SARS-CoV-2 Epidemic in the Israeli Defense Force—Lessons Learned From Our rt-PCR Screening Policy

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ABSTRACT

Background:
During the SARS-CoV-2 pandemic, multiple preventative measures were used to prevent the virus from spreading in the population. The Israeli defense force deployed further means to contain the disease, including putting units in quarantine, physical distancing and using masks, gowns and disinfectants when in contact with suspected patients.

Methods:
We used reverse transcriptase-polymerase chain reaction (rt-PCR) tests to screen for patients among asymptomatic soldiers within units participating in civilian aid or in close contact with known patients, using personal protective equipment. Positive results were repeated and followed with serological testing to verify the nature of results.

Results:
Between April and May 2020, we screened a total of 1,453 soldiers in 13 different units. We found 11 false positive results, leading to unnecessary measures until resolution, and three true positive results (0.2%). All true positive results had unreported symptoms concomitant with SARS-CoV-2 disease. These results led to the resolution of this screening policy.

Conclusion:
Screening asymptomatic army personnel in this setting with rt-PCR test for SARS-CoV-2 is not warranted and leads to unnecessary false positive results. Efforts should be directed at identifying symptomatic patients.

BACKGROUND

Severe acute respiratory syndrome coronavirus (SARS-CoV-2), a novel coronavirus with similarities to SARS-CoV and Middle East respiratory syndrome coronavirus, has spread worldwide leading the World Health Organization to declare it a pandemic.[1] Because of its high contagiousness and rapid spread within the population, an isolation policy was implemented worldwide as it was proven to be the most effective means to limit the spread of the disease.[2]

The common method to detect SARS-CoV-2 in the upper respiratory system is using real time reverse transcriptase-polymerase chain reaction (rt-PCR) test.[3] The primary, and preferred, method for diagnosis is the collection of upper respiratory samples via nasopharyngeal and oropharyngeal swabs. The sensitivity rate for this test is not clear but is estimated to be around 66%-80%.[4] The specificity of the rt-PCR test seems to be very high and false positive rate is estimated to be negligible, although there may be false-positive results due to swab contamination, especially in asymptomatic patients.[1,5]

One of the disadvantages of rt-PCR as a sole diagnostic method is its inability to detect past infection in case of a negative result.[6] Serology tests are comparatively easier to perform, requiring less technical expertise and equipment compared to nucleic acid detection and have a higher sensitivity and specificity rates.[7] The advantage of cheap, rapid tests for healthcare workers for example, would allow them to be cleared and return to work as the outbreak progresses.[7] The role of rt-PCR screening for asymptomatic patients is unknown.

The first confirmed COVID-19 case in Israel arrived in the country on February 11st, 2020.[8] Until May 12th, 2020, 237 Israeli Defense forces (IDFs) soldiers were confirmed positive for SARS-CoV-2 using rt-PCR test. Between March 4th and May 12th, there were up to 5,803 soldiers simultaneously in-home isolation because of contact with known patients. In order to limit the spread of the disease multiple measures were employed including minimizing contact with civilian population while using preventative measures (commanders were instructed to shorten contacts as much as possible while operating missions), strict social distancing of any population at risk for severe disease and central facilities for sick soldiers and those in quarantine. Another preventative measure was a screening process within the operational units using rt-PCR tests for asymptomatic personnel. The rationale was identifying asymptomatic patients or ones that are in the early stages of disease and disease limitation by using isolation

techniques. This report will describe our experience with this screening policy and its limitations.

METHODS

Study Design

The population were army personnel—healthy individuals who were deemed medically suitable to high combat army service without any chronic diseases. These soldiers serve in close quarters in an army setting. A designated panel chose the appropriate units on a weekly basis. Inclusion criteria were units who fulfilled one the following criteria:

1. Participating in civilian assistance in areas with a high prevalence of disease (peak 1,156 patients per 100,000 civilians)—in close contact with known patients.

Soldiers exposed to suspected COVID-19 patients used personal protective equipment, consisted of an isolation gown, overshoes, gloves, N-95 face mask, and a transparent face shield.

2. Participating in operational activity in high infectivity regions.
3. Soldiers serving in closed units after the army enabled the soldiers to visit their homes during the weekend—tests were performed a week after returning to the unit.

A flow chart of examples of this screening policy is described in Figure 1. Within each unit specific personnel were chosen and screened with rt-PCR tests (∼10% of the unit). Once the rt-PCR test was positive, each patient underwent an epidemiologic investigation, to identify and cross-reference his exposure to other SARS-CoV-2 positive patients and the general population. Each patient with a positive result was quarantined, and another rt-PCR test was obtained the following day. If this test was negative, another test was obtained after 3 days. In case the patient remained asymptomatic and had of two consecutive negative results, he was first declared cured and returned to duty. In order to evaluate whether the positive result was a false positive one a serology test was performed after 14-21 days.

rt-PCR Technique

The IDF medical corps military laboratory performed one-step real-time reverse transcriptase–polymerase chain reaction on all samples, using the SARS-CoV-2 CDC assay protocol. The Allplex 2019-nCoV assay (Seegene, Seoul, South Korea) was the kit of choice (for both extraction and PCR preparation) and for ease of use and compatibility the PCR of choice was the Biorad CFX 96 with the complementary Seegene software.[9] Cycle threshold (Ct) values were reported for three viral markers: RDRP, N gene and E gene, and an internal control marker. Values

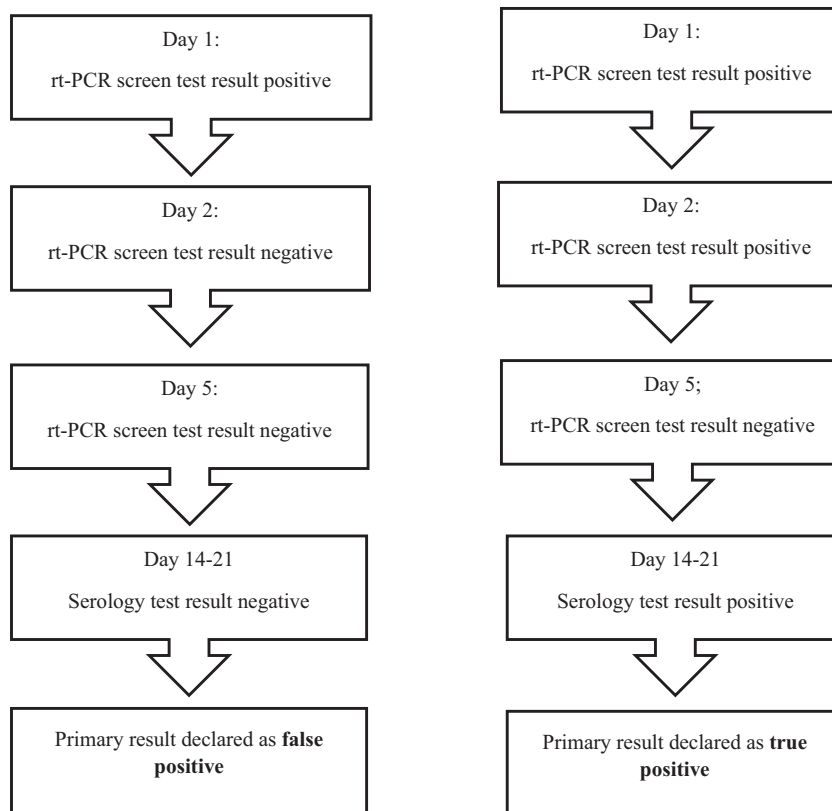| Day 1: rt-PCR screen test result positive	Day 1: rt-PCR screen test result positive
Day 2: rt-PCR screen test result negative	Day 2: rt-PCR screen test result positive
Day 5: rt-PCR screen test result negative	Day 5; rt-PCR screen test result negative
Day 14-21 Serology test result negative	Day 14-21 Serology test result positive
Primary result declared as **false positive**	Primary result declared as **true positive**

FIGURE 1. Example of tests performed for asymptomatic patients with a one positive rt-PCR.

below 40 cycles indicated a positive result for SARS-CoV-2. This laboratory was approved by the Israeli ministry of health and performed over 50,000 rt-PCR tests since march 2020. The first assessment of its performances by the manufacturer demonstrates a sensitivity of 70%, specificity of 100% and a limit of detection of 100 RNA copies/PCR reactions.[9]

Serology Tests

Immunoglobulin M (IgM), Immunoglobulin G (IgG) and Immunoglobulin A (IgA) levels were obtained using electro-chemiluminescence-based ELISA. Antibodies were directed toward the receptor binding domain of the spike protein (RBD) of SARS-CoV-2. Positivity toward COVID-19 seroconversion was determined by testing positive (using the ~98% specificity) for only one out of three specific RBD antibody classes.

RESULTS

Between April 1, 2020 and May 14, 2020, 1,453 rt-PCR tests were performed in 13 units (age 18-52 years, Table I). All patients in combat units were male, and this cohort included 217 non-combatant females (22%). We found 14 positive results leading to quarantine and preventative measures employed in these units. Three of these patients were found to be symptomatic (had unreported symptoms—mostly cough, muscle weakness, and fever).

The first three patients were admitted to the SARS-CoV-2 military rehabilitation center, as per the IDF medical corps guidelines, and were subsequently tested according to the protocol during the following days. Since all three had subsequent negative results, they were suspected as false positive. Following these findings, we changed our policy, and before declaring that a person with a positive result is sick, we performed two consecutive tests while they were quarantined at home. Patients with two consecutive negative results were then regraded as false positive and returned to their duties.

TABLE I. Number of Total Tests and Subsequent Positive Results

Unit	Number of tests	Positive results (%)	True positive (%)
A	192	1 (0.52)	
B	100	1 (1)	
C	100	0 (0)	
D	101	2 (1.98)	1 (0.99)
E	152	0 (0)	
F	129	1 (0.78)	
G	104	2 (1.92)	
H	93	2 (2.15)	
I	100	5 (5)	2 (2)
J	100	0 (0)	
K	140	0 (0)	
L	92	0 (0)	
M	50	0 (0)	
Total	1,453	14 (0.96)	3 (0.21)

Serology tests confirmed only 3 of the 14 patients to be true positive and 11 to be false positive. All three true positive patients were those with unreported symptoms concomitant with SARS-CoV-2 disease.

DISCUSSION

SARS-CoV-2 is an ongoing pandemic, and means to limit disease spread are needed.[10] SARS-CoV-2 rt-PCR test are currently considered to be the gold-standard for diagnosis, and data regarding false positive results is sparse.[11] Positive results are commonly regarded as true positive, and subsequent measures are commonly taken based on those result. Reports of using rt-PCR test to screen among asymptomatic adults are missing.

This report highlights our experience with SARS-CoV-2 rt-PCR screening within asymptomatic army personnel, exposed to COVID-19 patients using personal protective equipment. We found ~1% positive results, and after interpretation 0.7% were false positive. False positive results of SARS-CoV-2 rt-PCR results might originate from a contamination in the sampling process or in the laboratory itself.[12] False positive results led to unnecessary quarantines, isolations, and further tests, which has an operational and mental impact on those units. All three true positive cases all had unreported symptoms—a fact that strengthens the need to identify those patients and to actively search and encourage them to report symptoms to their medical personnel. Following our experience this screening policy using SARS-CoV-2 rt-PCR was abandoned.

This report has a few limitations. First, it is not a randomized trial—but a description of our early effort to mitigate the spread of the disease. Second, the group tested were healthy army personnel, not representing a normal cohort of the population. And third, most units are dense combat units, with multiple daily encounters within an army environment, not necessarily like civilians. Nevertheless, we believe that our findings might be relevant to other settings in which many young and apparently healthy adults live in a dense community, using protective measures against COVID-19.

CONCLUSION

In a setting with mandatory use of personal protective equipment and other countermeasures, screening asymptomatic army personnel with rt-PCR test for SARS-CoV-2 is not warranted and leads to unnecessary false positive results. Efforts should be directed at identifying symptomatic patients and testing only them and their close encounters.

CONFLICT OF INTEREST STATEMENT

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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