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DIAGNOSTIC ACCURACY OF PANBIO COVID-19 RAPID ANTIGEN METHOD FOR SCREENING IN EMERGENCY CASES

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ABSTRACT

Objective: To determine the diagnostic accuracy of PANBIO COVID-19 rapid antigen method in nasopharyngeal swab, for screening of COVID-19 infection in emergency cases.

Study Design: Cross-sectional validation study.

Place and Duration of Study: Department of Microbiology, Combined Military Hospital, Multan, from Jan to Mar 2021.

Methodology: After taking approval from institutional ethical review committee, total 1539 patients were included in this study according to sample size. With informed consent, nasopharyngeal swab specimens were taken for PANBIO COVID-19 rapid antigen method from each patient presenting as emergency medical/surgical case to Combined Military Hospital Multan as well as for Polymerase Chain Reaction for SARS CoV-2 RNA. PANBIO COVID-19 rapid antigen method and polymerase chain reaction for SARS CoV-2 RNA were performed simultaneously on swabs. Polymerase chain reaction for SARS CoV-2 RNA was considered to be the gold standard for comparison with the PANBIO COVID-19 rapid antigen method.

Results: A total of 21 patients had SARS CoV-2 RNA detected by polymerase chain reaction indicating COVID-19 infection. Out of polymerase chain reaction positive patients, PANBIO™ COVID-19 Ag test was able to detect 19 cases. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy was calculated and found to be 90.47%, 100%, 100%, 99.8% and 99.8% respectively.

Conclusion: PANBIO™ COVID-19 rapid antigen method was found to have excellent diagnostic accuracy in detection of COVID-19 infection. It can provide as a good alternate test for screening of masses with a short turnaround time of only 15 minutes.

Keywords: Antigen, COVID-19 serological testing immunochromatography, Polymerase chain reaction, SARS-CoV-2.

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INTRODUCTION

We live in a moment when the greatest act of love is to stay away from the object of your affection.[1] The reason for this is SARS-CoV-2, originated in late December 2019 in Wuhan, the capital of Central China's Hubei Province. It spread like wildfire, all over the world, impacting lives and norms.[2] It has been almost a year but still this pandemic is yet to be contained.[3] Due to highly contagious nature of SARS-COV-2, main focus has been on identification and isolation of COVID-19 patients in order to curb the spread.[4] In addition there was a hurdle of limited clinical sensitivity due to nature of specimen.[5] Studies have been conducted to evaluate if virus could be isolated from other biological specimens. It was ascertained that virus could also be found in feces of COVID-19 patients (29%) but mainly in respiratory specimens (93%).[6]

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At present, various testing modalities are being used to detect SARS-CoV-2. Serological tests are of lesser importance in diagnosing active cases due to prolong time to positivity as well as lower sensitivity and specificity.[7] Antigen detection tests based on lateral flow assays are being evaluated as they could help in early identification and may be used as point of care tests.[8] These are based on similar principle of colloidal gold membrane pre coated with immobilized anti-SARS-CoV-2 antibody.[9] PANBIO COVID-19 rapid antigen test method is one such novel modality being assessed by World Heatlh Organization (WHO) for emergency use.

In this study, we aimed to determine the diagnostic accuracy of PANBIO COVID-19 Ag Rapid Test Device for detection of SARS-CoV-2 in nasopharyngeal swab specimens in our setup to help in finding an alternate to PCR for SARS-CoV-2 with shorter turnaround time while being cost effective to enable prompt treatment and isolation for masses.

METHODOLOGY

This cross sectional validation study was carried out at Department of Microbiology, CMH Multan from January to March 2021. We calculated sample size by sensitivity-specificity calculator[10], using PANBIO rapid antigen method sensitivity at 90% and 99% specificity 8, COVID-19 prevalence of 7.2%[11], confidence level at 95% and margin of error at 5%. The estimated sample size was 481. However, in order to ascertain the performance of this method sample size was extended to 1539 patients. Non-probability, consecutive sampling was done.

Incluison Criteria: All those cases for emergency preoperative work-up and cases needing emergency medical intervention were included in this study.

Exclusion Criteria: Duplicate swabs of the same patient, to monitor disease progression and follow-up cases with confirmed PCR positive were excluded.

Permission was obtained from Institutional Ethics Committee (IRB no. 179/trg) and informed consent was taken from all the patients. Demographic information like name, age, gender and address was obtained. The PANBIO COVID-19 rapid antigen test device is a gold colloidal membrane-based lateral flow Immunochromatography assay by Abbott, USA, which detects the SARS-CoV-2 in nasopharyngeal swab samples. Nasopharyngeal swabs were inserted in buffer containing tubes and mixed properly as per manufacturer's instruction. All samples were analyzed, in a biosafety cabinet level 2, immediately within an average time of 20-30 min. These samples were processed and stored at room temperature 15-30^{o}C. Five drops of inoculated buffer were dispensed onto test cassette and results were recorded at 15 minute's time.

PCR for SARS CoV-2 was performed using two swabs; one nasopharyngeal and other oropharyngeal to increase the yield. The collected swabs were placed into 3ml Viral Transport Medium (VTM) and stored at 4^{o}C (±2) until further processing. Nucleic acid extraction was done on auto extractor (Genrui, China) followed by Reverse Transcription Polymerase Chain Reaction (RT-PCR). All results interpretation was done as per product manual (Sansure Biotech Inc., China), China. This method utilizes COVID-19 ORF 1ab and N (Nucleocapsid) gene as the target regions to achieve the detection through fluorescent signal changes. Nucleic acid amplification and detection was done on thermocycler (AMPLilab 96, Adaltis, Italy). The threshold Cycle (Ct) of 40 was taken as cutoff as per product's manual. A typical S shaped amplification curve at FAM and/or ROX channel and the curve at CY5 (internal control) with Ct<40 was taken as positive and vice versa.

The data obtained was entered Statistical package for social sciences (SPSS) version 25 for statistical data analysis. A 2x2 table was made to calculate sensitivity, specificity, Positive Predicted Value (PPV), Negative Predictive Value (NPV) and diagnostic accuracy of PANBIO COVID-19 rapid antigen test device against PCR for SARS CoV-2. Further descriptive statistics were used to ascertain the same by chi square test. Likelihood ratio and Receiver Operating Curve (ROC) curve were also measured. *p*-value was calculated by analysis in SPSS 25 by using covariation and Pearson equation for two-tailed study. The *p*-value of ≤0.05 was considered significant and results of PANBIO COVID-19 rapid antigen test device were validated against PCR for SARS CoV-2 as the reference method.

RESULTS

A Total of 21 patients had SARS CoV-2 RNA detected by PCR indicating COVID-19 infection out of 1539 total cases. PANBIO COVID-19 rapid antigen test was able to detect 19 true positive cases and no false positive ones. Of the remaining 1520 cases, 1518 were true negative while 2 were false negative. The two false negatives had Ct values of 28 and 30 respectively. Data analysis yielded *p*-value of <0.01 with AUC on ROC at 0.952. Comparison of PANBIO COVID-19 rapid antigen test with reference method PCR for SARS CoV-2 is given in Table-I.

The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy was calculated and given in Table-II.

Table-I: Comparison of PCR for SARS CoV-2 & PANBIO COVID-19 Ag rapid test.

		PCR for SARS CoV-2	
		Positive	**Negative**
PANBIO COVID-19 rapid antigen	Positive	19	-
	Negative	2	1518

Table-II: Diagnostic variables of PANBIO COVID-19 antigen rapid test.

Diagnostic Parameters	Values
Sensitivity= 19/(19+2) x 100	90.47%
Specificity= 1518/(1518+0) x 100	100%
Positive predictive value= 19/(19+0) x 100	100%
Negative predictive value= 1518/(1518+2) x 100	99.8%
Diagnostic accuracy=(19+1518)/1539 x 100	99.8%

DISCUSSION

It has been over a year and 3rd wave of COVID-19 virus is wreaking havoc all over the world.[12] The

silver lining appears to be in the two tiered approach of testing and isolating positive cases stopping spread while vaccinating masses with an aim to achieve herd immunity.[13,14] Vaccines are being administered but facing many hurdles like supply shortage and side effects.[15]

PANBIO COVID-19 rapid antigen method with short turnaround time while costing almost half as much as compared to PCR test has the potential to be a good alternate to nucleic acid testing. Being lateral flow assay its ease of use is also a salient point because PCR requires special expertise.

Sampling for SARS-CoV-2 is different in a way that swabs are taken from upper respiratory tract instead of blood samples. Hence, proper technique is essential for correct result that is quite lacking in even the developed countries. This was evident in study conducted by Mark *et al*, which studied the effect of simulation education on HCWs and revealed that post education sampling yield increased significantly.[16]

In a study conducted by Gremmels *et al*, l for real life validation of PANBIO COVID-19 rapid antigen test in symptomatic cases, the sensitivity and specificity of PANBIO™ COVID-19 Ag test was found to be >95% and 100% respectively while using Ct values <32 cycles as cut-off for PCR positivity.[17] Specificity is concordant with our study however sensitivity in our study is lower which could be due to our screening of selected population of asymptomatic cases having lower viral load or decreased prevalence.

Fluorescence Immunochromatography assay antigen detection test kit is another method by Shenzhen Bioeasy Biotechnology Co Ltd, China. It was evaluated by Porte, *et al,* for diagnosis of SARS CoV-2 in respiratory samples and it yielded sensitivity of 93.9% while specificity of 100%.[18] It is comparable to our antigen detection method, however, it requires fluorescence immunoassay analyzer rendering it difficult and equipment based to interpret the results.

Right test at right time is the key for expeditious diagnosis and same is true for COVID-19 infection. For the first week both serological tests and molecular tests are not as beneficial due to low viral load during incubation period.[19] However, PANBIO COVID-19 rapid antigen detection method has shown to have 100% sensitivity, in COVID-19 patients, 0-3 days after exposure. So this method can prove to be handy and reliable in contact tracing and diagnosis of patients during incubation period.

RECOMMENDATION

PANBIO COVID-19 rapid antigen detection method may be used for screening of masses for both suspected and non-suspected cases with proper sampling technique. This could be done at a centralized reference lab setup or peripheral satellite points without even the requirement of biosafety cabinet when the local risk assessment so dictates and proper precautions are in place.

CONCLUSION

PANBIO COVID-19 rapid antigen detection method was found to have excellent diagnostic accuracy. It can provide prompt diagnosis and effective isolation of positive cases with markedly shorter turnaround time. Lower cost means testing three cases in the cost of one RT-PCR enabling effective mass screening.

Conflict of Interest: None.

Authors' Contribution

RKA: Data analysis, results, and discussion of literature, SA: Data collection, analysis, interpretation, discussion of literature and review, FA: Discussion review and correction, SN: Data analysis and results, MY: Review of article and correction, TA: Discussion and literature review.

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