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Diagnostic Value of Rapid COVID-19 Antigen Test (Panbio, Abbott) Compared to RT- PCR in Suspected Cases of SARS-CoV-2 Infection at a Tertiary Care Center

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ABSTRACT

Objective: To determine the diagnostic value of rapid COVID-19 antigen test (Panbio, Abbott) in comparison with Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) in suspected community cases of SARS-CoV-2 infection at a tertiary care center in Pakistan

Study Design: Cross sectional study.

Place and Duration of Study: Pathology Department, Combined Military Hospital, Lahore Pakistan, from Jun 2020 to Jun 2021.

Methodology: The diagnostic value of the Panbio®COVID-19 Antigen Rapid Test (Panbio, Abbott), was determined in comparison with RT-PCR in suspected community cases of SARS-CoV-2 infection at a tertiary care center on samples taken simultaneously. 200 individuals reporting to the hospital with signs and symptoms of potential COVID infection or history of significant contact exposure (>1 hour without masking and social distancing) to a RT-PCR positive COVID patient and concurrently requiring a rapid COVID antigen test due to an underlying health condition were included in the study by consecutive sampling.

Results: Out of 200 individuals, 53(26.5 %) were COVID positive by RT–PCR whereas 147(73.5%) were clearly negative with no cases of indeterminate viremia on RT PCR. 32(60.3%) out of 53 RT-PCR positive COVID cases were also found to be positive by COVID-19 Antigen Rapid Test, whereas 21(39.6%) were negative. Out of 147 RT-PCR negative COVID cases, 146(99.3%) were negative by COVID-19 Antigen Rapid Test as well whereas 1(0.68%) was positive.

Conclusion: COVID-19 Antigen Rapid Test is suitable adjunct to RT-PCR testing in suspected cases in emergent settings in early days of admission.

Keywords: COVID-19, Rapid COVID-19 antigen test, RT- PCR.

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INTRODUCTION

COVID pandemic has affected more than 184 million people worldwide todate with 3.8 million deaths globally and almost 1% of all currently active cases being serious or critical.[1] The global average masks the great variance in healthcare costs imposed upon different health systems world over and the subsequent difference in case fatalities and disease burden in different countries.[2,3] Rapid diagnosis of an index COVID case and timely screening of possible contacts to stop further spread of source by effective home or hospital based quarantine has remained the bedrock of COVID public health policies.[4] Gold standard for diagnosis of SARS-CoV-2 infection is RT-PCR, however it is time consuming and laborious requiring well trained staff to ensure reliability of results.[5]

Rapid COVID antigen tests have now been introduced world over for aiding in a time efficient diagnosis of COVID infection at the bedside. However, their reliability has been called into question due to purportedly low sensitivity and WHO has recommended that they should not be used alone for clinical diagnosis.[6,7] Despite this caveat, the easy availability of the rapid test kits and their ease-of-use has prompted health authorities world over to evaluate their reliability to include them as an additional, adjunct or stand-alone tool for COVID diagnosis with varying results.[6]

Multiple types of rapid COVID antigen tests have been granted emergency use authorization by FDA since the start of pandemic and have since become available commercially.[7] Panbio ® COVID-19 Antigen Rapid Test (Panbio, Abbott) is a lateral flow assay based rapid test device which has shown a high sensitivity in early detection of COVID infection in ambulatory as well as in-patient settings. The test is based on the principle of detection of viral antigen in the patient's blood by the antigen binding to the SARS-CoV-2 antibody immobilized and coated on the test device which can be seen within twenty minutes.[8] In

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this way, the rapid tests can help in overcoming the delay in diagnosis thereby reducing the in-hospital preCOVID bed occupancy and improve the workflow.

The objective of this study was to determine the diagnostic value of rapid COVID-19 antigen test (Panbio, Abbott) by comparing it with RT-PCR as a reference standard and to determine it's sensitivity, specificity, positive and negative predictive values in suspected community cases of SARS-CoV-2 infection coming to the hospital in Pakistani population.

METHODOLOGY

The cross sectional study was carried out at Department of Pathology, Combined Military Hospital, Lahore Pakistan, from from June 2020 to June 2021, after approval by Ethical Review Board (Letter no 312/2021). Informed consent was taken from patients being involved in the study. Sample size was calculated using online sample size calculator (http://wnarifin.github.io) taking confidence level 95%, margin of error 5%, and an expected sensitivity and specificity of 0.538 and 1 respectively as per previously published study.[9] The estimated sample size came out to be 191 patients.

Inclusion Criteria: Individuals reporting to the hospital with clinical features of potential COVID infection or history of significant contact exposure (>1 hour without masking and social distancing) to a RT-PCR positive COVID patient and subsequently requiring a rapid COVID antigen test due to an underlying health condition were included in the study by consecutive sampling.

Exclusion Criteria: Cases of suspected COVID reinfection with one instance of previously confirmed RT-PCR based COVID positivity were not included. Additionally, COVID positive patients transferred to our hospital were also excluded.

As per hospital protocols, all suspected COVID cases reporting at emergency room were subjected to determination of COVID status by RT–PCR. However, in high risk cases such as poly injury, head injuries, emergency caesarians and urgent laparotomies rapid COVID antigen testing can be used to aid decision making till the PCR results become available. The rapid COVID antigen testing was therefore carried either as an aid to clinical triage in emergency cases to determine patient admission pathway in hospital or carried later during shifting of patients to intensive care unit or operation theatre in the settings of urgent surgery.

Oropharyngeal swabs were taken for RT-PCR for COVID-19 in all cases by a trained sampler on the day of admission. The samples were transferred to hospital laboratory within two hours of submission from outpatient department and were processed for viral RNA extraction by TANBead®Nucleic Acid Extraction Kit on Smart LabAssist®automated autoextractor the same day followed by amplification by Argene SARS-COV-2 R-Gene kit on 96 well RT PCR Amplilab, Adaltis thermal cycler. The final results were validated through an individual single channel positive control in all cases and repeated after fresh extraction in case of equivocal cases. Repeat equivocal/borderline cases with good positive control were labeled as borderline with an advice of repeat sampling at 48 hours. After sample submission, one consultant pathologist supervised all steps of RT-PCR in person at all times from viral RNA extraction to amplification and reporting.

The procedure for conducting Panbio®COVID-19 Antigen Rapid Test (Panbio, Abbott) was streamlined by designating one consultant pathologist as the focal person (principal investigator in this case, PI) who received all the requests for subject test from different wards, outpatient departments, emergency, ICU as well as preoperative settings. On receipt of request, a trained laboratory staff member was assigned who proceeded to perform this test at the bedside by taking a nasopharyngeal swab followed by the procedure as per manufacturer's instructions.[10] The final result was read in conjunction with controls by the PI and communicated to the requesting clinician within one hour of initiation of request.

Age, gender, date of admission, ward, date of PCR and rapid COVID antigen testing, clinical severity at presentation and number of symptoms were recorded in all cases on a specially designed questionnaire. Evidence of CT scan chest and CT scan severity score was also documented. The data were analyzed using SPSS version 20 as well as Microsoft Excel 2010. Frequency of rapid COVID antigen test results in RT-PCR positive cases was determined and a chi-square test of independence was performed to examine the relation between RT-PCR & rapid COVID antigen test positivity ($p<0.05$ considered significant). Sensitivity and specificity of rapid COVID antigen test as compared to RT-PCR were calculated.

RESULTS

A total of 200 study subjects were included in the study. Out of this, 167(83.5%) were males and 33 (16.5%) were females with the average age of males

and females being 41.9±20.96 and 43.2±22.74 respectively. The age distribution of study subjects was found to have a bimodal distribution with most of the patients (n=49, 24.5%) above 60 years of age. The second most common age group was 31-40 years with 42 patients (21%) followed by the age group 21-30 years with 35 patients (17.5%).

Out of 200 study subjects, 53 were COVID positive by RT–PCR (26.5%) whereas the rest were clearly negative 147(73.5%) with no cases of indeter-minate viremia on RT-PCR. 32(60.3%) out of 53 RT-PCR positive COVID cases were also found to be posi-tive by COVID-19 Antigen Rapid Test, whereas 21 (39.6%) were negative. Out of 147 RT-PCR negative cases, 146(99.3%) were negative by COVID-19 Antigen Rapid Test as well whereas 1(0.68%) was positive.

The over all sensitivity, specificity, positive predictive value & negative predictive value of COVID-19 Antigen Rapid Test as compared to RT-PCR was 60.4% (46% to 73.55% with 95% Confidence interval), 99.3% (96.27% to 99.98%), 97% & 87.4% respectively as shown in Table-I.

Table-I: Comparison of Rapid COVID 19 Antigen test (Panbio) and RT PCR for COVID 19 (n=200)

Rapid COVID 19 Antigen Test (Panbio)	RT-PCR COVID-19	
	Positive	Negative
Positive	32	1
Negative	21	146
Over all sensitivity	60.4%	

We evaluated the association of rapid COVID antigen test positivity with day of testing after admission with the admission day designated as day 0. It was seen that the test positivity declined with every passing day and was significantly reduced from day 5 onwards as shown in Table-II.

When only patients with active symptoms were considered at <3 days, <5 days or ≥5 days since admission, the sensitivity of rapid COVID antigen test as compared to RT-PCR was found to be 75.68% (95 % CI: 58.80% to 88.23%) , 69.05% (95% CI: 52.91% to 82.38%) and 36.3 % (95% CI: 10.93% to 69.21%) respectively as shown in Table-III.

Table-II: Association of Rapid COVID Antigen test Positivity with day of Testing Post-Admission(n=200)

Day of Testing after Admission	RAPID test positivity	
	No. of tests	Positive
0	16	12(22.6%)
1	14	11(20.75%)
2	7	5(9.4%)
3	3	0(0%)
4	2	1(0.53%)
5	4	1(0.53%)
6	5	1(0.53%)
9	1	1(0.53%)
32	1	1(0.53%)
	53	33

Table-III: Comparison between rapid COVID antigen test and RT-PCR (n=200)

<3 days			<5 days			≥5days		
Rapid COVID Antigen test	RT-PCR		Rapid COVID Antigen test	RT-PCR		Rapid COVID Antigen test	RT-PCR	
	Positive	Negative		Positive	Negative		Positive	Negative
Positive	28	1	Positive	29	1	Positive	4	0
Negative	9	90	Negative	13	130	Negative	7	17
Sensitivity	75.68%			75.68%			36.3%	

Finally, the association of rapid COVID antigen test & RT-PCR test result with disease severity was also evaluated. The rapid test result positivity did not show any significant association with the clinical severity of disease and was absolutely ineffective in detecting viremia in asymptomatic cases. In cases of mild, moderate and severe disease clinically, the results of rapid test were positive in 41.4%, 45.4% and 50% cases only respectively (as shown in Table-IV) indicating an inability to positively identify a large number of serious patients.

Table-IV: Association of rapid COVID Antigen test & RT-PCR test result with Disease Severity (n=200)

	RAPID test result	COVID PCR Result
	%age positivity	%age positivity
Disease severity		
Asymptomatic	0	6 (100%)
Mild	12 (41.6%)	17 (100%)
Moderate	11(45.4%)	16 (100%)
Severe	10 (50%)	14 (93.3%)

DISCUSSION

The rapid COVID tests have gained popularity due to easy availability and a short turn around time with minimum expertise to yield reproducible results.[11] However, the evaluation of their reliability has proved difficult and has yielded varying results in multiple studies over time leading to WHO cautioning against their sole use for diagnostic purposes.[12,13]

Furthermore, the extremely variable COVID case fatality rate per 1000,000 population in different countries signifies the stark difference in prevalence of

COVID in different populations and this prevalence in turn affects the predictive value of a test like the rapid COVID antigen test making it absolutely essential to base the usage guidelines for this test on local experience.[14,15]

Our results indicated a low overall sensitivity for this test at around 60.4%. This goes against established scientific consensus that, "It is clearly desirable to have a test that is both highly sensitive and highly specific".[16] We also compared our results with twelve international studies carried out to evaluate diagnostic accuracy of Panbio®rapid COVID antigen test over the last one year. These studies showed great variation in reported sensitivity of this test in different settings ranging from 42.5% to 91.7%.[17,18] One possible cause could be the differences in prevalence of COVID in different populations. It has been shown conclusively that a change in prevalence from the low to high value results in a corresponding statistically significant variation in sensitivity of a diagnostic test as well.[19,20]

Various authors have determined that the limit of detection (LOD) of this rapid test is two orders of magnitude less than RT-PCR with the calculated LOD at 10−4 viral copies.[21,22] This explains the inadequate sensitivity of this test in positively identifying COVID infection in asymptomatic cases and at >7 days at presentation due to low viremia. The relationship of decreasing sensitivity with the increasing number of days from presentation was borne out in our study with overall sensitivity improving when the test was utilized in first three days only after presentation.

The outcome of the study clearly highlighted the necessity of tailoring the COVID rapid antigen testing guidelines to local milieu due to variability in disease prevalence as well as hitherto unknown host factors which affect disease incidence as well.[24] Judicious use of these tests with clear identification of patients who might benefit from these is imperative.[25] In our study, we found that these tests are of value as an adjunct test in addition to RT-PCR in symptomatic cases in first few days of presentation.

CONCLUSION

Our study in Pakistani population demonstrated an inability of Panbio®rapid COVID test to positively identify COVID cases in upto 50% of cases despite clinical symptoms and total inability to identify any asymptomatic COVID cases. The overall sensitivity of test (60.4%) was increased upto 75% if it was utilized in the first three days of presentation in symptomatic cases only, making it a good adjunct test to RT-PCR but a poor standalone choice of diagnostic modality especially in asymptomatic cases.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MOR: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

ND & SWK: Data acquisition, data analysis, critical review, approval of the final version to be published.

SM & BP: Concept, critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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