ORIGINAL ARTICLE

EFFICACY OF PANBIO™ COVID-19 AG RAPID TEST IN SARS-COV-2 DETECTION: COMPARISON WITH RT-PCR TEST

Shabana Asif[1], Aashi Ahmed[2], Ambreen Gul[2], Tariq Abbasi[3]

Department of Pathology, Margalla Hospital, Taxila, Department of Biochemistry, HITEC Institute of Medical sciences (IMS, Taxila) NUMS, Rawalpindi, [3]Department of Anaesthesia, Ayub Teaching Hospital, Abbottabad-Pakistan

Background: Evidence on performance of Rapid Antigen Detection Tests to recognize SARS-CoV-2 symptomatic patients in our context is limited. This study was aimed to evaluate Panbio™ COVID-19 Ag Rapid Test Device (Abbott Diagnostics, Jena, Germany) in identifying SARS-CoV-2 infection in comparison with RT-PCR test. **Methods:** This cross-sectional validation study was carried out at Margalla Hospital, Taxila from October, 2020 to March, 2021. Three hundred and eighty-two participants of both gender and all ages, symptomatic for 3–4 days were included in this study. For each participant, two nasopharyngeal swabs were collected by trained lab technicians according to SOPs, one for Rapid Antigen Test and other for RT-PCR.Covid-19 antibodies were checked 4-6 weeks after symptoms among 77 randomly selected participants to further evaluate the performance of Rapid Antigen Test. Data was analyzed using SPSS-26. **Results:** The mean age of the participants was 43.1 years (SD=15.9). More than half of participants were males (n=213%=55.8) and 169 (44.2%) were females. Sensitivity of Rapid Antigen Test was calculated to be 94.3%, whereas the specificity was 39.7%. Out of 34 RT-PCR negatives that were initially detected positive on Rapid Antigen Test, 33 demonstrated presence of COVID-19 antibodies. **Conclusion:** Panbio™ COVID-19 Ag Rapid Test was found to have 93.4% overall sensitivity and relatively low overall specificity (37.9%). Rapid antigen testing using Panbio™ COVID-19 Ag Rapid Test Device can be effectively used to scale up mass testing to interrupt transmissibility of COVID-19 infection by generating quick result.

Keywords: SARS-CoV-19; COVID-19; Rapid antigen detection; Reverse transcriptase polymerase chain reaction; Sensitivity; Specificity

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INTRODUCTION

COVID-19 caused by novel severe acute respiratory coronavirus-2 (SARS-CoV-2), was declared a global pandemic by WHO on 12th March, 2020. Associated with significantly high morbidity and mortality, the disease has disrupted societies and economies globally. The disease presents clinically with fever, fatigue, myalgia, headache, dry cough, dyspnoea, loss of smell and taste in mild cases. Manifestations among severe and critically ill patients include respiratory distress syndrome, respiratory failure, and other serious complications including death.[1] Early diagnosis is crucial for control of outbreak and for patient management. A specific and highly sensitive standard test for screening and diagnosis of COVID-19 by RNA assays is reverse transcription-quantitative polymerase chain reaction (RT-qPCR) analysis using respiratory samples.[2] The sensitivity of RT-PCR test in identifying COVID-19 cases is reported to range from 71–98%, with 2–29% of false negative rates.[3] This test is expensive, time consuming and requires facilities setup, special materials, biosafety measures and skilled laboratory staff. Testing operation for at least four hours may lead to delayed reporting ultimately leading to anxiety of the suspected COVID-19 patients and a gap in which infection can spread.[4] Under ideal conditions turnaround time of RT-PCR is 6–8 hours that signifies the need of rapid diagnostic tests. In addition to this, many health care facilities have limited testing capacity by molecular method, either due to manpower or resources deficiency linked to inadequate equipment and reagents for testing.[5] According to standard operating procedures recommended by WHO for collection, storage, transportation and handling of potentially infectious sample, safety of healthcare personnel is a big issue due to highly infectious nature of disease. Quality of specimen and cold chain maintenance during transportation is mandatory for accuracy of RT-PCR test result. Inappropriate sample collected at improper time may generate false positive result.[6] Testing for presence of COVID infection among symptomatic patients and contact tracing in well controlled clinical settings is focused on therapeutic care and is not sufficient for containing transmission. In order to reduce viral transmission among population, mass screening to identify infectious individuals followed by isolation is focused on improving public health outcomes. However, massive testing for diagnosis of

SARS-CoV-2 testing is limited due to dependence on RT-PCR test.[7] To overcome these concerns and to detect COVID-19 quickly, Rapid Antigen Tests (Ag-RDT) are approved as valuable alternative to RT-PCR for clinical use. The SARS-CoV-2 Rapid Antigen Tests are rapid chromatographic immunoassay for the qualitative detection of specific antigens of SARS-CoV-2 present in nasopharyngeal or combined nasopharyngeal/oropharyngeal samples. A Rapid Antigen Test with at least 80% sensitivity and a specificity higher than 97% is recommended to obtain reliable results.[8] The Panbio™ COVID-19 Ag Rapid Test is a lateral flow assay which detects SARS-CoV-2 nucleocapsid protein in nasopharyngeal specimens. These tests have lower sensitivity than molecular assays and are known to perform best with high viral load specimens, preferably within seven days after onset of symptoms.[9] These tests are relatively inexpensive and do not require expensive equipment. These tests are found to be highly effective in identifying COVID-19 infection in asymptomatic contacts. This early detection of potentially highly infectious contacts contributes to control the spread of SARS-CoV-2 infection in community.[10] Analysis of sensitivity and specificity of rapid antigen testing in comparison to gold standard Rt-PCR is required to be established in Pakistan to curb the burden on health system and to provide a relatively economic and quick testing alternative to population to curtail ongoing COVID-19 pandemic. We aimed to assess efficacy of Rapid Antigen Test with RT-PCR that might contribute in framing new and effective strategy for screening and diagnosis of SARS-CoV-2 infection in Pakistan.

MATERIAL AND METHODS

This single-centre cross sectional validation study to evaluate efficacy of Rapid antigen testing (Ag-RDT) in detecting COVID-19 infection was carried out in Margalla Hospital Taxila from October, 2020 to March, 2021 during the second wave of corona pandemic, after approval of Ethical Review Committee of the hospital. Patients of all age groups irrespective of their gender were included consecutively after informed consent. The confidentiality of the patients was preserved. Based on a prevalence of 20% of disease, 380 samples were needed to determine sensitivity and specificity with a 95% confidence interval (CI) and a target significance level of 0.05 to achieve a minimum power of 80%.[11] A total of 382 participants were included in the study who presented in the outpatient and inpatient department of hospital, having symptoms for 3–4 days. In order to determine the efficacy of Rapid Antigen Testing device, we performed Rapid Antigen Test of all participants, using Panbio™ COVID-19 Ag Rapid Test Device (Abbott Rapid Diagnostics, US), followed by confirmation of the positive/ negative results using RT PCR technique. For each participant, an asopharyngeal swab was collected by trained lab technician after wearing proper PPEs according to standard operating procedure for sample collection. Result was read at 15 minutes. The second nasopharyngeal swab was taken from the contralateral nostril 6–12 hrs after the first sample following the same SOPs. Each specimen container was labelled with the patient's ID number and the date. These samples were then transported to tertiary care center for RT-PCR. Delayed specimens were stored at 2–8 °C for up to 72 hours after collection. To further evaluate the validity of antigen testing we performed serum antibody screening for SARS-CoV-2 among 71 randomly selected participants 4–6 weeks after their symptoms by Cobas E-411 analyzer using combo Roche antibody kit.

RESULTS

Out of total 382 participants, 213 (55.8%) were males and 169 (44.2%) were females. The mean age of the participants was 43.1 years (SD=15.9). Minimum age was 1 year and maximum age of the participant was 82 years. All 382 participants were tested by Panbio™ COVID-19 Ag Rapid Test Device, confirmation of diagnosis of all participants for COVID-19 infection was done by RT-PCR test. Out of total 382 COVID-PCR tests, 211 turned positive, thereby producing a test positivity rate of 55.2%. Test positivity rate for Rapid Antigen Test was 79%.

Table-1: Cross tabulation of Rapid antigen test and RT-PCR Results

Rapid antigen Test	RT-PCR		Total
	Positive	Negative	
Positive	199	103	302
Negative	12	68	80
Total	211	171	382

Sensitivity of Rapid antigen test was calculated to be 94.3%, whereas the specificity was 39.7%. Predictive value of positive Rapid antigen test was 60%, whereas predictive value of negative rapid antigen test was 85%. False negative rate was 5.6% whereas false positive rate was 60.2 %.

Serum antibody for COVID-19 infection was checked randomly among 71 participants on Cobas c-311 analyzer using combo Roche antibody kit. Out of 34 RT-PCR negatives, antibodies were detected among 33 individuals, showing that they were not identified by RT-PCR test. Covid antibodies were detected among 6 participants only who were tested negative on rapid antigen test thereby

confirming that rapid antigen test missed lesser number of individuals as compared to RT-PCR test.

Table-2: Detection of Covid-19 antibodies among RT-PCR and Rapid Antigen Test positives and negatives

Test		Covid-19 antibodies		Total
		Positive	Negative	
RT-PCR	Positive	37	0	37
	Negative	33	1	34
Rapid Antigen Test	Positive	64	1	65
	Negative	6	0	6

DISCUSSION

This study was aimed to evaluate the efficacy of Panbio™ COVID-19 Ag Rapid Testin detecting SARS-CoV-2 infection in comparison with RT-PCR test. Sensitivity and specificity of Panbio™ COVID-19 Ag rapid test in present study was 94.3% and 39.7% respectively. These findings contradict the results of studies conducted at Netherlands and Aruba, which showed test sensitivity of 72.6% (95%CI: 64.5–79.9%) and 81.0% (95% CI: 69.0-89.8%) respectively. Whereas, the specificity established both in Netherlands and Aruba was 100% (95% CI: 99.7–100%). Probability of low specificity and high false positivity (60%) of Panbio™ COVID-19 Ag rapid testing present study might be associated with varying duration of symptoms and non-segregation of samples according to Ct values.[12] In present study, sensitivity of Rapid Antigen Test was found to be 94.3%, whereas the specificity was 39.7%. These findings are comparable with results of study conducted by K Alexander *et al* in Germany, according to which sensitivity of Rapid Antigen Test (Rosch) was 100 for samples with a high viral load (Ct <25). The sensitivity was 95% for specimens with a medium viral load (Ct 25 -<30), 44.8% for low viral load (Ct 30- <35) and 22.2% for samples with very low (Ct >035) viral load. However, in present study no segregation of specimens according to viral load was done before conducting Rapid Antigen Test. Secondly in contrast to methodology of present study, K Alexander et al performed RT-PCR first and RT-PCR positives and negatives were then tested by using Rapid Antigen Test using Roche Kit. Specificity reported by same study was 96% which contradict the findings of present study.[13] Overall sensitivity and specificity of Panbio™ COVID-19 Rapid Antigen Test reported by another study was 57.1% (95% CI 45.9–67.9%) and 100% respectively. Sensitivity was found to vary with duration of study. Reported sensitivity during 3–4 days of onset of symptom was 66.7%. Sensitivity was found to decrease 63%, 47.1% and 50% when testing done on 2nd day, within 24 hours and on 5th day after onset of symptoms respectively.[9] These findings contradict the results of present study. Sensitivity and specificity of Rapid Antigen Test estimated was 94.3% 39.7% respectively. However, a high false positive rate of 60.2% and detection of COVID-19 antibodies among 33 participants out of 34, who tested negative by RT-PCT might support that they were not identified by RT-PCR contributing to low specificity in this study.

More than 150 SARS-CoV-2 RNA detection kits have been approved by the Food and Drug Administration. Our results suggest that Panbio™ COVID-19 AG Rapid Test correctly identified 94.3% of SARS-CoV-19 patients who actually had the disease latter on confirmed by RT-PCR. Overall sensitivity and specificity of same kit reported in Spain was 73.3% (95% IC: 62.2–83.8) and 1% respectively. Sensitivity according to duration of symptoms was found to slightly increase from 85.3% (95 % IC: 73.4–97.2) to 86.5% (95% IC: 75.5–97.5) with symptoms for <5 days and <7 days respectively. However, for symptomatic patients with >7 days since onset, sensitivity was found to decrease to 53.8%. Specificity in all cases was 1.0% opposing specificity established by present study that was 39.7%.[14] Panbio™ COVID-19 AG Rapid Test has established acceptable accuracy among symptomatic patients at Primary Health Care setup too. The overall sensitivity was of 71.4% (95% CI: 63.1%, 78.7%), the specificity of 99.8% (95% CI: 99.4%, 99.9%), the positive predictive value of 98.0% (95% CI: 93.0%, 99.7%) and a negative predictive value of 96.8% (95% CI: 95.7%, 97.7%). These findings are comparable to Sensitivity (94.3%), specificity (39.7%), positive predictive value (60%) and negative predictive value (85%) established in present study conducted on symptomatic patients.[15] Overall sensitivity and specificity of Panbio™ COVID-19 AG Rapid Test was 48.1% (95% CI 37.4–58.9) and 100% (95% CI 99.3e100), respectively among asymptomatic close contacts of SARS-CoV-19 patients. However, those tested positive by Panbio™ COVID-19 AG Rapid Test later became symptomatic compared with their negative counterparts (p<0.001).[16]

Sensitivity and Specificity of Panbio™ COVID-19 AG Rapid Test was found to be highly variable compared to that documented by manufacturer. According to a study in Germany, the sensitivity and specificity was 42.57% (95% CI: 33.38–52¢31%) and 99.68% (95% CI: 99.48–99.80%) respectively.[17] According to a systematic review carried out to assess sensitivity and specificity of rapid antigen tests, overall sensitivity of Panbio™ COVID-19 Ag Rapid Test was 78.41% (95% CI:76.7–79.9%) and overall specificity was 99.61% (95% CI: 99.4–99.7%).[18] Sensitivity (94.3%) and specificity (39.7%) established by our study is comparatively higher and lower than results reported by this meta-analysis respectively.

CONCLUSION

Panbio™ COVID-19 AG Rapid Test has acceptable sensitivity and low overall specificity. It detected 94.3% of SARS-CoV-2 positive cases among symptomatic individual as in real life settings and missed 5.6% of cases latter confirmed with RT-PCR. However, a high false positive rate of 60.2% yielding a specificity of 39.7% may lead to overstressing of health facilities. Although less sensitive than RT-PCR, this test can be preferred when rapid identification of positive patient is critically required on part of its low complexity, speed and low-cost. These tests can effectively contribute in combating the COVID-19 pandemic in low resource densely populated settings especially when prompt diagnosis is vital.

Limitations: A delay of 6–12 hours between two samples by two different lab staff and temperature variation during transportation of PCR samples to tertiary care hospital might have contributed to low specificity established by this study and detection of COVID-19 antibodies in serum of individuals who tested positive on Panbio™ COVID-19 Ag Rapid Test but had negative RT-PCR result.

AUTHORS' CONTRIBUTION

SA: Concept & Study design, data collection. AA: Data analysis, data interpretation. AG: Literature review, write-up. TA: Proof reading

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Address for Correspondence:

Ambreen Gul, Department of Biochemistry, HITEC Institute of Medical sciences (IMS, Taxila) NUMS, Rawalpindi-Pakistan

Email: ambreengul0300@gmail.com