)
Dyspnea	5 (21.7%)	6 (13%)	21.74% (7.46%-43.70%)	86.96% (73.74%-95.06%)	45.45% (22.12%-70.97%)	68.97% (63.55%-73.91%)
Contact History	2 (8.7%)	0 (0%)	8.7% (1.07%-28.04%)	100% -	100% -	68.66% (65.88%-71.30%)
Lymphocytopenia	5 (21.7%)	8 (17.4%)	21.74% (7.46%-43.70%)	82.61% (68.58%-92.18%)	38.46% (18.71%-62.92%)	67.86% (62.11%-73.11%)
Chest X-Ray	12 (52.2%)	24 (52.2%)	52.17% (30.59%-73.18%)	47.83% (32.89%-63.05%)	33.33% (23.64%-44.67%)	66.67% (54.25%-77.13%)
Rapid Antibody Test	18 (78.3%)	32 (69.6%)	78.26% (56.30%-92.54%)	30.43% (17.74%-45.75%)	36% (29.66%-42.86%)	73.68% (53.48-87.21%)

Figure 2. Screening Results in SARS-COV-2 Positive by RT-PCR

Symptomatic Cases												
Parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	
Symptoms	+	+	+	+	+	+	+	+	+	+	+	
Contact (+)	+	-	-	-	-	-	-	-	-	-	-	
Lymphocytopenia	-	+	-	+	-	-	-	+	-	+	-	
Chest X-Ray	-	+	+	-	+	-	+	+	-	+	+	
Rapid Antibody Test	-	-	+	+	+	+	+	+	-	+	-	
Asymptomatic Cases												
Parameters	Case 12	Case 13	Case 14	Case 15	Case 16	Case 17	Case 18	Case 19	Case 20	Case 21	Case 22	Case 23
Symptoms	-	-	-	-	-	-	-	-	-	-	-	-
Contact (+)	-	+	-	-	-	-	-	-	-	-	-	-
Lymphocytopenia	-	-	-	-	-	-	-	+	-	-	-	-
Chest X-Ray	-	-	+	-	+	-	+	-	+	+	-	-
Rapid Antibody Test	+	+	+	+	+	+	+	+	+	-	+	+

DISCUSSION

Currently, the world is suffering from a global crisis in fronting the COVID-19 pandemic. It sets enormous pressure on the health system around the world. Nearly all health service centers in entire countries are overwhelmed. Excellent anticipation with appropriate and adaptive strategies to reduce transmission is wholly needed and considered to increase exponentially. Even though some specific health services have been postponed, maternal health services must remain to be performed and cannot be discontinued at any time. Recent evidence from areas with a high transmission prevalence will also present many pregnant women with COVID-19³.

Out of 190 patients admitted to the delivery room, it found 23 COVID-19 positive cases (12.1%). Related studies from the American Journal of Obstetrics and Gynecology (AJOG) revealed a higher proportion of maternal COVID-19 cases (19.9%)². Sutton's investigation also reported a similar result, with a proportion of 15.3% from 33 positive cases in 215 pregnant women³. The different numbers of overall COVID-19 cases between the US and Indonesia can differentiate this study's results. Furthermore, the two comparative studies conducted universal RT-PCR. In contrast, this study conducted RT-PCR testing based on the initial screening.

The mean COVID-19 positive maternal age was 29 years old, and the majority was in the range of 20 to – 35 years old. Most patients came for delivery or pregnancy termination (60.9%). Then most subjects at term gestational age (62.5%). This study is compatible with a systematic review study, where 108 COVID-19 pregnancy women were obtained with the average age from 29 to 32 years and mostly came to the delivery room in the 3rd trimester. In this review, labor also occurred in 80% of cases⁷. The characteristics of obstetrics patients were different compared to the general population. Guan's research explained a median age of 47 years old⁸. The pregnant patient's population always has a younger age range. Moreover, maternal COVID-19 patients' identification is not due to the COVID-19 problem but correlates with specific obstetric problems in the delivery process. Therefore, the screening and identification of

COVID-19 in pregnant women who came to the hospital have a vital role.

The most obstetric complication related to COVID-19 comorbidities in the studies was obesity (4 cases, 17.4%). Other studies have also confirmed that obesity is the most commonly found in diabetic mellitus and hypertension during pregnancy^{9,10}. Breslin's investigation showed that patients who need health services at the Intensive Care Unit (ICU) are at a Body Mass Index (BMI) > 35, however further studies are needed to reconfirm the correlated morbidity findings¹¹.

The majority of patients with COVID-19 positive were asymptomatic (12 cases, 52.2%). Coughing is the most often complained (39.1% from all cases and 81.8% from symptomatic cases). Insignificantly different from Zaigham's study, fever was found to be the most frequent symptom⁷, while Breslin's observation explained that cough was the most prevalent ailment¹⁰. Breslin's study is more in line with this study because the samples were taken by universal screening. Typical screening protocols will also give different characteristics. Significant COVID-19 contact history was only found in 2 cases (8.7%). In contrast, a different study showed contact history in a higher proportion of about 34.5% of cases¹⁰. Yan's study revealed 38 out of 116 cases with a positive contact history⁹. In contrast, a different study showed contact history in a higher proportion of about 34.5% of cases. Yan's study revealed 38 out of 116 cases with a positive contact history⁹. Evaluating contacts is quite challenging, notably in a developing country due to patients' negative stigma, fear of isolation care, and risk of separating newborns from their mothers. This affects the contact history covered.

Lymphocytopenia obtained only 21.7%, while other studies from Zaigham reported lymphocytopenia in 59%⁷. This study also examined a chest X-ray and revealed that half of COVID-19 positive showed abnormal results (52%). A retrospective study from Yan on 116 COVID-19 pregnant women informed abnormal radiologic findings in 96.3% of cases and a higher proportion of symptomatic cases (76.7%)⁹.

The Centers for Disease Control and Prevention (CDC) does not recommend that chest radiography to diagnose COVID-19. The findings on chest imaging are not specific and overlap with other infections. Therefore, this

modality should not be accepted as a first-line test to diagnose COVID-19. However, in the low-resource testing areas, this option can be considered. The most obstetric complication related to COVID-19 comorbidities in the studies was obesity (4 cases, 17.4%). Other studies have also confirmed that obesity is the most commonly found in diabetic mellitus and hypertension during pregnancy⁹. Breslin's investigation showed that patients who need health services at the Intensive Care Unit (ICU) are at a Body Mass Index (BMI) > 35, however further studies are needed to reconfirm the correlated morbidity findings.

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The protocol in this study involved a rapid antibody test due to our limited testing capability. This revealed that the majority (78.3%) of maternal COVID-19 cases had a positive antibody test. Almost all patients with COVID-19 will test positive for antibodies within 10–20 days after symptoms, but the antibody test's clinical significance cannot be explained in either the pregnant population or obstetric cases. There were also various methods for antibody testing for SARS-CoV-2 with different sensitivity and specificity¹⁴. In general, if the results of rapid antibody tests are positive, we will continue with swab RT-PCR to distinguish whether this patient is still infected¹⁵.

It should be known that triage or COVID-19 cases sorting must be performed at the hospital¹⁶. Unlike many gynecological visits that can be postponed, obstetric

patients' arrival, especially during labor, frequently cannot be planned. It is fundamental to develop strategies to secure the safety of patients and health workers. Therefore, the implementation of universal testing must be strongly considered in all obstetric cases¹⁷. The safety of women, babies, partners, and health staff remains an absolute priority. Offering testing to women receiving maternity care can reduce nosocomial transmission. However, universal testing can only be arranged in high-resource hospitals with adequate laboratories. Bowling's recommendations were to take universal testing if the hospital's capacity could adhere to the high number of asymptomatic COVID-19¹⁸. Therefore, other approaches need to be considered.

This study added more parameters (lymphocytopenia, abnormal chest x-ray, and rapid antibody test) in COVID-19 screening to increase the testing capacity. With this screening protocol, we can detect more COVID-19 patients. If only symptoms are used, this strategy can only detect 11 out of 190 patients (5.8%), while if we expanded the screening strategy also by attending at lymphocytopenia, abnormal chest X-ray, and rapid antibody tests, the detected cases increased more than 2-fold to 23 cases per 190 patients (12.1%). Tests based on symptoms will not be effective and endanger the maternal delivery ward of new COVID-19 transmissions.

The symptoms only have a sensitivity and specificity of 48% and 74%. There is still a few research that looks at COVID-19 screening capabilities. A study of Vintzileos revealed lower sensitivity (34.4%) but higher specificity (96.1%) in maternal symptoms. The highest specificity was found in the history of COVID-19 contact, but as explained earlier, evaluating contacts especially in extensive local transmission conditions is not easy, patients sometimes not know whether she was exposed or try to avoid COVID-19 testing by hiding past symptoms and contact history².

No other studies have observed the ability to select other parameters (lymphocytopenia, chest X-rays, and rapid antibody tests). As revealed earlier, by supplementing these parameters, the COVID-19 detection raised almost twice. The antibody test had the highest sensitivity (78.3%), while chest X-rays and lymphocytopenia had a lower sensitivity (52% and 22%). A good screening test has several characteristics, including being used for critical health problems, diagnosis and therapy facilities are available, not expensive, and has good sensitivity¹⁹. COVID-19 can be detected indirectly by measuring the immune response; therefore, serological diagnosis is vital for mild problems¹⁴. Although the highest antibody detection is obtained after the first week, Guo's analysis confirmed that the fastest detection even starts from the first day symptoms appear²⁰.

This study focuses on finding ways to detect asymptomatic cases of COVID-19 in RT-PCR limited testing situations. Asymptomatic cases are important because the potential for transmission remains reported by asymptomatic transmission from Bai²¹ and several Lancet publications that showed asymptomatic pediatric patients in family clusters with abnormal radiographs. A different study has shown that the detectable viral load in asymptomatic cases is almost the same as in symptomatic shows the potential transmission ability from asymptomatic case²².

Some studies have shown that most obstetric cases with COVID-19 are asymptomatic; hence universal testing is extremely recommended²³. Although this cannot be generalized in low infection states, COVID-19 status is essential to determine isolation in hospitals, bed allocation, CDC's newborn protocol, and management of Personal Protective Equipment (PPE) procedure^{24,25}. This study presents an excellent alternative to the COVID-19 screening protocol in maternal health services. This protocol can increase the detection of up to 12 asymptomatic patients. Indeed, if universal testing is implemented as in developed countries, we need 190 swab tests, whereas, with this protocol, we only perform RT-PCR swab tests only on 69 patients at risk, which can reduce costs and keep the test for other patients who also need it.

A limitation of this study was that we did not perform RT-PCR swabs on all patients who had negative results on initial screening. So that the possibility of an undetected COVID-19 case was not ruled out. Further studies to compare our screening protocols and universal testing will allow us to see the screening protocol's capabilities more precisely. Our screening protocol can detect more asymptomatic patients and saving medical personnel who have essential inpatient care roles. The conditions in Italy that reported the death of several health workers with 3000 or more affected by COVID-19 indicate the importance of identifying cases, especially in maternal care that can never be delayed and always requires direct contact services for delivery¹⁸.

CONCLUSION

More asymptomatic cases of COVID-19 can be detected using our hospital screening protocol (Dr. Soetomo General Hospital) than the RT-PCT swab test in selected symptomatic cases. Rapid antibody testing has high sensitivity and a beneficial role in screening for COVID-19, particularly in areas with high COVID-19 rates with limited testing capacity. This study reveals the importance of identifying COVID-19, notably in asymptomatic cases, to prevent infection transmission to newborns, other patients, patients' families, and health workers urgently required in this pandemic.

Conflict of interest: The authors declared there were no competing interests in the study.

Ethical approval: This research was declared an ethical pass test by the Ethics Committee of Dr. Soetomo General Hospital, Surabaya East Java Indonesia.

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