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Rapid Antigen Tests for COVID-19: Are Their Specificity, Sensivity and Accuracy Sufficient?

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Abstract

Objective: The aim of our study was to determine the sensitivity and specificity of rapid antigen and Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) tests which are widely used today in patients presenting with Covid-19 complaints and to evaluate these tests' routine usability.

Methods: Two samples were taken from oropharyngeal and nasopharyngeal from 100 patients (50 women, 50 men) who applied to the Covid-19 outpatient clinic of our hospital between April and May 2022. The patients attended to the study were volunteers between the ages of 18-90. One of the samples was studied with the BNG SARS-CoV-2 Antigen Rapid Test (Saliva) and evaluated with the naked eye after 15 minutes according to the company's recommendations. The other sample was studied with RT-PCR on BIO-RAD CFX Real Time System with DSCoronex Covid-19 QPCR Test Kit. The epidemiological data and clinical conditions of the patients were determined by questionnaires. The age, gender, symptoms (fever, cough, headache, diarrhea, sore throat, shortness of breath, loss of taste and smell, myalgia) of the patient and the day of the symptoms were noted down.

Results: It is known that technically rapid antigen tests generally have lower sensitivity and higher specificity than RT-PCR. In our study, the sensitivity was 71% and the specificity was 100%. The Accuracy (Diagnostic Value) rate of the rapid antigen test was determined as 90%. Our results suggest that rapid antigen tests are inexpensive and practical tests to reduce transmission, especially in epidemics however they should be selected carefully by the health care authorities.

Conclusion: The prevalence of self-reported FA based on web-based survey in Eastern Black Sea residents is relatively high and specific to the region.

Key words: Covid-19, PCR, Rapid antigen test

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INTRODUCTION

Policies regarding SARS-CoV-2 testing approaches and services vary from country to country, including rapid antigen testing for the current ongoing Covid-19 infection. RT-PCR is recommended as the gold standard test in the diagnosis of Covid-19 infection all over the world, including Turkey. However, molecular tests are expensive, require experienced personnel and equipped laboratories. Rapid antigen tests are suitable tests for several advantageous such as short lead times, user-friendliness, being able to be used anytime, anywhere, requiring minimum equipment, no preparation step, low cost and reduced personnel load. Antigen tests investigate proteins of the infectious agents and have lower specificity and sensitivity for technical reasons than nucleic acid amplification methods, depending on the infectious agent, the course of the disease and the sample type. Since the onset of the Covid-19 pandemic antigen tests have gained momentum and they have been approved for use by the World Health Organization, Centers for Disease Control and Prevention (CDC), US. Food and Drug Administration (FDA), European Center for Disease Control and Prevention (ECDC) (1-4).

Commonly used parameters to evaluate diagnostic tests are sensitivity and specificity. The Sensitivity rate is the ability of a test accurately identifying individuals with the disease, while the Specificity ratio is the test's accurately identification ability of patients without the disease. The Accuracy (Diagnostic Value) ratio indicates how confidently the results of the test can be used for diagnostic purposes. (1,3). The tests that will be used for diagnostic or screening purposes should be compared with the reference test in terms of sensitivity and specificity, The prevalence/incidence data of the population in which the test will be applied should be known in order to create the algorithms of the countries. The sensitivity of SARS-CoV-2 antigen tests is highest within the first 5 days after the onset of symptoms. The sensitivity of the test decreases especially in upper respiratory tract samples after the 5th day in symptomatic patients. (4).

Rapid antigen tests can be replaced by molecular tests when urgent decision is required in clinical patients, but symptomatic cases with negative test results and contact with a COVID-19 case should be confirmed with PCR (Polymerase Chain Reaction) or new antigen tests within 48 hours (5,2,3).

Apart from diagnostic purposes, rapid antigen tests can also be used for screening the disease. ECDC states that these tests can be used for screening purposes by repeating them at 3-day intervals in public areas. However, WHO says that nucleic acid amplification tests should be the first choice when there are sporadic cases in a country, if there is risky

patients who will undergo surgery and at the airports (4,1).

In our study, it was aimed to evaluate the routine usability of rapid antigen tests by studying simultaneous rapid antigen and PCR tests in patients who applied to the outpatient clinic with complaints suggestive of Covid-19.

METHODS

Our study was carried out with the approval of Local Ethics Committee, dated 23.02.2022 and numbered 2022/1 and with the permission of the Ministry of Health of the Turkish Republic. Informed consent form was obtained from each participant before starting the study. Our study was single blinded. Since the rates of male and female patients who applied to our hospital's Covid-19 outpatient clinic were equal, between April and May 2022, 100 patients aged between 18-90 years and who filled out the patient consent form were randomly selected, and 50 male and 50 female patients were included in the study. With the questionnaires made, the patients were questioned for age, gender, symptoms (fever, cough, headache, diarrhea, sore throat, shortness of breath, loss of taste and smell, myalgia) and the day of the symptoms.

Simultaneously, two different oropharyngeal and nasopharyngeal samples were taken for Covid-19 rapid antigen and RT-PCR test. While one of the samples was studied and evaluated with the BNG SARS-CoV-2 (saliva) rapid antigen test at the bedside, the other sample was studied with the DS Coronex Covid-19 QPCR Test Kit and the BIO-RAD CFX Real Time System. Negativity status and Ct values were noted.

Statistical Analysis

Statistical analyses were conducted with SPSS for Windows version 26.0. The sensitivity and specificity of two diagnostic tests in the same patient group were compared using the McNemar test. An independent two-sample t-test was performed to compare the Ct values of these two groups because it was assumed that each group had a normal distribution ($p>0.05$). The Spearman's rho correlation coefficient used to determine a relationship between the Ct levels and the day that symptoms first appeared. The specificity, sensitivity, and accuracy (diagnostic value) rate (diagnostic test evaluation calculator) was used to compare a rapid antigen test to a PCR test.

RESULTS

The median age of 100 patients participating in the study was 41.5 (Min-Max: 19;85). The distribution of cases by gender was equal (50%).

Sore throat was present in 23%, cough in 13%, and fever in 8% of the patients. It was observed that the patients intensified on the 2nd, 3rd and 1st days of their symptomatic phase, respectively (Figure 1).

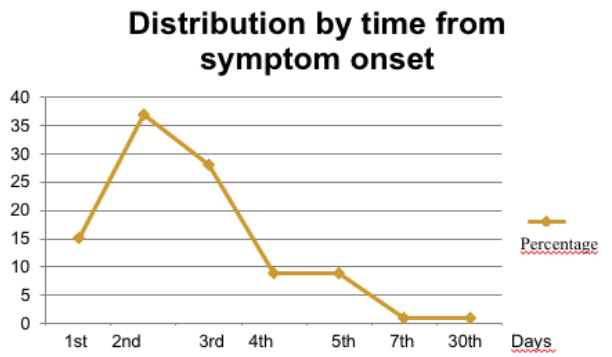

Figure 1. Distribution of patients according to the time from the onset of symptoms

As a result of PCR test, 66 (66%) of the patients were negative and 34 (34%) were positive. All of the patients who were found to be negative with the rapid antigen test were also found to be negative with the PCR test. Only 24 of the 34 PCR positive patients were also positive with the antigen test (Table 1).

Table 1. Distribution of test results

		PCR		McNemar p-value
		Negative	Positive	
Antigen	Negative	66	10	0.002*
	Positive	0	24	

* $p \leq 0.05$ was considered as statistically significant

The Specificity rate of the test was 100%. According to the PCR test results, 24 of the 34 patients who were positive were also positive with the rapid antigen test, and 10 were negative. Therefore, the Sensitivity rate of the test was 71%. The Accuracy (Diagnostic Value) rate, which shows how confidently the results of the rapid antigen test can be used for diagnosis, was determined as 90%.

When the Ct values obtained by PCR test and rapid antigen test results of the patients were compared, no significant difference was found between them ($p>0.05$). The results are given in Table 2.

Table 2. Independent two-sample t-test results

	Group	Patient Number (n)	Average	Standard Deviation	t test (p-value)
CT	Antigen negative	10	26,8000	4,15799	1.817 (0.079)
	Antigen positive	24	24,2083	3,63532	

* $p \leq 0.05$ was considered statistically significant

In our study, Ct values for both groups were compared with the onset days of symptoms, but no significant relationship was found between the two groups ($p>0.05$) (Table 3)

Table 3. Relationship between Ct values and day of onset of symptoms

		Spearman's rho	p-value
Antigen negative	CT- Day of onset of symptoms	0.034	0.926
Antigen positive	CT- Day of onset of symptoms	0.227	0.287

* $p \leq 0.05$ was considered statistically significant

DISCUSSION

According to the detailed statistical analysis results; The rapid antigen test of our study was able to detect the diagnosis of SARS-CoV19 virus infection with 100% specificity, 71% sensitivity and 90% accuracy. Our results were in line with some publications in the literature, however the rapid antigen test we used could not meet the specificity and sensitivity criteria of WHO and ECDC for SARS-CoV-2 (1,4).

The Covid-19 pandemic has once again reminded us of the importance of fast and accurate diagnosis in the treatment of patients.

Rapid antigen tests provides many advantages with their short delivery times, ability to be used anytime, anywhere, no need for extra equipment, low cost and laboratory workers especially for the diagnosis of symptomatic patients who are in the first 5 days of the disease with high viral load (6). However rapid antigen tests' sensitivity and specificity need to be determined in order to be used more widely (7).

While the specificity of antigen tests has been found to be quite high in many studies, the sensitivity rates are variable. In a study of Scohy et al., the sensitivity of the rapid antigen test was 30.2%, the specificity was 100%, while the sensitivity was determined as 94% in the study of Porte et al., the specificity was determined as 100%. In another study with a sample size of 1186, the sensitivity was found to be 86.7% and the specificity as 100% with the rapid antigen test (8-10). The specificity rate of the test we used in our study was 100% and the sensitivity was determined as 71%. The sensitivity and specificity criteria suggested by WHO and ECDC for the antigen tests are ≥80% sensitivity, ≥97% specificity and ≥90% sensitivity, ≥97% specificity, respectively (1,4). Our test was far from these sensitivity criterias. This might be due to the the limitations of our study such as low sample number or the patients who applied to our outpatient clinic after the symptomatic period.

In our study, no significant relationship was found between antigen positivity and the time elapsed since the onset of symptoms. However positive cases were seen to be intensified especially in the first days of their disease. Consistent with our study, in the study of Porte et al., 93.7% of the positive samples were concentrated in the first week after symptom onset. In a study by Ristic et al., they said that the sensitivity of rapid antigen tests changed according to the day of the symptoms of the patients, and therefore the sensitivity of the test they used could vary from 67.7% to 100% (8,11).

Although there was no statistically significant relationship between Ct values and antigen test results in our study, it was observed that the Ct values of the samples with positive antigen test were lower. This might be again due to the inadequacy of the sample size, which was the limitation of our study. In the study performed by Mak et al., it was observed that the sensitivity of antigen test results of 160 respiratory tract samples with positive PCR test was higher in samples with a Ct value of less than 18.7 (12) In a study of Ford et al., RT-PCR positive samples with higher Ct values were found to have lower antigen positivity, while the antigen test was found to be >90% positive in samples with Ct values <29. (13).

CONCLUSION

As a result, when we look at the findings obtained from our research and literature, in order to reduce the workload of health professionals working in emergency services,

hospitals, cargo companies, nursing homes, schools, prisons and etc. rapid antigen tests can be used to for both diagnosis and screening. However, the performance of the selected kits must be officially approved by independent institutions, how the performances of the tests are determined must be clearly written in the kit content and each country must create its own algorithm. For these reasons, more studies with larger samples and different antigen test kits are needed to evaluate the specificity and sensitivity of these tests.

Ethical Approval: Ethics committee approval was received for this study from Scientific Research and Publication Ethics Committee of Gumushane University and Ministry of Health of the Republic of Turkey.

Peer-review: Externally peer-reviewed.

Author Contributions:

Concept: HS, EU, MCU, EA, CA, SD, Design: HS, EU, MCU, EA, CA, SD, Supervision: HS, EU, Data Collection and/or Processing: HS, EU, MCU, EA, CA, SD, Analysis and/or Interpretation: HS, EU, EA, Writing: HS, EU, MCU, EA, CA, SD

Conflict of Interest: No conflict of interests

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