Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Correlation Between Low-Dose Chest Computed Tomography and RT-PCR Results for the Diagnosis of COVID-19: A Report of 27,824 Cases in Tehran, Iran

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Rationale and Objectives: Real-time polymerase chain reaction (RT-PCR) remains the gold standard for confirmation of Coronavirus Disease 2019 (COVID-19) despite having many disadvantages. Here, we investigated the diagnostic performance of chest computed tomography (CT) as an alternative to RT-PCR in patients with clinical suspicion of COVID-19 infection.

Methods: In this descriptive cross-sectional study, 27,824 patients with clinical suspicion of COVID-19 infection who underwent unenhanced low-dose chest CT from 20 February, 2020 to 21 May, 2020 were evaluated. Patients were recruited from seven specifically designated hospitals for patients with COVID-19 infection affiliated to Shahid Beheshti University of Medical Sciences. In each hospital, images were interpreted by two independent radiologists. CT findings were considered as positive/negative for COVID-19 infection based on RSNA diagnostic criteria. Then, the correlation between the number of daily positive chest CT scans and number of daily PCR-confirmed cases and COVID-19-related deaths in Tehran province during this three-month period was assessed. The trends of admission rate and patients with positive CT scans were also evaluated.

Results: A strong positive correlation between the numbers of daily positive CT scans and daily PCR-confirmed COVID-19 cases ($r = 0.913$, $p < 0.001$) was observed. Furthermore, in hospitals located in regions with a lower socioeconomic status, the admission rate and number of positive cases within this three-month period was higher as compared to other hospitals.

Conclusion: Low-dose chest CT is a safe, rapid and reliable alternative to RT-PCR for the diagnosis of COVID-19 in high-prevalence regions. In addition, our study provides further evidence for considering patients' socioeconomic status as an important risk factor for COVID-19.

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Key Words: COVID-19; computed tomography; RT-PCR; polymerase chain reaction; socioeconomic; correlation; diagnosis.

INTRODUCTION

In late 2019, an outbreak of pneumonia occurred in Wuhan, China that was later found to be associated with a novel coronavirus, now known as the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (1). The disease caused by this highly contagious virus was designated Coronavirus Disease 2019 (COVID-19) and was declared a pandemic on March 13, 2020 by the World Health Organization (WHO). The morbidity and mortality associated with this disease, as well as its economic burden has already posed a serious threat to healthcare systems worldwide and still, the future of this pandemic remains unknown and there is a high probability of a second wave in the upcoming months (2). As like any other contagious infection, one of the first steps in mitigating COVID-19 and reducing its burden is to employ efficient and universally-accessible methods for timely detection of the disease in order to reduce its transmissibility. Thus, appropriate management of COVID-19 highly depends on utilizing rapid, widely-available and safe diagnostic tools, which at the same time are cost-effective and sensitive.

Previously, chest computed tomography (CT) had been demonstrated to be a beneficial imaging modality in the diagnosis and management of viral pneumonia outbreaks such as the severe acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (3,4). Therefore, from the beginning of the current pandemic, CT was used as a valuable tool for the identification of patients with COVID-19 (5,6). Several initial studies reported a high sensitivity for chest CT, which was superior to that of reverse transcriptase-polymerase chain reaction (RT-PCR) (7,8); however, RT-PCR remained the preferred test for confirmation of COVID-19 (9,10). Despite being used as the reference standard, there are many downsides to RT-PCR such as limited global accessibility to kits, high rate of false negative results, and an undesirable delay in diagnosis, making the efficacy of this test suboptimal (11−12).

During the COVID-19 pandemic, there were limited referral centers in Iran with access to RT-PCR assay. Thus, the Iranian Society of Radiology recommended the use of low-dose chest CT as the first modality for diagnosing patients clinically suspected of COVID-19 in regions with established COVID-19 circulation and limited access to RT-PCR (5,13). In this study, we aimed to evaluate the correlation between the number of daily positive chest CT scans and number of daily PCR-confirmed cases and COVID-19-related deaths in Tehran during a three-month period. We also assessed the trend of admission rate and the trend of patients with positive CT scans during this three-month period.

METHODS

Study Design

This was a descriptive cross-sectional study conducted on 27,824 patients who underwent at least one chest CT due to high clinical suspicion of COVID-19 during a three-month period from 20 February, 2020 to 21 May, 2020. Patients were recruited from any of the general hospitals affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran including Labbafinejad, Modarres, Shohada-e-Tajrish, Imam Hossein, Masih Daneshvari, Taleghani, and Loghman hospitals. These tertiary referral hospitals provide health coverage for about 5.4 million people with different socioeconomic status living in the north, northeast and east of Tehran and were specially designated for COVID-19 during this pandemic. Shahid Beheshti University of Medical Sciences was the core unit of COVID-19 management in Tehran province during this pandemic.

Chest CT Scanning

All CT images were obtained using a 16−64 multi-slice CT scanner. Non-enhanced CT was performed for all patients while being placed supine and during end-inspiration. Scanning was performed at a tube voltage of 100−120 Kvp and current modulation of 50−100 milliampere-seconds with a spiral pitch factor of 0.8−1.5 and slice thickness of 1−3 mm (13). CT slices were assessed using picture archiving and communication system (PACS) and a dedicated workstation. Then, all images were independently interpreted and reviewed by two experienced board-certified radiologists at each hospital. Disagreements were resolved by consensus. The decision for considering the findings of a CT scan as positive for COVID-19 was based on Radiology Society of North America (RSNA) diagnostic criteria (14).

Ethical Considerations

Our study was conducted in accordance with the ethical standards of 1964 Declaration of Helsinki and its later amendments. The ethical review board of our institution approved the study. Due to the retrospective nature of the study and no potential risk of harm to patients, the need for informed consent was waived. All data regarding patients' personal information was anonymized and kept confidential.

Statistical Analysis

In this descriptive study, continuous variables are presented as mean (standard deviation) and categorical variables are

reported as frequency (percentage). Pearson's correlation test was used to assess the correlation between daily number of cases with positive CT scans and daily number of RT-PCR confirmed COVID-19 cases and also daily number of COVID-19-related deaths based on officially-reported data for Tehran province. All statistical analysis was performed using Microsoft Excel (Microsoft Office 2010) and the SPSS software version 16.0 (IBM, Chicago, Illinois). A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 shows in detail the rate of admission in each specific hospital during this three-month period. Overall, the mean (SD) number of patients admitted to the hospitals during this period was 43.6 (27.1) patients per day. The highest number of patients ($n = 193$) were admitted on 6 March, 2020 in Imam Hossein hospital.

As shown in Figure 1, the number of admissions steadily increased throughout the study period and a peak in admitted patients was observed in the first half of March (approximately from 3 March, 2020 until 12 March, 2020). Despite this, there was a gradual decrease in the trend of positive cases during the study period. Figure 2 shows the trend of total patients who underwent chest CT due to high clinical suspicion and also the trend of cases with positive CT scan in each specific hospital during this three-month period. As shown, Loghman and Imam Hossein hospital had higher admission rates and more cases with positive CT scans; however, a relatively similar trend was seen in the rest of the hospitals.

The mean ±SD percentage of positive cases to total admitted patients was 21.9% ± 9.9% during this three-month period. The highest and lowest percentage was 38.5% and 7.7%, observed on 13 March, 2020 and 2 May, 2020, respectively (Figure 3).

Figure 4 shows the correlation between the number of daily positive CT scans and number of daily PCR-confirmed COVID-19 cases and COVID-19-related deaths in Tehran province during a three-month period. As shown, there was a strong positive correlation between number of daily positive CT scans and number of daily PCR-confirmed COVID-19 cases in Tehran province ($r = 0.913$, $p < 0.001$). We also observed a significant positive correlation between number of daily positive CT scans and number of daily COVID-19-related deaths in Tehran province during the period evaluated in this study ($r = 0.79$, $p < 0.001$).

DISCUSSION

Pulmonary involvement of COVID-19 predominantly manifest as subpleural ground glass opacities and consolidation. Early identification of typical CT findings provides timely diagnostic evidence of the disease and enables early decision-making and treatment (15,16). In this study, we observed a strong positive correlation between number of daily positive CT scans and daily PCR-confirmed COVID-19 cases. A

TABLE 1. Trend of Admission Rate and Positive CT Scan During a Three-month Period From 20 February, 2020 to 21 May, 2020 in Each Specifically Designated Hospital for COVID-19.

	Imam Hossein		Shohada-e-Tajrish		Modarres		Loghman		Taleghani		Masih Daneshvari		Labbafinejad		Total	
	Total*	Positive†	Total	Positive	Total	Positive	Total	Positive	Total	Positive	Total	Positive	Total	Positive	Total	Positive
Mean (SD)	84.5 (24.3)	17.1 (13.4)	29.5 (12.1)	6.1 (3.8)	33.1 (17.1)	7.4 (7.2)	59.2 (18.9)	10.9 (9.3)	36.7 (17.0)	6.46 (5.52)	45.9 (19.8)	15.6 (8.5)	16.7 (9.6)	6.14 (6.04)	43.7 (27.1)	9.98 (9.8)
Median	82	12	28	5	36	5	57	8	38	5	47	15	16	4	40	7
Minimum	20	1	2	0	0	0	11	0	4	0	4	0	0	0	0	0
Maximum	193	55	64	15	82	38	101	38	85	27	107	36	44	23	193	55
First day of study period	20	3	87	6	8	0	11	0	8	0	31	0	5	1	20	3
Last day of study period	20	4	55	6	0	0	25	0	57	6	50	8	11	0	11	0

* Total (n/day): number of daily admitted patients with clinical symptoms highly suggestive of COVID-19 who underwent at least one chest CT during the study period.
† Positive (n/day): daily number of patients with clinical symptoms highly suggestive of COVID-19 and a chest CT consistent with COVID-19 findings based on RSNA diagnostic criteria.

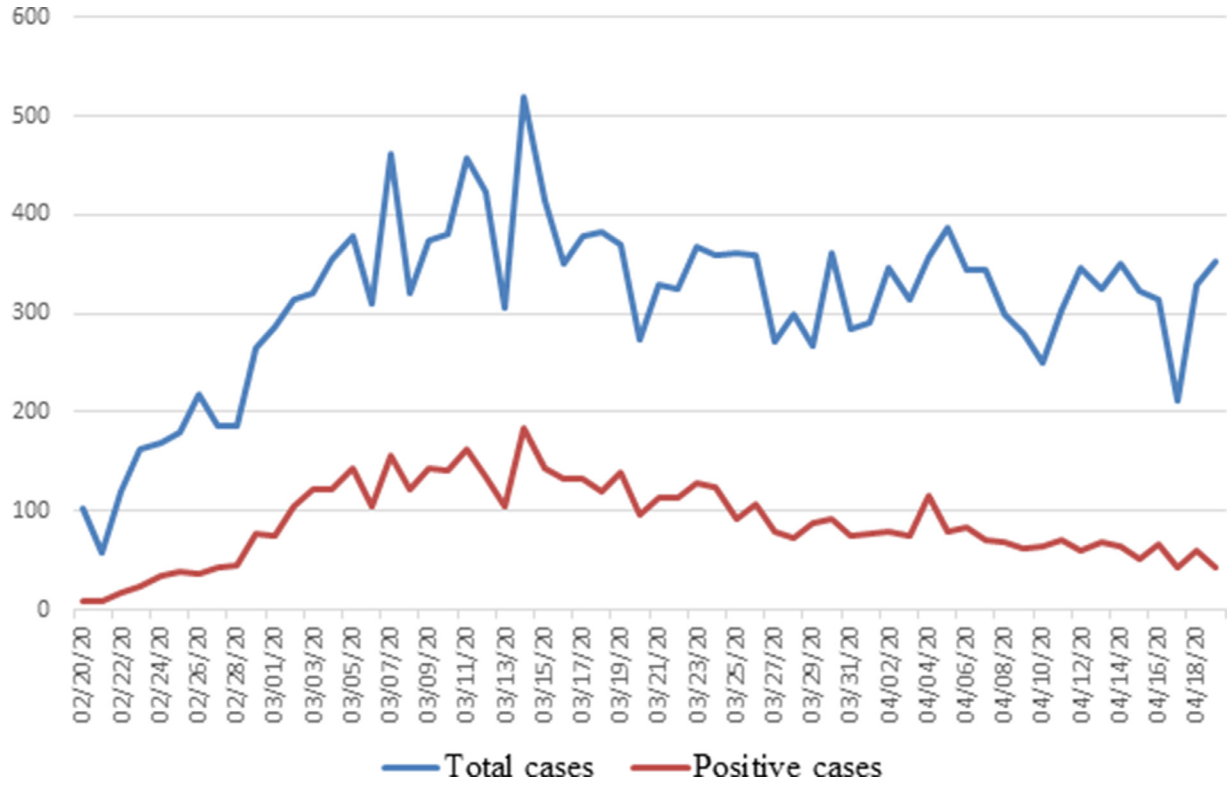

Figure 1. Total admitted patients with clinical suspicion of COVID-19 who underwent chest CT versus total cases with positive CT scans† during a three-month period from 20 February, 2020 to 21 May, 2020. † Cases with positive CT scan were defined as patients with clinical symptoms highly suggestive of COVID-19 and a chest CT scan consistent with COVID-19 findings based on RSNA diagnostic criteria. (Color version of figure is available online.)

significant positive correlation also existed between number of daily positive CT scans and daily COVID-19-related deaths during a three-month period from 20 March, 2020 to 20 May, 2020. This observation suggests that RT-PCR and low-dose chest CT have fairly comparable diagnostic ability in detecting patients with clinical suspicion of COVID-19 and that, low-dose chest CT could be used as a reliable alternative confirmatory test in epidemic regions with limited access to RT-PCR.

Routine confirmation of SARS-CoV-2 infection is based on molecular tests such as RT-PCR that detect the presence of viral RNA in patients' nasopharyngeal, oropharyngeal, tracheal, or saliva specimen (17). RT-PCR, as the current gold standard for the diagnosis of COVID-19, has a high specificity; however, the sensitivity of this test can be as low as 50%–62% at initial presentation (9,18,19). Even in highly-suspected individuals displaying typical clinical manifestations and characteristic CT imaging, serial false negative RT-PCR results might develop at early clinical stage; increasing the risk of delayed diagnosis and subsequently, hinders isolation and initiation of treatment (20). There is also a risk of false negative RT-PCR result if the patient presents late in the disease course (10). This may result in the misdiagnosis of patients who are likely to develop more severe form of the disease due to later presentation. On the other hand, CT not only has the capability to detect changes when patients are asymptomatic and before RT-PCR becomes positive (7), it can also predict infection time course. An early study from China reported a sensitivity of 97% for chest CT in predicting COVID-19 (8). Another study comparing the diagnostic value of CT and initial RT-PCR showed a sensitivity and specificity of 79% and 100% for initial RT-PCR and 77% and 96% for chest CT, suggesting comparable diagnostic performance of these two techniques (7). Fang and his colleagues also demonstrated a higher sensitivity of CT compared to RT-PCR (98% vs 71%), supporting the use of chest CT for the screening of COVD-19 in patients with consistent clinical findings (21).

RT-PCR is associated with several disadvantages that make it a not-so-efficient and reliable method for the diagnosis of COVID-19. For instance, different kit manufacturer, amount of patient viral load and improper clinical sampling can affect the detection rate of COVID-19 by RT-PCR. Furthermore, in many developing countries, there is a shortage in supply of RT-PCR kits; another major drawback to RT-PCR, which also affects developed countries, is limited medical staff to perform and process the test. This not only places a burden on healthcare workers but also increases their risk of infection due to high load of exposure (22). Nevertheless, the benefit of conventional CT is also limited by the fact that it imposes a high risk of radiation, especially if repeated. Moreover, CT is proposed to be less specific, particularly in

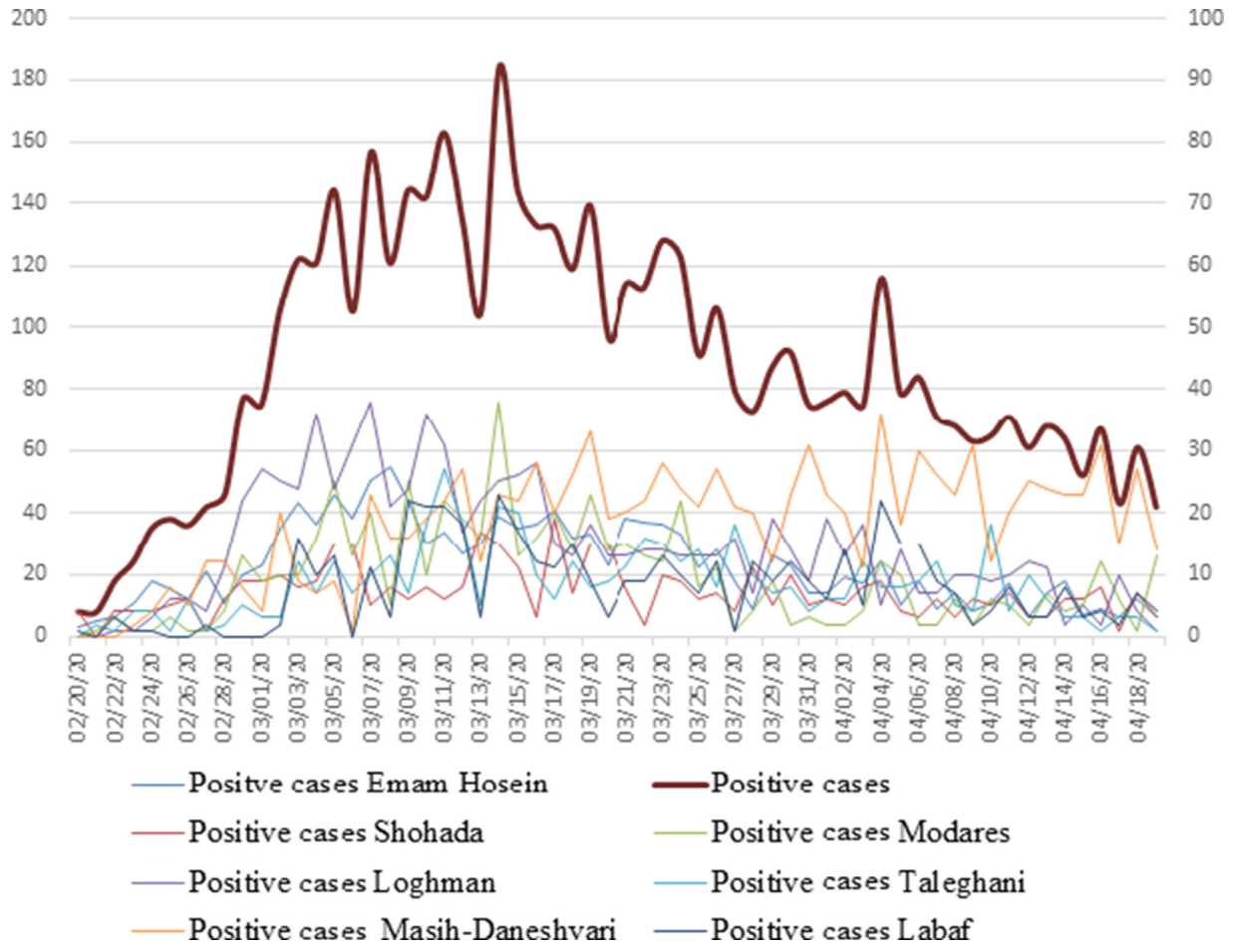

Figure 2. Comparison of the trend of cases with positive chest CT† in each specifically designated hospital for COVID-19 during a three-month period from 20 February, 2020 to 21 May, 2020. † Cases with positive CT scan were defined as patients with clinical symptoms highly suggestive of COVID-19 and a chest CT scan consistent with COVID-19 findings based on RSNA diagnostic criteria. (Color version of figure is available online.)

non-endemic regions (23). From the beginning of the COVID-19 pandemic, the Iranian Society of Radiology designed a low-dose CT protocol to evaluate patients with high probability of COVID-19 infection (14). Later on, other studies also pointed to the effectiveness and benefit of low-dose chest CT over standard-dose CT for evaluating lung involvement in COVID-19 (24,25). Interestingly, in the study by Dangis et al. (26), a high specificity rate of 93.6% was observed with low-dose CT. This was similar to the results of another study conducted on 424 patients, showing a specificity rate of 93-100% with standard CT (26).

As we progress through this pandemic, novel approaches that detect viral RNA more rapidly are being introduced; methods such as loop-mediated isothermal amplification and CRISPR-Cas12 or -Cas13-based diagnostic tests are already under investigation. These tests, while being cheaper, will probably offer more sensitive and specific results as compared to the current RT-PCR test (17); though, to date, these tests have not yet been validated for clinical use in the detection of SARS-CoV-2. Thus, until then, the use of a non-invasive technique such as low-dose CT seems to be a more rapid and sensitive method, as compared to PCR, with reasonably equal diagnostic performance, particularly in regions with high prevalence of COVID-19. More importantly, this relatively inexpensive imaging modality is widely accessible throughout the world and ensures patient's safety if used with a low-dose protocol. In addition, it is not associated with the sampling flaws of RT-PCR.

Besides CT scan, another imaging modality that is recommended for the detection of pulmonary involvement in patients with the clinical suspicion of COVID-19 is lung ultrasound. This modality has many advantages in terms of availability, reliability and relatively low cost. Furthermore, there is no risk of radiation and less risk of contamination (due to its' portability), which make it a safer method compared to CT. In addition, Point-of-Care Ultrasound can provide vital information regarding any possible involvement of the cardiovascular system as well being used as

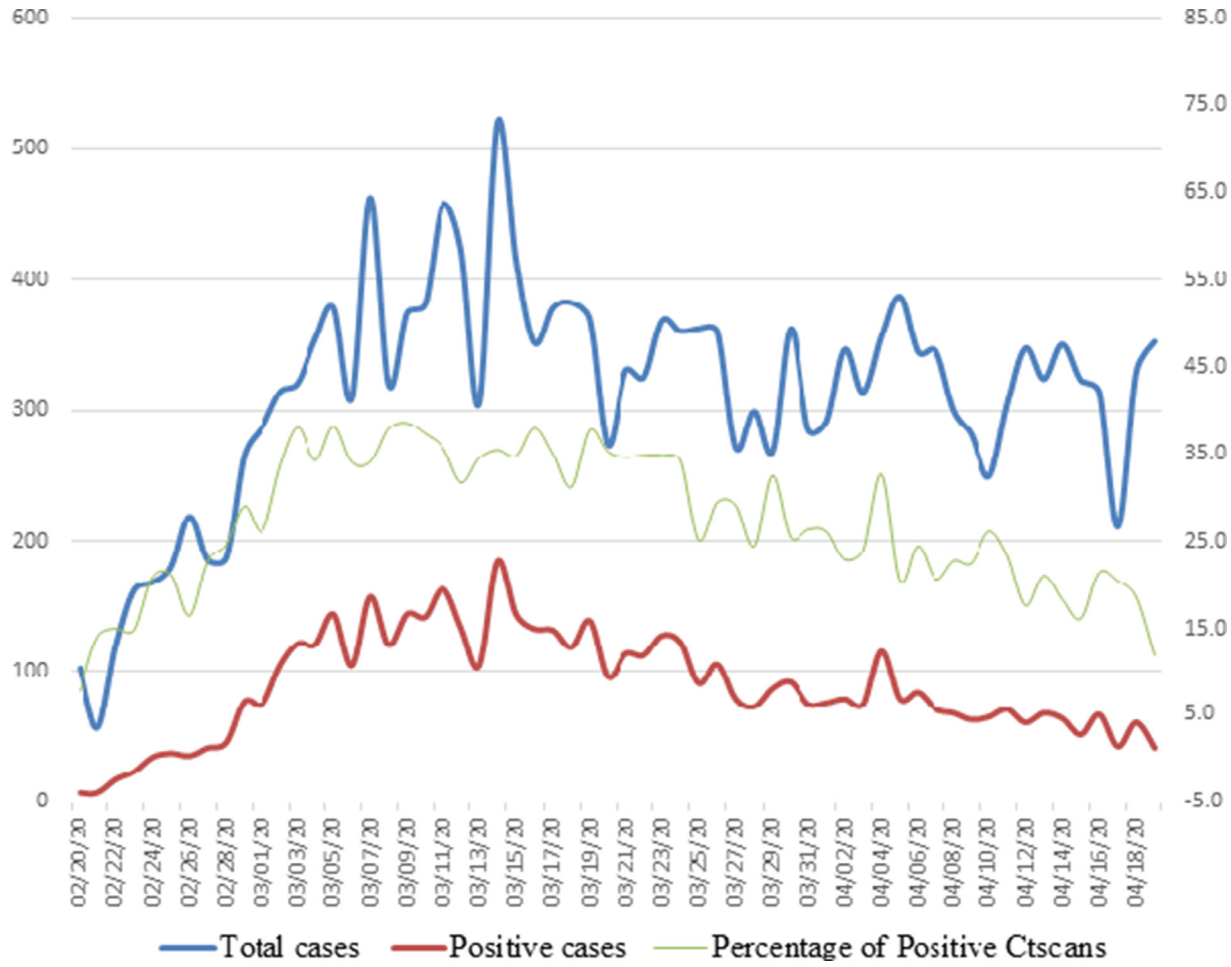

Figure 3. Percentage of cases with positive chest CT† to total admitted patients with clinical suspicion of COVID-19 who underwent chest CT during a three-month period from 20 February, 2020 to 21 May, 2020. † Cases with positive CT scan were defined as patients with clinical symptoms highly suggestive of COVID-19 and a chest CT scan consistent with COVID-19 findings based on RSNA diagnostic criteria. (Color version of figure is available online.)

echocardiography during the same session (27). However, the reported sensitivity of this diagnostic tool is controversial, particularly when it is performed by a non-expert sonographist (28–30).

As a secondary objective, we also assessed the trend of total COVID-19-related admissions and positive cases (based on CT) within this three-month period. The results of our study showed that both of these rates were higher in Loghman and Imam Hossein hospitals. This might be because these two hospitals are located in regions of Tehran where underrepresented minorities and patients with a lower socioeconomic status live. According to existing literature, regions of Tehran with lower socioeconomic status and specifically, the districts where these hospitals are located have higher prevalence rates of overweight BMI and obesity (31,32). Consistent with our finding, many studies have reported a disproportionate rate of burden in socioeconomically-disadvantaged individuals with COVID-19 (33–35). This might be due to the fact that because of high housing density, performing social distancing is not as practical. Also, it is now widely accepted that higher BMI and obesity are major risk factors for COVID-19 (36). Hence, our observation provides further evidence for considering patients' socioeconomic status as an important risk factor for COVID-19.

As like any other study, this study has some limitations. One of the main limitations was that due to shortage of kits, RT-PCR had not performed for all of the patients admitted to the hospitals included in this study; thus, a different dataset that included the daily-reported number of PCR-confirmed COVID-19 cases for all hospitals in Tehran province was used to assess the correlation between CT and RT-PCR. Another limitation was the low diagnostic ability of chest CT in diagnosing patients who present with complications other than pneumonia, such as individuals manifesting with neurologic or gastrointestinal symptoms without any signs of lung involvement. Another point which should also be considered is that such results might not be achieved in regions with lower prevalence of COVID-19 compared to Iran.

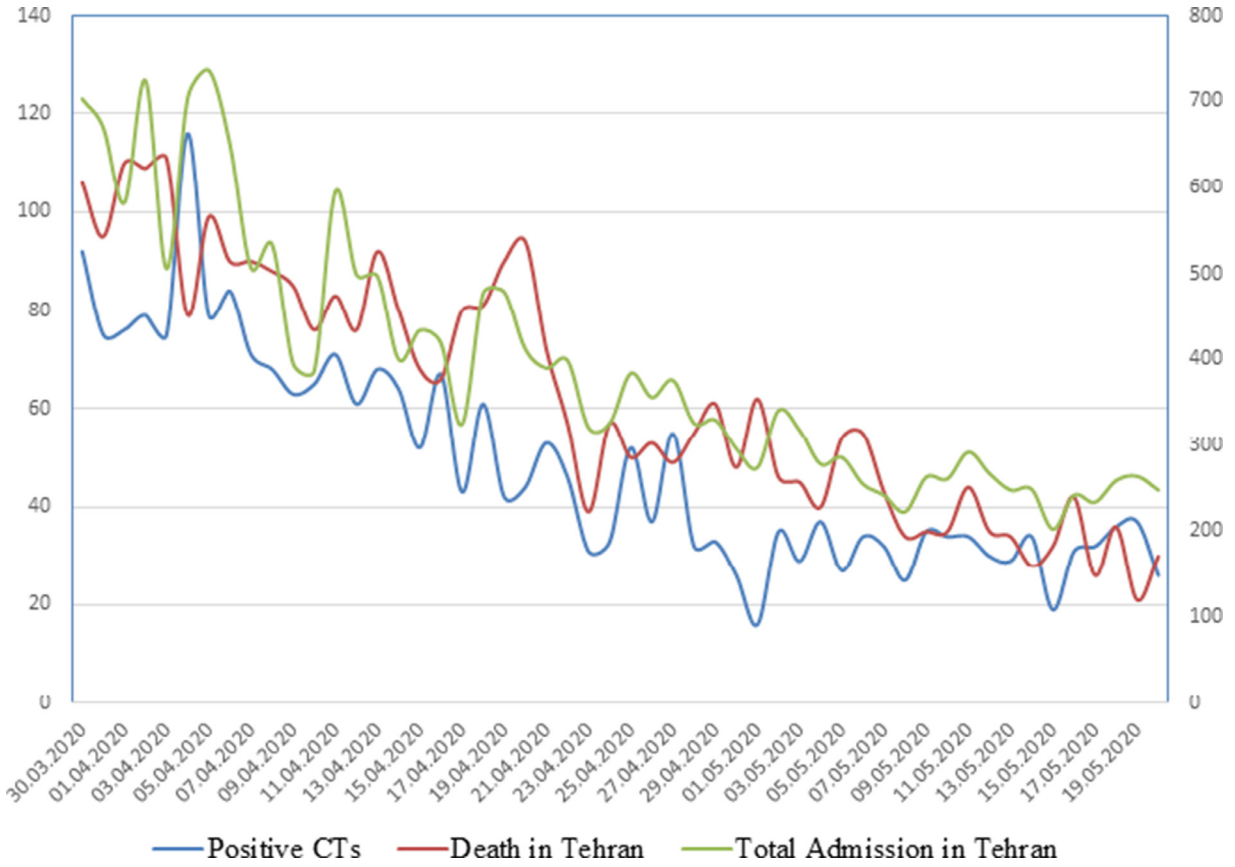

Figure 4. Correlation between the number of daily COVID-19 cases with positive chest CT scan † and number of daily PCR-confirmed COVID-19 cases and COVID-19-related deaths‡ in Tehran province. † Cases with positive CT scan were defined as patients with clinical symptoms highly suggestive of COVID-19 and a chest CT scan consistent with COVID-19 findings based on RSNA diagnostic criteria. ‡ Deaths attributed to COVID-19 through confirmation by PCR or other diagnostic tests. (Color version of figure is available online.)

CONCLUSION

The results of our study, along with the findings of previous reports, provide evidence for policymakers and healthcare leaders to consider low-dose chest CT as a safe, rapid and reliable diagnostic tool to for the detection of COVID-19, particularly in high-prevalent regions with constraint of resources such as insufficient SARS-CoV-2 molecular test kits. Although we did not compare CT scan with lung ultrasound in this study; based on reports from other studies, lung ultrasound might also provide benefit as a safe and reliable tool in the absence of RT-PCR kits. Furthermore, in this study, the observed higher rate of COVID-19-related admission and positive CT in hospitals located in socioeconomically-disadvantaged regions emphasizes on the role of socioeconomic status as an important risk factor of COVID-19 infection.

AUTHORS' CONTRIBUTION

Ali Mahdavi, Ali Maher, and Mohammadreza Sohrabi concieved of the presented idea.

Alireza Zali and Morteza Sanei Taheri designed and supervised the study.

Mohammadreza Sohrabi performed the analysis, interpreted the data and provided the figures.

Mohammadmehdi Sadoughi, Afshin Zarghi, Seyed Ali Ziai, Nastaran Khalili and Reza Jalili Khoshnoud performed the literature search, drafted the manuscript and performed critical revision.

Abbas Arjmand Shabestari, Mehrdad Bakhshayeshkaram, Hamidreza Haghighatkhah, Babak Salevatipour, Alireza Abrishami, Masoomeh Raoufi, Pooneh Dehghan, Arash Khameneh Bagheri and Morteza Sanei Taheri participated in data collection.

Khatereh Hanani participated in data analysis.

All authors revised and approved the final draft of the manuscript.

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DECLARATION OF COMPETING INTEREST

The authors declare no conflict of interest.

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