Potential applications of the rapid COVID-19 antibody test kit screening in comparison to the real-time RT-PCR in patients and personnel at the Department of Obstetrics and Gynaecology

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Abstract

Objective To evaluate the real clinical-setting feasibility of the rapid antibody test for COVID-19 screening, compared to RT-PCR for emergency obstetric and gynaecological procedures, and medical personnel in the Department of Obstetrics and Gynaecology, a cross-sectional survey was conducted with 232 patients and 60 medical staff, during the four-month national COVID-19 outbreak period (Aug – Sep 2020, and Dec 2020 – Jan 2021). All participants underwent rapid antibody tests and RT-PCR (at admission for patients).

Results A total of 270 participants (210 patients and 60 medical personnel) completed the study. Fever and URI symptoms were present in 6/210 patients (2.8%), while one patient (0.5%) had a history of travelling to a high-risk area. However, only two (1%) asymptomatic patients had positive IgM results. Concerning the medical personnel, 10% fell into the 'patient under investigation (PUI)' category. 4/60 (6.7%) IgM positive was observed in the staff cohort, in which 3/4 came from non-PUI participants. Neither participant had RT-PCR positive, demonstrating a 1.9% total false positive rate. A rapid point-of-care antibody test can be used to screen either a pregnant woman coming for delivery, a patient who requires urgent/emergency operative procedures, or medical personnel, at least in the defined lower-prevalence COVID-19 situation.

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Introduction

Developed in early 2020 by the Baiya Phytopharm company (Bangkok), Baiya's rapid Coronavirus Disease (COVID-19) IgG/IgM test kit is a point-of-care antibody test in either serum or plasma, utilizing 'the lateral flow immunoassay' technique. The result is read within 15 minutes. Patient's antibodies, both immunoglobulin G (IgG) and immunoglobulin M (IgM), to SARS-CoV-2 spike protein (S-protein) are detected when bound to the kit's conjugate membrane coated with recombinant antigen protein produced from the tobacco plant, or 'Baiya' in Thai, in the laboratory. The lateral flow immunoassay has proven effective in the literature with 88.66% sensitivity and 90.63% specificity.[1] The kit post-manufacturer evaluation in the laboratory utilizing 51 samples of confirmed positive cases and 150 sample controls observed 94% (48/51) sensitivity and 98% (147/150) specificity of either positive IgM or IgG results when compared to the real-time reverse transcription polymerase chain reaction (RT-PCR) (unpublished data). To overcome the limitations of RT-PCR, including its high cost, taking time to get the results (usually 12-48 hours depending on the batch running cycle), and the requirements of experienced staff and sophisticated equipment, our obstetrics and gynaecology department was interested in adopting this rapid antibody test kit for the COVID-19 screening besides using the high-risk contact criteria. Pregnant women have a higher rate of asymptomatic infection (49-68%).[2] Nonetheless, few other studies investigated the efficacy of rapid antigen/antibody test kits for urgent/emergency obstetric and gynaecologic conditions. Therefore, the study was conducted i) to evaluate the actual clinical-setting feasibility of the Baiya's rapid IgG/IgM test kit as a point-of-care COVID-19 screening in comparison to real-time RT-PCR in patients and medical personnel, and ii) to evaluate the seroprevalence of the COVID-19 in patients visiting the hospital for obstetric and gynaecological procedures (including childbirth), and personnel within the department.

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Materials and Methods

Trial registration

Thai Clinical Trials Registry (TCTR20210613001;

https://www.thaiclinicaltrials.org/).

Participants

This cross-sectional study was performed at the Department of Obstetrics and Gynaecology, Srinakharinwirot University Hospital, during the periods between August – September 2020 and December 2020 – January 2021. A total of 290 participants were expected: i) 230 patients and pregnant women visiting the hospital for either an emergency medical procedure or an elective unpostponable surgery including vaginal delivery, cesarean section, uterine curettage for miscarriage, and exploratory laparotomy, ii) 60 medical personnel, comprising physicians, nursing staff, technicians, in the department. Participants were excluded when they denied or could not complete both the rapid-antibody test kit and real-time RT-PCR testing. This study was approved by the Institutional Review Board of Srinakharinwirot University (IRB SWUEC119/ 2563F). Written informed consent was obtained from all participants.

Methods

Demographic data and risks associated with COVID-19 infection were recorded by a physician. A blood sample was taken either by fingertip collection or venipuncture for the rapid antibody test. The rapid test result was read at 15 minutes by a trained physician. Subsequently, the nasopharyngeal swab was obtained. The real-time RT-PCR for SARS-CoV-2 was performed on the ABI7500 real-time PCR machine (ThermoFisher, Waltham, USA) using a commercial kit (Sansure Biotech Inc, China). This assay detects two specific SARS-CoV-2 genes, including ORF-1ab and N genes (lower detection limit; LOD = 0.2 copies/μL). The RNase P gene was used as an internal control (IC) to ensure appropriate specimen collection. The cut-off cycle threshold (ct) was assigned at less than 40 for interpretation with 'detectable.' The real-time RT-PCR tests were analysed by a molecular pathologist (WJ) who was blinded from the rapid test results.

Statistical analysis

The sample size of patients visiting the hospital for medical procedures was calculated using a statistics formula and a prevalence of COVID-19 infection in pregnancy previously reported by Sutton D. et al. (2020).[3] A total participant (plus 20%) of 230 patients were expected. Other 60 participants who are health personnel were anticipated. Data are presented using descriptive statistics. We had planned to evaluate the sensitivity, specificity, and predictive values of Baiya's rapid COVID-19 IgM/IgG test kit, compared to the real-time RT-PCR, if seroprevalence was allowed.

Results

The cumulative number of confirmed COVID-19 cases in Thailand was 3312 cases with 58 deaths on 1st August 2020 which was increased to 19,618 cases with 77 deaths on 1st February 2021. During the 4-month study period, we enrolled 292 participants including 232 OB-GYN patients, who were admitted to the hospital for an operative procedure, and 60 medical personnel, involved in the OB-GYN clinical practises. In the patient cohort, 22 participants were excluded, all due to real-time RT-PCR was not performed, either by participants withdrawing consent or technical/clinical issues. The median age of the remaining 210 participants was 29 years (interquartile range 25-36 years). A majority (83.3%) of participants were admitted to the hospital for childbirth delivery, either vaginal delivery (57.6%) or cesarean section (25.7%). There were 14% of patients admitted for gynaecological surgery, including oncological operations and emergency laparotomies/laparoscopic surgeries (ruptured ectopic pregnancy, torsion ovarian cyst) (Table 1).

There were 6 (2.9%) symptomatic participants.

Table 1 The demographic data of patients and pregnant women.

Demography; n = 210	
Age (years): median [IQR]	**29 [25, 36]**
Reason for admission: n (%)	
Vaginal delivery	121 (57.6%)
Cesarean section	54 (25.7%)
Gynaecologic oncology/Gynaecology major operation	29 (13.8%)
Curettage for obstetric/gynaecologic conditions	6 (2.9%)
Race: n (%)	
Thai	174 (82.9%)
Burmese	18 (8.6%)
Cambodian	13 (6.2%)
Laotian	5 (2.4%)
History of travelling to high-risk area (without mask); n (%)	**1 (0.5%)**
History of contact with patient under investigation / confirmed positive; n (%)	**0 (0.0%)**
Healthcare worker; n (%)	**2 (1.0%)**
Presence of symptoms†; n (%)	**6 (2.9%)**
Fever 37.5 ℃	6 (2.9%)
Cough	2 (1.0%)
Rhinorrhoea	1 (0.5%)
Sore throat	1 (0.5%)

†A patient could have multiple symptoms; IQR, interquartile range.

Fever, cough, rhinorrhoea, and sore throat were observed in 6 (2.9%), 2 (1%), 1 (0.5%), and 1 (0.5%) participants, respectively. Neither had contact with a confirmed COVID-19 case. Only one patient (0.5%) reported that she had been visiting a declared high-risk area. Overall, two participants (1%) had the positive rapid antibody test result, both having only IgM positive. These two patients neither had symptoms of upper respiratory tract infection (URI), travelled to the high-risk area, nor had contact with a confirmed COVID-19 patient. The real-time RT-PCR for SARS-CoV-2 was negative in all patients. Information regarding these two patients' treatment plans is found in Table 2.

Table 2 Characteristics of participants with positive rapid IgM/IgG antibody test

Case	Status	Indication	Age (Sex)	Risk factors			Rapid Ab test		RT-PCR	Intervention
				Travelled to a high-risk area	Hx of contact	Symptoms	IgM	IgG		
1	Patient	Surgical staging	61-65 (F)	No	No	None	(+)	(-)	Negative	Operation postponed for 1 week; Repeated RT-PCR - negative prior operation
2	Patient /HCW	Caesarean section (Emergency)	36-40 (F)	No	No	None	(+)	(-)	Negative	Requested for emergency RT-PCR Operation delayed for 3 hours (patient waited in the negative pressure suite)
3	HCW	Volunteer to research	31-35 (F)	No	No	None	(+)	(-)	Negative	Leave and self-quarantine until RT-PCR result known (1 day)
4	HCW	Volunteer to research	36-40 (M)	No	No	None	(+)	(-)	Negative	Leave and self-quarantine until RT-PCR result known (1 day)
5	HCW	Volunteer to research	25-30 (F)	No	No	Rhinorrhoea No fever	(+)	(-)	Negative	Leave and self-quarantine for 2 days until symptoms decrease / RT-PCR results known (1 day), then self-monitoring for 14 days

Ab, antibody; HCW, healthcare worker; IgG, immunoglobulin G; IgM; immunoglobulin M; RT-PCR; reverse transcription polymerase chain reaction.

A total of 60 medical personnel participated in the study from December 2020 to January 2021, the second nationwide outbreak of COVID-19 in Thailand. The median age was 28 years old (interquartile range 24.8-38). The majority were women (78.3%) and nursing staff (60%). Approximately 28% were physicians (interns, residents, clinical fellows, and consultants). The cohort also included 5 prelicensed final-year medical students who had just been relocated from a provincial hospital considered a high-risk area. Also, one resident had just visited the declared high-risk area, and one intern had contacted a confirmed COVID-19 patient while working in the other hospital after hours. Six medical personnel had upper respiratory tract symptoms. Overall, 12 (20%) medical staff were classified as patients under investigation (PUI) for COVID-19, including one physician who had contacted with a confirmed COVID-19 case, five medical students who travelled from the high-risk area, and six medical personnel who had upper respiratory tract symptoms (Table 3). The rapid antibody test results showed positive IgM-only antibodies in four participants (6.8%). None of the medical personnel tested had a positive real-time RT-PCR for SARS-CoV-2 (Table 2).

Discussion

The major challenge during the pandemic is to balance between prevention of nosocomial SARS-CoV-2 transmission and the provision of patient-centred care for emergency/urgent conditions. Pregnant women are considered a vulnerable population for COVID-19 infection, with higher probabilities of requiring invasive ventilation support, ICU admission, obstetrics complications, and maternal death. However, data demonstrates that they are less likely to show symptoms.[4] Thus, they are potentially a silent spreader when visiting the hospital. There was no definite practise guideline for screening obstetrics and gynaecology patients before being admitted to the hospital. Most authorities recommend that real-time

Table 3 The demographic data of medical personnel

Demography; n = 60	
Age (years): median [IQR]	**28 [24.8, 38]**
Sex	
Female n (%)	47 (78.3%)
Male n (%)	13 (21.7%)
Role n (%)	
Physician	17 (28.4%)
Registered / Practical Nurse	36 (60.0%)
Final-year medical students	5 (8.3%)
Technician/ Laboratory scientist	2 (3.3%)
Recent travelled to or worked in high-risk area; n (%)	**6 (10%)**
Number of IgM/IgG rapid test positive	0 (0%)
History of direct/indirect contact with patient under investigation /confirmed positive; n (%)	**1 (1.7%)**
Number of IgM/IgG rapid test positive	0 (0%)
Presence of symptoms (fever, cough, rhinorrhoea, sore throat); n (%)	**6 (10%)**
Number of IgM/IgG rapid test positive	1/6 (16.7%)

IgG, immunoglobulin G; IgM; immunoglobulin M; IQR, interquartile range

RT-PCR be performed on admission in every case.[5] Concerns have been raised regarding the universal RT-PCR screening because of its high cost, time to get results, and in-house availability. Zullo and colleagues suggested screening SARS-CoV-2 antibodies utilizing a rapid antibody test in pregnant women before receiving care in both inpatient and outpatient settings.[6] The Baiya's rapid COVID-19 IgG/IgM test kit was selected as it was developed within the country and tested for efficiency both in the laboratory and in a few other clinical trials during our study period.

Our research shows that though there were two nationwide outbreak episodes, the seroprevalence of patients with positive IgM/IgG antibodies was only 1% (2/210). Neither of these two was symptomatic. On the contrary, six pregnant participants had fever (and URI symptoms), demonstrating a 3.4% (6/175) rate of intrapartum fever. Intrapartum fever is not uncommon in obstetric practise, reported between 3-7% in the literature.[7] This condition generated significant concern about whether patients were having COVID-19 infection. The rapid test could immediately guide the management concerning prioritising personal protective equipment (PPE) and facilities, i.e., negative pressure theatre or cohort ward, which shall be limited during the pandemic. However, the rapid antibody test should be interpreted with caution also due to the odds of false-negative results, especially during the early clinical course.[6,8] In our current practise, we performed both rapid antibody test and real-time RT-PCR in all patients at admission, either for an emergent/urgent or elective procedure.

The research also studied the seroprevalence of SARS-Cov-2 antibodies among medical personnel, considered healthy and active, thus possessing a risk of becoming a 'silent spreader.' We included 74% of all staff in the department. All frontline workers, including residents, interns, nursing staff, and technicians, participated in the study. In contrast, only 10% of the consultants took part in the study. In the current study cohort, 21.6% (12/60) were at risk for COVID-19 infection. About half of these high risk were symptomatic (6/20), while the others were either indirectly contacting the COVID-19 patient or recently travelling to the high-risk area. Contracting the disease from outside of the organisation either by working or non-working related is one of the greatest threats of the department in which, despite precautions, the incidences still occurred.[9] Nonetheless, we observed 6.7% (4/60) positive IgM from the rapid test in the study cohort, while the majority of the positive (3/4) came from participants without PUI risks.

Real-time RT-PCR is the current standard of COVID-19 detection. In our study, the results from the rapid antibody test corresponded with the RT-PCR with a 1.9% presumed false-positive rate (5/270; range 1% to 6.8% in patients and medical personnel, respectively). Other epidemiological studies utilizing Baiya's rapid COVID-19 IgG/IgM kit observed 0.8-3.7% and 12.1% seroprevalence of COVID-19 antibodies in medical personnel and patients, respectively.[10,11] Neither our nor these published studies observed a correlation between positive rapid antibody test results with PUI risks and symptoms. A difference in the timing of positive test results between the nucleic acid (real-time RT-PCR) and antibody (rapid antibody kit or standard immunoassay) tests should be considered. The real-time RT-PCR will detect with the highest chance in the first week following symptom onset, while antibodies (mainly IgM) are commonly found in the 2nd week.[6,12] In asymptomatic participants, it is rather difficult to pinpoint the onset of the disease, thus may pass the detection period of real-time RT-PCR. Nonetheless, further study is needed to confirm the serologic status of the positive rapid antibody test before concluding that the result is not a false positive one.

An array of assays, including i) point-of-care (POC) nucleic acid amplification test (NAAT), ii) POC antigenic detection, and iii) POC or laboratory-based serology IgM/IgG detection, offers aid in COVID-19 diagnosis with different purposes.[13] In our study, during the first wave of the pandemic but still considered low prevalence, the Baiya's rapid COVID-19 IgG/IgM antibody test had been developed. The knowledge regarding the COVID-19 infection was still immature. It was concerned that there were asymptomatic patients; especially in a specific population e.g., pregnant women and healthcare personnel, who had never been detected as they were not accessible to RT-PCR due to limited resources and availability. A rapid antibody test could provide a prevalence (indicating recent or prior infection) for monitoring and responding to the COVID-19 pandemic in a particular population especially when the infection is primarily asymptomatic.[13] Nonetheless, the utility of serologic tests for diagnosing acute infections is limited at timing around the symptom onset (highest transmission rate). At present, both symptomatic patients and asymptomatic patients with contact risks are screened or even diagnosed by the rapid antigenic test due to the infection's high prevalence in both total and symptomatic cases. The viral load decreases 6-14 days following the onset of symptoms.[14,15] On the contrary, the mean duration of IgM and IgG detection in serum are 5 and 14 days, respectively, following the onset of symptoms.[14,16] Zhao J, et al. reported that the sensitivity of antibody detection was significantly lower than the RT-PCR within the first week from the onset of the disease (38.3% vs. 66.7%). While the sensitivity of RT-PCR is reduced to approximately 50% (45.5%-54%) after the first week, the sensitivity of the antibody test reached 90% by day 12 after onset overtaking the RT-PCR sensitivity.[17] Hence, the rapid antibody test (which should be later confirmed by the standard serological assays) is also helpful in confirming the diagnosis in the late phases of the disease for example patients with complications and history/clinical compatibility with COVID-19

infection who had been RT-PCR test negative.[18] Confirmation of adaptive immune response either from previous infection[19-21] or vaccination[22,23] reduces the incidences of reinfection and severe disease. False-positive rapid antibody tests should be cautiously considered especially in individuals with previous infection/vaccination and in other non-SAR-CoV-2 viral infections e.g. other human coronaviruses (HCoVs).[24] False-negative, nonetheless, is technically more concerned, particularly during the first week of infection. It should not replace the nucleic acid test (RT-PCR) for the diagnosis of acute COVID-19 infection. The antibody test is not recommended to determine immunity following COVID-19 vaccination, to evaluate the need for a vaccination booster, or to avoid quarantine in cases of high-risk contact.[25] Utilizing a multiple-antigen approach on various specific antigenic targets (Nucleocapsid, N-protein; S1 subunit of spike glycoprotein, S1-protein; and receptor binding domain, RBD) with knowledge of their cross-reactivity to other antigenic targets can differentiate between previous infection and vaccination (commonly developed against the S-protein).[26]

We anticipated that all participants (Table 2) with a positive rapid antibody test were anxious while waiting for their real-time RT-PCR results, which could have been worse if the hospital did not have an in-house PCR facility (up to 3 days). Nonetheless, while a positive rapid test result caused concern and anxiety to both personnel and patients, a negative result reassured them significantly. PPE should be offered for all emergency surgical procedures during the pandemic. Though the rapid test can guide and facilitate the management of PPE and the negative room more efficiently.

In conclusion, the rapid point-of-care antibody test can be used as either a screening tool for patients who require urgent/emergency operative procedures or a seroprevalence survey on medical personnel on service. In the defined low-prevalence subpopulation, i.e., pregnant or gynaecologic patients, the test kit was relatively accurate in the negative result compared with real-time RT-PCR with a false positive rate of 1%. The rapid antibody test ensures, while reducing anxiety, patients and healthcare workers at the point of care and facilitates the management of PPE more efficiently, at least in the low to moderate COVID-19 prevalence area. Moreover, the development of serologic tests either rapid POC or laboratory-based should be designed to accurately determine prior infection and immunity to the SARS-CoV-2. They are beneficial for epidemiologic surveillance either for COVID-19 infection or vaccine coverage among patients and healthcare workers. Further elucidation on diagnostic efficacy and optimal application is required.

Limitations. The study was conducted during the low prevalence period of COVID-19 infection in obstetrics and gynaecology patients, thus the rapid antibody test's performance, i.e., sensitivity/ specificity, could not be calculated. In addition, there was no standard immunoassay for COVID-19 available onsite during the study period, therefore the serologic status of the positive rapid test kit could not be confirmed.

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Conflict of Interest

None to declare. All authors declared no conflict of interest upon the Baiya Phytopharm company, owner/developer of the rapid antibody test kit.

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