Journal of Health Sciences

RESEARCH ARTICLE Open Access

Application of rapid antigen tests in the prevention of the transmission of SARS-COV-2 in a hospital setting

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ABSTRACT

Introduction: The pandemic of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) presented a major challenge to health-care systems around the world. To ensure the continuity of hospital care for patients with cardiovascular diseases, the clinic has formulated the strategy for prevention of transmission of SARS-CoV-2 across the hospital environment. The purpose of this paper is to present the strategy for the prevention of transmission of SARS-CoV-2 in a healthcare facility, using Antigen Rapid Diagnostic Tests (Ag-RDTs).

Methods: A description of the work from the hospital committee for the prevention and control of the SARS-CoV-2 epidemic is presented. The hospital has adopted the zero-case strategy. Each positive Ag-RDTs test was sent for confirmation by real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR).

Results: During the observed period, 6569 tests were performed at the Magdalena Clinic. Of these, a total of 6100 Ag-RDTs were performed, while 469 were recorded by RT-PCR test. Of these tests, a total of 181 tests showed a positive result, which is a share of 2.75% of all tests performed, of which 144 (2.19%) positive findings were detected among staff. In Ag-RDTs alone, a total of 86 positive people were detected, which is 1.41% of those tested on this type of test.

Conclusion: The use of antigen rapid diagnostic tests is an effective and reliable method for the early detection of asymptomatic individuals infected with SARS-CoV-2 in a hospital setting. This strategy can significantly contribute to the insurance of uninterrupted healthcare, providing regular workflow processes, and the care of patients in the safest possible way.

Keywords: Rapid antigen tests; COVID19; prevention; transmission; hospital

INTRODUCTION

Over the past 2 years, the world has been faced with one of the most serious public health threats recorded in recent history. According to current data from the Croatian Institute of Public Health in the Republic of Croatia, a total of 392,281 cases of the Coronavirus Disease 2019 (COVID19) were detected, with over 2.5 million tests performed (1) to identify infected people and prevent virus transmission in the population.

According to experts, global health-care systems had not been appropriate prepared to deal with this type of burden caused primarily by rapidly growing numbers of infected and seriously ill persons (2,3). Efforts to bring the spread of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) under control have highlighted the need to diagnose the disease as early as possible, and quickly, accurately, reach as many people as possible (4,5). Introduction of Antigen Rapid Diagnostic Tests (Ag-RDTs) as a base for routine analysis offered the possibility of identifying and isolating positive individuals and their contacts at an early stage of infection (6,7).

According to the definition of the US Centers for Disease Control and Prevention (CDC), Ag-RDTs are actually immunological tests, designed to detect the protein of a pathogen on a person's mucosa, indicating the current existence of a possible infection or its source (7). Rapid, point-of-care diagnostics tests, targeting mainly viral antigens and antibodies were widely performed amongst communities globally (8-10). Although Reverse Transcription Polymerase Chain Reaction (RT-PCR) technique is still considered the gold standard in the detection of nucleic acid of SARS-CoV-2, its shortcomings, which are manifested primarily in availability and limitations to centralized laboratories, problems of sample transport, processing time and some delay in delivery of findings to the end user, make this methodology inaccessible to the general population

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Submitted: 01 December 2021/Accepted: 21 March 2022

DOI: https://doi.org/10.17532/jhsci.2022.1618

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FACULTY OF HEALTH STUDIES

(11-17). Therefore, the availability of Ag-RDTs intended for "point-of-care" testing has made a significant step forward in the diagnosis and detection of potentially infected individuals in the current environment (15).

The main advantages of Ag-RDTs are considered to be accessibility, ease of use, short sample processing time and high accuracy of findings (18). However, performing rapid antigen testing requires some skill and training of staff, as technical difficulties and/or irregularities in taking, processing, and analyzing results, can yield false-negative findings (6,16,19). False negative findings are also possible when a nasopharyngeal swab is taken during the incubation phase of the virus (5-7 days), which usually lasts 1–2 days before the onset of the disease symptoms themselves (6). On the other hand, there are many known reasons for false positive results among which it should be noted mislabeling at the point of collection and at the point of processing, contamination during sampling and processing, presence of interfering substances and improper operating or storage of test kits (20-22). However, their main shortcomings are considered to be limited by clinical and diagnostic sensitivity, that is, the relationship between false-positive and false-negative findings, which according to certain studies range from 30.2% to 60% (23-26). It has been estimated that sensitivity of Ag-RDTs strongly depends on viral load of infected person which points to a fact that broader use of these tests in asymptomatic individuals in a low prevalence setting may result in a large number of false positive results (21).

The basic premise of the application of the Ag-RDTs is the early introduction of preventive measures, which are one of the most important steps in a control of pandemic (27). Therefore, in 2021, the World Health Organization issued recommendations suggesting the use of Ag-RDTs to achieve the greatest possible coverage of SARS-CoV-2 testing, especially in symptomatic individuals, while testing of asymptomatic individuals is recommended in groups. Particularly groups exposed to the virus transmission, such as health professionals and staff, employed in long-term care facilities (28). Their use is especially recommended in situations of low probability of infection, for example, in asymptomatic individuals in low prevalence environments (schools, workplaces, travel, and mass gatherings), because their high negative predictive value can be reliably used to exclude the possibility of SARS-CoV-2 infection (29). Development of rapid antigen testing programs for employees, along with other preventive measures, significantly helps to achieve a safe work environment (30).

METHODS

During September 2020, due to the current increase in the number of patients with COVID19 disease, the hospital's Commission for the Prevention of COVID19 Disease decided to start conducting rapid antigen tests for all employees of the institution, their family members who have been identified with SARS-CoV-2 infection, and patients with suspected symptoms of COVID19. According to the current recommendations of the Croatian Institute of Public Health, it was decided to confirm any positive findings of the Ag-RDTs by taking a sample of nasopharyngeal swabs and sending them for RT-PCR testing. The aim of this preventive strategy was identification potentially ill and/or infected employees and their close family members (who share the same household) as well as patients admitted to hospital treatment as soon as possible. This approach enabled the separation of infected persons and their contacts from the work collective in order to prevent further transmission of SARS-CoV-2 within the hospital. The following Ag-RDTs were used during the implementation of the employee testing strategy: Roche Sars-CoV-2 Rapid Antigen Test, CoviGnost Ag Test, Abbott Panbio Rapid Antigen Test, and Hangzhou All test Biotech (31). All these tests have been validated and approved for use by the Croatian Institute of Public Health.

To ensure optimal sampling technique, processing speed, and supervision of testing of all employees, a team of trained nurses were organized. They sampled swabs, with the use of appropriate protective equipment, and a suitable space for testing outside the hospital was provided. At the beginning of the test, samples of nasopharyngeal swabs were transported in appropriate conditions to a collaborating authorized laboratory, which analyzed them, issued written findings, and reported the detected positive persons, by telephone. On the arrival of Ag-RDTs, which had been validated and intended for wider application on the Croatian market, the hospital was able to distribute a significant amount of tests, and further testing was carried out within the premises of the Magdalena Clinic. Persons who had positive Ag-RDTs for SARS-CoV-2 were immediately referred for RT-PCR testing, and self-isolation measures were taken until the findings arrived. Patients who tested positive were also referred for RT-PCR testing by place of residence, and were instructed on isolation measures and reporting to the family physician.

All positive Ag-RDTs were reported to the competent epidemiological service, and further preventive measures were agreed. Furthermore, from the beginning of the testing, a careful record was kept of all tests performed, their findings and measures taken against the tested persons. Study is approved by clinic Magdalena ethical board.

RESULTS

From October 1, 2020, to June 30, 2021, 6569 tests were performed in Clinic Magdalena (Figure 1). Of these, a total of 6100 antigen rapid diagnostic tests were performed, while 469 were recorded by RT-PCR tests (Figure 1). Of these tests, a total of 181 tests showed a positive result, which is a share of 2.75% of all tests performed. It is important to emphasize that an antigen rapid diagnostic tests detected a total of 86 positive individuals, which is 1.41% tested on this type of test.

The results showed that the testing included mostly clinic staff (5474 tests), followed by patients (841) and family members of employees (254) (Figure 2). Of the tests performed, most of the positive samples were detected among the clinic staff (144), which makes a share of 2.19% of positive employees within a total of 2.75% of all positive findings. During the observed testing period, a total of 104 people positive for SARS-CoV-2 were detected (Figure 3). Samples of those individuals who were identified as positive

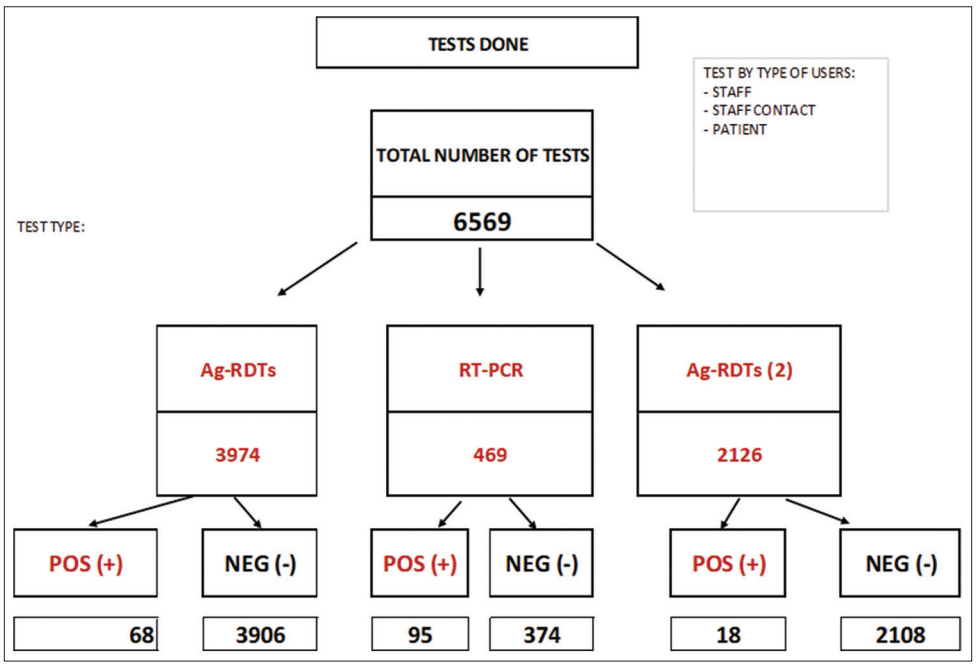

FIGURE 1. Overall testing statistic data.

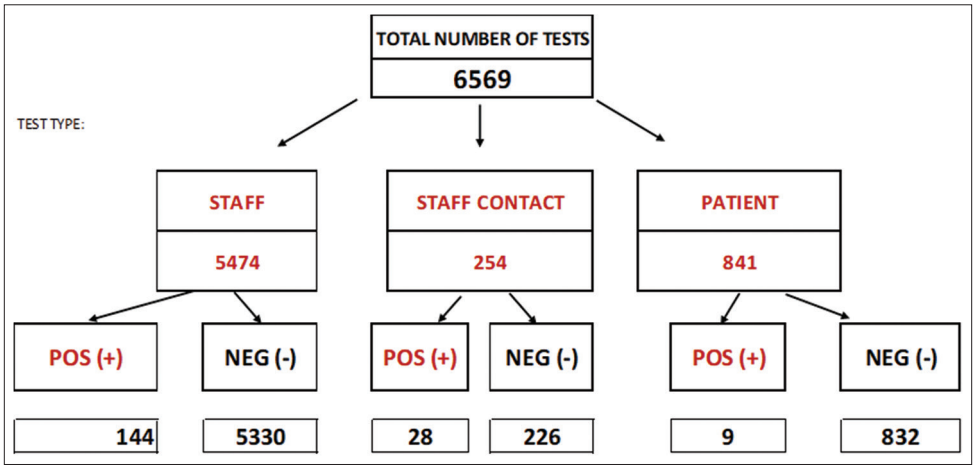

FIGURE 2. Testing statistic data by type of user.

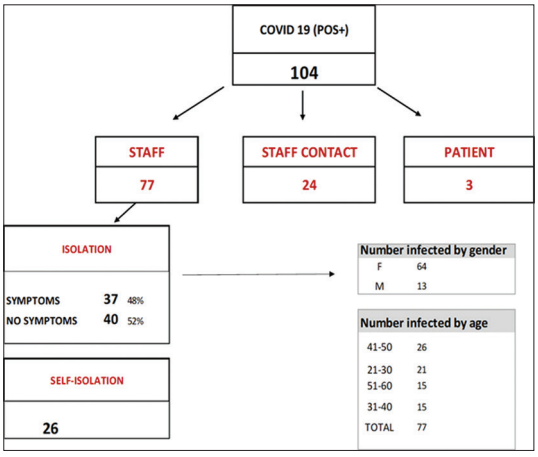

FIGURE 3. Analysis of SARS-CoV-2 positive findings.

on Ag-RDTs were sent for confirmation with RT-PCR. Of the 77 positive employees at the clinic, 52% had no symptoms of the disease. The largest number of positive individuals was in the age group of 40 to 50 years, while the observed sample of positive persons consisted mainly of women.

In Figure 4, we have shown the numbers of employees tested in the weeks of June. The above data presents still high share of tested staff in the Intensive Care Unit, which is considered to be one of the most risky places for infection transmission within the hospital. Likewise, a high frequency of preventive testing was maintained in the cardiology departments and in the Catheterization laboratory. These measures included staff who was not fully vaccinated and who had contracted SARS-CoV-2 but had more than 8 months since recovering from the illness (in accordance with the Croatian Institute of Public Health guidelines).

Table 1 shows the number of total antigen rapid diagnostic tests performed on staff by months and the number of positive findings detected. The data show that during the third pandemic wave, the largest share of positive employees (60) was detected, which makes up more than half of all detected positive cases (57.69%). Table 2 shows the total number of antigen rapid diagnostic tests performed in the period from October 2020 to June 2021 according to the departments of the clinic. As can be seen from the attached table, the largest number of tested persons was recorded in

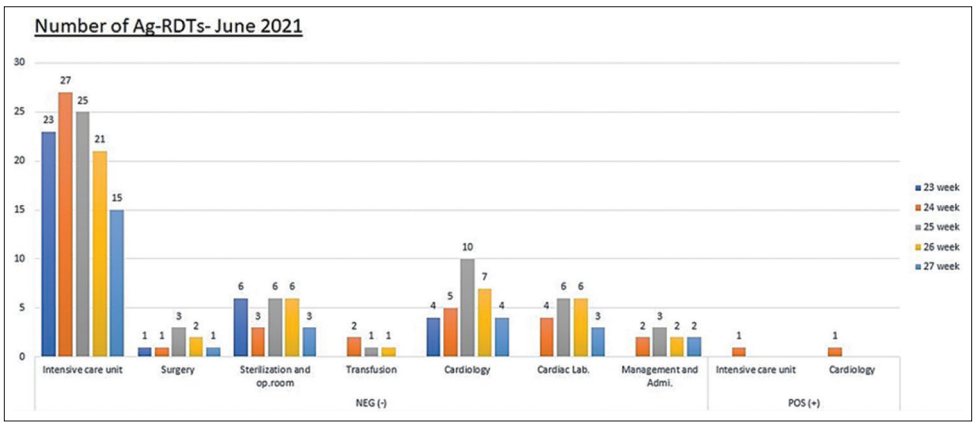

FIGURE 4. Statistic data of the number of employees tested in June 2021.

TABLE 1. Number of antigen rapid diagnostic tests by months

Number of Ag-RDTs									
MONTH	10	11	12	1	2	3	4	5	6
NEG (-)	621	1270	1046	790	445	330	216	171	207
POS (+)	10	24	20	6	1	0	1	2	2
TOTAL	631	1294	1066	796	446	330	217	173	209
Share POS (+)/TOTAL	1,6%	1,9%	1,9%	0,8%	0,2%	0,0%	0,5%	1,2%	1,0%

Ag-RDTs: Antigen rapid diagnostic tests

the Intensive Care Unit (27.8%) during November 2020. At the same time, the most positive results were recorded among employees in cardiology departments (45.83%) during the same period.

Table 3 shows the results of similar studies published recently. The results of these studies showed that the share of positive findings is very different and ranges from 0.44% to 16.7%, regardless of sample size. The vast majority of studies used RT-PCR to confirm the accuracy of the tests.

DISCUSSION

The use of the rapid antigen tests for the purpose of early screening of persons potentially infected with the SARS-CoV-2 is one of the ways to help prevent the transmission of the virus in work and other environments. As can be seen from the presented results, during the implementation of the preventive testing strategy at the Magdalena Clinic, a total of 77 infected employees were detected, as well as 24 persons who were their closest contacts. This approach made it possible to identify people who are carriers of the SARS-CoV-2, even before the onset of symptoms of the disease, and their timely elimination from the work environment. These steps are part of a zero-case strategy chosen by the hospital management as the only safe option that will prevent the transmission of the virus between employees within the work environment, but also to the patients of the clinic.

However, the introduction of this methodology for testing and detecting individuals who are potential carriers of the virus and transmitters of infection in the early stages of the disease has its limitations. Among the main deficiency is the variation in sensitivity in different types of the antigen tests. The susceptibility range of most Ag-RDTs overlaps with the SARS-CoV-2 viral load commonly observed in the 1st week of symptom onset and indicates a period of infectivity in most patients (32). Although this was developed as a first line of screening for SARS-CoV-2, research has shown that the main disadvantage of this method is precisely the poor sensitivity of tests, especially at low levels of viral load that most tests fail to detect (33). Various studies conducted at the beginning of the COVID19 pandemic have shown that the sensitivity of these tests can vary from a low 41.2% to a relatively acceptable 71.4% in asymptomatic carriers (34-37). Therefore, Pray et al. (34) in their study concluded that affirmative RT-PCR testing should be done in all negative Ag-RDTs results in symptomatic carriers and positive results in asymptomatic carriers. The authors of studies presented in our paper had a very similar approach, where all results showed high specificity of Ag-RDTs tests, which varied from 81% to maximum 100% and very different determined sensitivity of the applied tests ranging from 48% to a high 87% (37,39-44). However, sensitivity is a nothing as Ag-RDTs' performers and doctors who consider the test results should bear in mind all the reasons for a potential false test result (16).

Bello-Chavolla et al. (38) state in their study that Ag-RDTs has optimal diagnostic performance up to 3 days after the onset of disease symptoms. The same authors suggest the use of these tests as an alternative to RT-PCR tests in cases of extensive testing, noting that the interpretation of Ag-RDTs results should be approached with caution to avoid risks associated with false-negative findings.

The use of Ag-RDTs testing is recommended in pandemic conditions where test results can be used to timely isolate infected people, prescribe appropriate treatment, and closely monitor a person's contacts to limit the spread of SARS-CoV-2 in the population as much as possible (45-47). Here, we must mention that the management of the Magdalena Clinic decided to introduce a strategy of preventive testing in early October 2020, while the same strategy was introduced at the level of health institutions in the Republic of Croatia a year later, in October 2021. A study by Koeleman et al. (48) conducted on users and employees in long-term care institutions and emergency departments confirmed that rapid immunoassays are useful for detecting infected persons with short-term symptoms of the disease, especially among employees in these institutions. Users of emergency services showed slightly more false negative findings which makes this method relatively inappropriate for this group

TABLE 2. Proportion of tested by department

Number of Ag-RDTs									
Number of Ag-RDTs by department	YEAR, MONTH								
	2020			2021					
	10	11	12	1	2	3	4	5	6
TEST OUTCOME	631	1294	1066	796	446	330	217	173	209
NEG (-)	621	1270	1046	790	445	330	216	171	207
Polyclinic Zagreb	14	24	12	29	0	0	0	0	0
Intensive care unit	117	360	291	209	122	149	91	99	111
Cardiology	256	343	280	202	103	14	31	25	30
Cardiac Lab.	72	108	64	67	58	50	20	12	21
Surgery	52	134	123	87	44	24	11	0	8
Sterilization and op.room	72	194	175	118	76	71	46	16	24
Transfusion	11	35	27	14	13	10	6	6	4
Management and Admi.	27	72	74	64	29	12	11	13	9
POS (+)	10	24	20	6	1	0	1	2	2
Polyclinic Zagreb	0	1	1	0	0	0	0	0	0
Intensive care unit	2	3	3	2	0	0	0	1	1
Cardiology	6	11	6	3	1	0	1	0	1
Cardiac Lab.	0	4	0	0	0	0	0	0	0
Surgery	1	4	4	0	0	0	0	0	0
Sterilization and op.room	0	0	3	1	0	0	0	1	0
Transfusion	1	0	1	0	0	0	0	0	0
Management and Admi.	0	1	2	0	0	0	0	0	0

Ag-RDTs: Antigen rapid diagnostic tests

TABLE 3. Comparison of published reports

Ag-RDTs	Sample	Positive (%)	Negative (%)	RT-PCR	Study
Roche/Sd Biosensor	1465	94 (6.41)	1368 (93.37)	Yes	Jegerlehner et al. 2021
Various	7471	773 (10.34)	6393 (85.57)	Yes	Krüger et al. 2022
Roche Sd Biosensor	970	162 (16.70)	808 (83.29)	Yes	Igloi et al. 2021
Jiangsu Bioperfectus Tech.	317	-	120 (37.85)	Yes	Lombardo et al. 2021
SD Biosensor	1100	38 (3.45)	1062 (96.55)	Yes	Mungomklang et al. 2021
SD Biosensor Standard Q	193	27 (13.99)	123 (63.73)	Yes	Abdul-Mumin et al. 2021
SD Biosensor	49,542	222 (0.44)	49,320 (99.55)	Yes/No	Wachinger et al. 2021

Ag-RDTs: Antigen Rapid Diagnostic Tests, RT-PCR: Reverse transcription polymerase chain reaction

of patients. It has been observed that age, the presence of comorbidities, and the onset time of symptoms significantly affect Ag-RDTs performance, and that the optimal efficacy of these tests decreases after 7 to 10 days of disease onset (38).

According to the World Health Organization (28), the use of Ag-RDTs is recommended to achieve high coverage of testing, especially in symptomatic individuals, while testing of asymptomatic carriers should be performed in groups of those particularly exposed to the virus, such as healthcare workers and long-term care providers. Although a pilot study by Šterbenc et al. (49) conducted to determine the usefulness of Ag-RDTs screening among healthcare professionals in a hospital setting showed that such tests were not completely reliable in detecting newly infected individuals due to a number of false negative findings in the presymptomatic phase of the disease, confirmed the credibility of the RT-PCR methodology which still needs to be implemented if we want to prove or rule out the existence of infection. The ECDC (50) states in its guidelines that the application of Ag-RDTs in professional settings can significantly complement existing occupational safety measures and non-pharmaceutical interventions aimed at preventing the spread of the virus and the increase in the number of those infected. A study conducted by Wong et al. (51) among students and staff at a university in Canada, found that Ag-RDTs are useful in detecting asymptomatic infected individuals, rapid detection of their contacts, self-isolation, and controlling the spread of infection especially in shared housing conditions. This would contain a certain proportion of false-positive findings. Nevertheless, according to Mouliou et al. (52), it should be highlighted that epidemiological screenings with mass-testing like our study detect pre- or post-symptomatic carriers, or paucisymptomatics, and a definite asymptomatic case without having contacted with COVID-19 identified individuals or in places with low burden of SARS-CoV-2, may be just a false result.

According to Schulte et al. (30), the development of a rapid employee antigen testing program, along with other preventative measures, contributes significantly to achieving a safe work environment. Study provided by Kotsiou et al. (53) highlighted the importance of preventive rapid antigen testing among workers in different professions and interestingly showed that significantly higher vulnerability to COVID19 has employees in lower-status professions such as catering workers, while employees in higher-status professions such as health professionals, despite increased risk of contact with infected persons, have lower susceptibility

to infection probably due to better access to risk mitigation measures, such as frequent sanitation, enforced distancing, personal protective equipment, and better ventilation and air filtration systems.

According to the recommendations issued by the CDC (54) at the beginning of the pandemic, it is advisable to introduce early testing as part of the SARS-CoV-2 prevention strategy in critical infrastructure workplaces that allows identifying infected people, isolating them from the collective, preventing the spread of infection and protecting other workers, and openness of the workplace to regular jobs. Preventive testing of all employees at the Magdalena Clinic enabled the complete absence of intrahospital transfer of the infection to the patients themselves, thus the smooth running of regular work processes and the provision of health services. The identification of active cases among employees of institutions not only stops the transmission of the virus in the workplace, but is also a vital component in broader national efforts aimed at combating the spread of the pandemic (30).

Finally, it should be mentioned that the availability of vaccines against COVID19 has significantly contributed to the overall safety and prevention of the transmission of infection within the work environment. Despite the high vaccination coverage of hospital staff of 87%, there is still a number of health and non-health staff who refuses vaccinations, and the strategy of preventive testing by Ag-RDTs at regular intervals (usually twice a week) is applied to the same employees. It is also important to emphasize that the emergence of new types of the virus requires the correction and supplementation of existing preventive measures. Therefore, according to new guidelines issued by the CDC (55), all fully vaccinated health-care professionals who have been in close contact with infected people should perform Ag-RDTs in health-care settings aimed to prevent transmission to particularly vulnerable groups or patients in hospitals. A recent study revealed that job environment had a positive impact on the response to the vaccine against COVID19 for half of the vaccinated responders (56). May mass-testing be exclusively important especially for people with underlying medical conditions that could possibly lead to a likely severe COVID19, and another study showed that rates of risk factors are high in society (57). Furthermore, self-testing through Ag-RDTs was characterized as unreliable by 2 / 3 of the responders of a recent study, and this may trammel people from accepting and supporting mass-testing (58).

The introduction of a testing strategy for health professionals at the Magdalena Clinic required the engagement of additional organizational, financial, and material resources. Likewise, testing of close contacts and the proportion of patients admitted to the clinic further emphasized the importance of planning and a comprehensive approach in designing measures to control and prevent the spread of infection in the hospital setting. The implementation of a defined testing plan, careful monitoring of results and cooperation of all employees in its implementation, along with other measures to prevent the spread of the virus, enabled continuous and uninterrupted regular work processes, and provided health services in a way that does not endanger patient safety during hospital stay.

CONCLUSION

The application of antigen rapid diagnostic tests is an effective and reliable method for the early detection of SARS-CoV-2 positive individuals in a hospital setting. Although there are still discussions about their sensitivity and specificity, especially in the detection of asymptomatic and presymptomatic carriers, it is undoubtedly a method that can serve to screen potentially infectious individuals in the population. Despite the fact that their regular and long-term application requires certain financial resources, staff training and organization of testing sites, the introduction of preventive testing by Ag-RDTs can help prevent the entrance and transmission of the virus among staff and patients. Therefore, it should be noted that this approach is certainly one of the key steps in ensuring the continuity of healthcare in a pandemic, the smooth running of regular work processes and the care of patients in the safest possible way.

ACKNOWLEDGMENTS

We sincerely thank all study participants for taking part in this study as well as to registered nurses for helping in data collection.

DECLARATION OF INTERESTS

The authors declare that they have no conflict of interest.

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