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Original article

Epidemiological profile and performance of triage decision-making process of COVID-19 suspected cases in southern Tunisia

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ABSTRACT

Introduction: During an epidemic, screening processes can play a crucial role in limiting the spread of the infection. The aim of this study was to describe the epidemiological profile of COVID-19 suspected cases and to evaluate the performance of the triage process in predicting COVID-19 in Southern Tunisia.
Methods: It was a prospective study including all patients consulting to the Hedi Chaker University Hospital departments from March to June 2020. A clinical triage score (CTS) was used to assess the risk of the infection and to refer patients to the appropriate part of the facility accordingly.
Results: Overall, 862 patients were enrolled, among whom 505 patients (58.6%) were classified as suspected cases (CTS $\geq$4). Of these, 46.9% (n = 237) were of mild form. Samples were collected from 215 patients (24.9%), among whom five were COVID-19 positive, representing a positive rate of 2.3%. The in-hospital cumulative incidence rate of COVID-19 was 580/100000 patients. The total daily incidence decreased significantly during the study period ($p < 0.001$, chi-square for linear trend = 25.6). At a cut-off of four, the CTS had a sensitivity of 40%, a specificity of 32.4%, and negative and positive predictive values of 95.8% and 1.4%, respectively.
Discussion: Although the triage process based on the CTS was not as performant as the RT-PCR, it was crucial to interrupt virus spread among hospitalized patients in "COVID-19-free departments".

African relevance

- The lack of resources in Africa limits triage strategies meant to mitigate the spread of the COVID-19 pandemic..
- A modified COVID-19 triage strategy based on a clinical triage score could address this issue in limited resources countries.
- We find the triage process was not as performant as RT-PCR in identifying COVID-19 cases in some African hospitals.
- African physicians should continue to rely on their medical expertise to diagnose and manage COVID-19 suspected cases.

Introduction

In December 2019, a novel coronavirus now known as SARS-CoV-2 and later identified as the cause of COVID-19 suddenly emerged in Wuhan, China. COVID-19 rapidly spread throughout the world, becoming, according to the WHO, a Public Health Emergency of International Concern on January 31st, 2020 [1,2]. As of April 16th, 2020, the emerging COVID-19 infection had been spreading worldwide, causing over two million cases and over 137 thousand deaths [3].On March 2nd, 2020, the first imported case of COVID-19 was reported in Tunisia, announcing the beginning of the COVID-19 pandemic in our country. In as much as this disease continues to appear and poses a major

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public health concern, due to its higher rates of transmissibility, hospitalization, intensive care unit admission, the severity of disease, and mortality, health institutions should increase as better as possible measures to prevent COVID-19 spread among hospitalized patients in "COVID-19-free departments". Studies from China, where the initial outbreak took hold, reported that triage strategies, aimed both at regulating patient access and separating them within the hospital, could mitigate many problems related to the spread of the pandemic, such as hospital overcrowding, diffusion of the virus within the hospital and infection of healthcare personnel [4,5]. In northern Italy, the structure of a hospital, which was specifically equipped for the management of COVID-19 patients, was immediately modified with the introduction of a pre-triage protocol to divide patients according to the risk of infection [6]. This hospital held the "zero infection" record in healthcare workers, which indicated the flexibility and validity of the pre-triage system. Despite major advances in epidemic preparedness, Africa remains uniquely susceptible to COVID-19 [7]. The high prevalence of HIV, tuberculosis and other pathogens might potentiate the severity of this disease and contribute to diagnostic uncertainty [7]. On February 27th, 2020, the first case of COVID-19 in sub-Saharan Africa was reported in Nigeria, making the spread in the region more probable [8]. Unfortunately, COVID-19 triage strategies adopted in response to COVID-19 outbreak in Wuhan, China, such as chest Computed Tomography (CT), complete blood counts with differential, and c-reactive protein, would not be feasible in low-income settings due to lack of logistics, human and material resources [7,9]. Accordingly, a modified COVID-19 triage strategy was proposed for use in resource-limited settings that do not have established local transmission [7]. It was a simple approach used to decide who requires isolation and targeted testing for SARS-CoV-2. The most advanced tool required was a thermometer. In Southern Tunisia, Hedi Chaker University Hospital (HCUH) has adopted, according to the Tunisian national guidelines, a triage process based on a clinical triage score (CTS) in order to improve its function during the pandemic and to avoid patients with suspected COVID-19 to be carrying the infection from coming into contact with non-infected patients. However, to the best of our knowledge, the effectiveness of this strategy and whether the adopted CTS was conforming to the local epidemiological context have not yet been evaluated. Thus, the aim of this study was to describe the epidemiological profile and the chronological trends of COVID-19 suspected cases in Southern Tunisia during the first wave and to evaluate the performance of the triage process in predicting COVID-19.

Methods

It was a prospective study including all patients consulting to the HCUH departments in Southern Tunisia during the first epidemic wave, from March to June 2020. This hospital has been nominated as the referent centre of COVID-19 management in Sfax, Southern Tunisia, hosting patients from both private and public health structures. Moreover, an isolation ward was launched in HCUH, receiving all cases with confirmed or suspected COVID-19, with clinical symptoms not manageable outside the hospital settings, and who required immediate hospitalization.

A two-level triage operation was established in HCUH to guide patients during their hospital visits. All patients entering the hospital had to pass through pre-triage. Moreover, this process included all individuals entering the hospital: outpatients, emergency cases, inpatients, healthcare professionals, and visitors. The first level of the triage process, called pre-triage, aimed to identify patients who might be infected. The second-level and final evaluation, called triage, aimed to evaluate the degree of the disease severity. Before being qualified for a pre-triage or triage position, all medical and nursing staff personnel received systematic and strict training. The pre-triage was performed inside the purpose-built structure, opened 24 h a day, and introduced at the entrance to the HCUH by a team comprising a doctor and a nurse. This team measured the body temperature using an infrared thermometer and underwent an oral questionnaire. Data were collected using a pre-established fact sheet. These data included gender, age, residency, comorbidities, such as diabetes, hypertension, chronic respiratory diseases, cardiovascular diseases, chronic renal failure and obesity, a history of fever (Temperature ≥ 38.5), clinical symptoms, and potential community exposure to SARS-CoV-2, defined as a history of travelling within the last 14 days before the disease onset or having contact with people with acute respiratory symptoms or having close contact with returning travelers. Then, this information was compiled into a CTS, which was established by Tunisian national guidelines of the National Authority for Accreditation in Healthcare (INEAS) in order to stratify those at higher risk of COVID-19, which was continuously updated according to the epidemiological evolution in the country [10]. The CTS was calculated as follows: community exposure (2 points), fever (2 points), cough and/or dyspnoea (2 points), sore throat (1 point), nausea/vomiting/diarrhoea (1 point), renal/respiratory or cardiac failure (1 point). A cut-off of four was adopted to classify all patients consulting to the hospitals into suspected cases if the score was ≥ 4 points and not suspected cases if the score was <4 points. The doctor had to calculate the CTS for each patient. If this score was less than four, then the patient would be allocated to the relevant department dedicated to patients presumed not to be infected. Otherwise, suspected patients (CTS ≥ 4) were referred for the second-level triage, re-evaluated by an expert team of specialised physicians, and classified according to the severity of the disease using specific criteria established by Tunisian national guidelines of INEAS, as follows [10]: mild form (i.e., suspected patients who had a respiratory rate (RR) <30 breaths/min and a peripheral oxygen saturation on pulse oximetry (SpO2) $>92\%$ on ambient air), moderate form (i.e., suspected patients with shortness of breath or a RR >30 breaths/min or SpO2 $\leq 92\%$ on ambient air or a severe tare decompensation requiring hospitalization), and severe form(i.e., suspected patients with respiratory distress or systolic blood pressure less than nine or neurological disorders). Further biological and radiological explorations were done when necessary, i.e., indication of hospitalization or exacerbation of existing comorbidity or suspicion of another diagnosis other than COVID-19. Then, after a physical examination and further complementary biological or radiological exams, patients who had another diagnostic other than COVID-19 were ruled out from the study. Despite its relatively low sensitivity, the real-time reverse-transcription polymerase chain reaction (RT-PCR) was described as the gold standard to confirm COVID-19 diagnosis during the study period [11]. The RT-PCR analysis of nasopharyngeal swab specimens was carried out for patients with clinical CTS ≥ 4 and/or for those with high clinical suspicion of COVID-19 after expert re-evaluation.

Statistical analysis was performed using SPSS.20. Continuous variables with normal distribution were presented as means $\pm$ standard deviation (SD); non-normal variables were reported as medians and interquartile ranges (IQR). Categorical variables were summarised as numbers and percentages. Chronological trends analysis was done using Chi-square for trends. The diagnostic performance of CTS was evaluated by calculating the area under the receiver operating characteristics curve (AUROC). At a cut-off of 4, the score performance in predicting COVID-19 was also evaluated through a 2×2 contingency table RT-PCR result (Positive RT-PCR vs. Negative RT-PCR) with the patient's CTS (<4 vs. ≥ 4). Through this contingency table, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPP) of CTS were calculated. P values lower than 0.05 were considered statistically significant.

Results

From March to June, 862 patients were successively evaluated at the pre-triage stage. Their median age was 39 years (IQR = [29.5–54.8]). The distribution by age groups showed that the largest age group of included patients was [15–60 years[(n = 670;77.7%), followed by ≥ 60 years (n = 153;17.7%). Five hundred and fifteen patients were males

(59.7%), with a sex ratio (Male/Female) of 1.48. According to the urbanity of residence, 688 cases (79.8%) came from urban areas. Community exposure to SARS-CoV-2 was noted in 133 patients (15.4%). Four hundred sixty-six cases (54.1%) reported having at least one comorbidity. The most prevalent comorbidities were chronic respiratory diseases (n = 116;24.9%), hypertension (n = 96;20.6%) and cardiovascular diseases (n = 79;17%). Common clinical symptoms included dry cough (40.8%), headache (33.9%), fever (32.1%), dry throat (30.6%), and dyspnoea at rest (30.6%). Of patients who arrived in pre-triage during the study period, 58.6% (n = 505) had a CTS ≥ 4 and were referred for second-level triage according to the described protocol. Of these, 46.9% (n = 237) were with mild form, 145 cases with moderate form (28.7%), and 3 cases with severe COVID-19 form (0.6%). The COVID-19 diagnosis was ruled out in 120 cases (23.8%) (Table 1).

The RT-PCR analysis of nasopharyngeal swab specimens was carried out for 215 cases out of the 862 enrolled cases, representing a screening rate of 24.9%. Of these, five tested cases were COVID-19 positive, accounting for a positive rate of 2.3%. Of all patients consulting to the pre-triage box, the in-hospital cumulative incidence rate of COVID-19 was 580/100000 persons.

The median daily number of suspected cases was 6 cases/day (IQR = [3–11.75]). It had increased gradually since March 25th, 2020, and peaked on April 7th, 2020, with 22 new cases (Fig. 1).

Meanwhile, the peak of not suspected cases appeared on April 13th, 2020, with 21 new cases, and then the daily new cases started to gradually decline in both groups (Fig. 1).

Chronological trends analysis showed a significant decrease in the total daily incidence of the COVID-19 suspected cases during the study period ($p < 0.001$, chi-square for linear trend (CST) =25.6), as well as in COVID-19 mild ($p = 0.02$, CST = 9) and moderate forms ($p = 0.01$, CST = 6). However, the daily incidence of COVID-19 severe form did not change over the study period ($p = 0.28$, CTS = 12) (Fig. 2).

Performance of clinical triage score in predicting COVID-19.

Receiver operating characteristics (ROC) curve analysis showed that the CTS had an AUROC of 0.35 in predicting COVID-19 ($p = 0.26$) (Fig. 3).

At a cut-off of four, the CTS had a sensitivity of 40% and a specificity of 32.4%. In addition, this score showed an NPV of 95.8% and a PPV of 1.4% (Table 2).

Table 1
Description of the study population.

Variables	Number (%)[c]
Total	862
Gender	
Males	515 (59.7)
Females	347 (40.3)
Age groups (years)	
< 15	39 (4.5)
[15–60[	670 (77.7)
≥ 60	153 (17.7)
Urbanity of residence	
Urban areas	688 (79.8)
Rural areas	174 (20.2)
Community exposure[a]	
Yes	133 (15.4)
No	729 (84.6)
Comorbidities	
Yes	466 (54.1)
No	396 (45.9)
Clinical symptoms	
Dry cough	352 (40.8)
Fever	277 (32.1)
Headache	292 (33.9)
Dry throat	264 (30.6)
Dyspnoea at rest	264 (30.6)
Exertional dyspnoea	133 (15.4)
Productive cough	169 (19.6)
Diarrhoea	155 (18)
Arthralgia	145 (16.8)
Shivering	137 (15.9)
Vomiting	133 (15.4)
Myalgia	111 (12.9)
Rhinorrhoea	117 (13.6)
Clinical triage score	
< 4	357 (41.4)
≥ 4	505 (58.6)
Mild form	237 (46.9)
Moderate form	145 (28.7)
Severe form	3 (0.6)
Ruled out COVID-19 diagnosis	120 (23.8)
COVID-19 diagnostic testing based on RT-PCR[b]	
Yes	215 (24.9)
No	647 (75.1)

[a] People who travelled within the last 14 days or who were exposed to people with acute respiratory symptoms or who had close contact with returning travelers.
[b] The real-time reverse-transcription polymerase chain reaction;
[c] percentage.

Discussion

During the study period, the in-hospital cumulative incidence of COVID-19 was 580/100000 patients. At a population-based level, the cumulative incidence of COVID-19 ranged between 3 and 5/100000 inhabitants in Southern Tunisia and was equal to 9.66/100000 inhabitants at the national level [12]. This latter was much lower than the cumulative incidence rates reported in developed countries such as the United States (403.6/100000 persons) [13] and Germany (223/100000 persons) [14] as well as in the developing countries, such as Brazil (36.58/100,000 inhabitants), Morocco (15.2/100000 inhabitants) and Algeria (11.02/100000 inhabitants) [15].

The screening rate found in the present study (24.9%) reflected the low testing capacity, especially at the very beginning of the pandemic spread. To be noted, the laboratory testing capacity (RT-PCR) in Tunisia was highly limited compared with France and Italy. Indeed, the maximum recorded tests made in Tunisia were 724 daily, while only the city of Marseille in France provided more than 11,000 tests per day [16]. Additionally, there was a testing inequality among the regions: the testing was focused on the capital but was not adequately performed over all the regions. As for Southern Tunisia, there was an extremely low testing activity in the region, and the majority of infected individuals had not been tested [16].

Taking these facts into account, it is getting clear that there is a huge discrepancy between the officially recorded and real infection cases. Accordingly, our hypothesis was that the recorded positive rate in the present study (2.3%) might be underestimated. This rate was higher than those of Australia, South Korea, and Uruguay (<1%) and lower than positives rates reported in Mexico and Bolivia (20%–50%) [17]. According to criteria published by the WHO in May 2020, a positive rate of less than 5% is one indicator that the epidemic is under control in a country [17].

Most of the COVID-19 suspected cases were classified as mild to moderate cases, which was in line with previous studies [3,18–20]. In fact, in Italy, which was the first European COVID-19 cluster, 5% to 6% of cases required admission to intensive care unit [19], which was higher than that reported in our study population. As the population median age in Italy is higher than North-African countries [21] and given that the severe form of the disease becomes significantly and progressively higher after 50 years of age, the observed discrepancy in the severity of COVID-19 symptoms could be explained by differences in population age structures [19].

During the study period, a significant decrease in the total daily incidence of the COVID-19 suspected cases was noted. In fact, since the very beginning of the pandemic spread in our country, Tunisian authorities adopted a containment strategy, which started on March 22nd in order to halt the spread of COVID-19 and limit the number of fatalities [16]. Compared to France and Italy who had applied similar

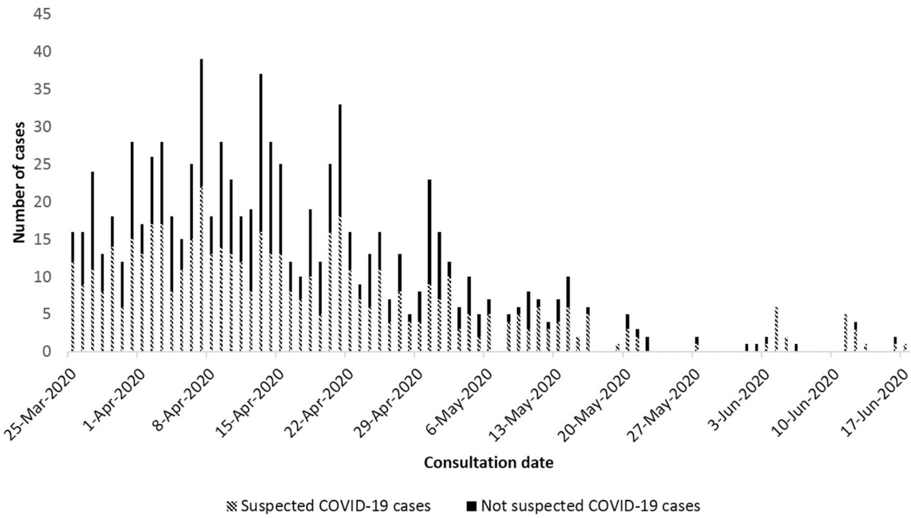

Fig. 1. Daily change in the number of new suspected and not suspected cases from March 25th, 2020 to June 17th, 2020.

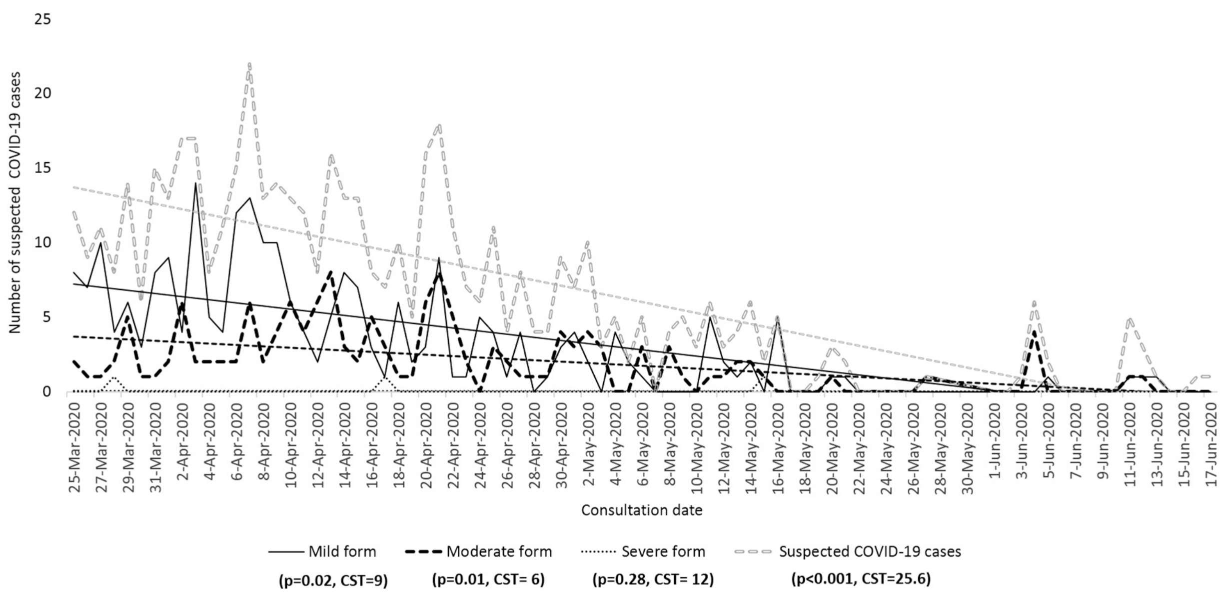

Fig. 2. Chronological trends of suspected cases according to the severity of the disease from March 25th 2020 to June 17th 2020.

containment rules [16], this early preventive measure allowed Tunisia to reduce faster the number of infected people. However, containment measures have entailed large economic costs and were likely to continue to aggravate the economic recession with sharp reductions in production and interruptions to trade and supply chains [22]. Besides, this strategy had a negative impact on the management of patients with non-communicable diseases (NCDs). Resources were mainly allocated to enhance emergency care and were deflected from facilities for NCDs [23].

In the present study, the ROC curve and the corresponding AUROC analysis showed that CTS did not have a predictive ability to discriminate COVID-19 cases from those not infected with SARS-CoV-2. Moreover, in comparison with the RT-PCR, CTS had lower sensitivity and lower specificity, impeding its use for screening symptomatic patients and for confirming COVID-19 diagnosis. In fact, data from in vitro analyses along with minimal clinical data suggested that RT-PCR had a very high specificity but lower sensitivity ranging from 63% to 78% [24]. A non-peer-reviewed publication reported that, based on 87 Chinese patients who were ultimately diagnosed with COVID-19, RT-PCR tests had a sensitivity and a specificity of 78.2% and 98.8%, respectively [25]. Therefore, CTS adopted in the triage process cannot substitute RT-PCR in diagnosing COVID-19, although the same reagent, process, and technique were used. This might be explained by the small number of confirmed cases, which may lead to lower reliability and validity of the score. However, the identification criteria for suspected COVID-19 cases cannot achieve 100% sensitivity and specificity at the same time. Giving preference to sensitivity will cause more patients to be admitted into the infected area, increasing the risk of transmitting the infection to healthy patients incorrectly placed there. Conversely, preferring specificity will allow infected patients to enter a clean area where they may infect healthy patients. Although the sensitivity and the specificity were relatively low in this study, these rates could be arguably acceptable since the incidence of COVID-19 in this region was very low. In fact, the disease incidence or the prevalence is a key determinant of the effectiveness and reliability of public health screening strategies. With a highly sensitive test, few false-negative results would be recorded, and the diagnosis could be ruled out. Besides, NPV of CTS was high, suggesting its performance in excluding the COVID-19 diagnosis rather than confirming it. The low PPV found in our study could be explained in part by the fact that the chosen cut-off was low. On the other hand, other

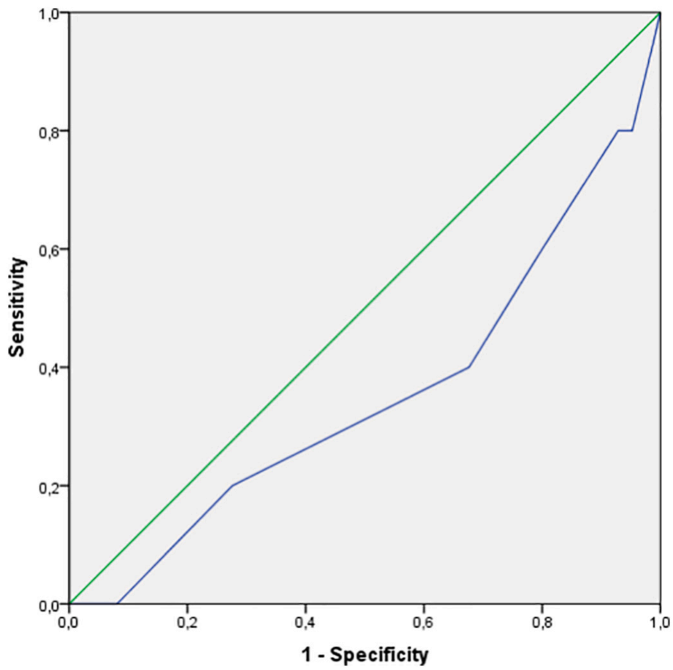

Fig. 3. Receiving operating curve of the clinical triage score in predicting patients with COVID-19 infection, referred to the RT-PCR as a gold standard. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Performance of clinical triage score in predicting COVID-19.

	Positive RT-PCR[a]	Negative RT-PCR[a]	Total
CTS[b] $\geq$ 4	2	142	144
CTS[b] <4	3	68	71
Total	5	210	215
Sensitivity: 40% (95%CI[e] = [5.4–85.3])			
Specificity: 32.4% (95%CI[e] = [26.1–39.2])			
NPV[c]: 95.8% (95%CI[e] = [88.1–99.1])			
PPV[d]: 1.4% (95%CI[e] = [0.2–4.9])			

[a] Real-time reverse-transcription polymerase chain reaction.
[b] Clinical triage score.
[c] Negative predictive value.
[d] Positive predictive value.
[e] Confidence interval.

triage strategies were established in several countries, such as in northern Italy, particularly in Piacenza, where a point-of-care ultrasound lung was used in the triage decision-making. This technique was strongly recommended as an effective, safe, low-cost, and easy method to early detect pulmonary and pleural findings in patients without suspicious symptoms of COVID-19 [1].

This manuscript provides a lot of concise data from a prospective assessment of a novel triage tool. The results studies described demographic, chronological, as well as a gold-standard comparison. This CTS could be proposed as a useful algorithm in other low-income countries to better predict patients at high risk of COVID-19 infection. Yet, regardless of the adopted triage strategy, physicians should generate their reasoning skills to make effective judgments about the diagnosis and management of suspected cases on a case-by-case basis.

Nevertheless, some limitations associated with conducting survey screenings need to be mentioned. In fact, not all patients were tested with the gold standard (RT-PCR). Although the RT-PCR referenced has a relatively high sensitivity in most countries, the CTS had a low sensitivity which is not well-matched with what is desired for large public health screenings. That is, when doing public health screenings for outbreaks identification, the compromise is generally to sacrifice specificity for sensitivity, notably in mass screening, in order to avoid a high rate of misdiagnosed and false-negative cases. Indeed, this scoring system was effective based on the overall low incidence of cases, however, due to overall low sensitivities, it may not be suitable for high-incidence diseases regions and need to be more amended to generalise it in other health settings. These findings confirmed that the physician should rely on their medical expertise to suspect a diagnosis, rather than adopting blindly a rational score independently of their clinical sense. Moreover, clinical triage scores based on an absurd measure of temperature using an infrared thermometer could bias the objective evaluation of the patient status, and then it should be interpreted according to the reliability of this method as well as its dependence on technique.

Conclusion

This original study highlighted that triage decision rules adopted in predicting COVID-19 suspected cases represented a real challenge in the local context. Although the triage process based on the CTS was not as performant as the RT-PCR, it was crucial to interrupt virus spread among hospitalized patients in "COVID-19-free departments" and to avoid local outbreaks. Nevertheless, since the COVID-19 outbreak is not over yet, every detail should be evaluated carefully, and the updates should be followed closely to monitor the epidemiological properties of COVID-19.

Dissemination of results

The results of this study were shared with the clinicians at the study site through an informal presentation.

Authorship contribution statement

Authors contributed as follows to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: MBJ, HBA, MK, and MBH contributed 10% each; MT, HM, NK, SY, JT, YM, MT, CM, SM, MBJ, HB, and JD contributed 5% each. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of competing interest

The authors declared no conflicts of interest.

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