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Short Communication

Clinical and epidemiological features discriminating confirmed COVID-19 patients from SARS-CoV-2 negative patients at screening centres in Madagascar

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ABSTRACT

Early and fast detection of COVID-19 patients help limit the transmission and wide spread of the virus in the community and will have impact on mortality by reducing the incidence of infection among vulnerable people. Therefore, community-based screening is critical. We aimed to identify clinical signs and symptoms and epidemiological features that could help discriminate confirmed cases of COVID-19 from SARS-CoV-2 negative patients. We found that age (aOR:1.02, 95%CI:1.02–1.03, p < 0.001), symptoms onset between 3 and 14 days (aOR:1.35, 95%CI:1.09)1.68, p = 0.006), fever or history of fever (aOR:1.75, 95%CI:1.42–2.14, p < 0.001), cough (aOR:1.68, 95%CI:1.31–2.04), sore throat (aOR:0.65, 95%CI:0.49–0.85, p = 0.002), ageusia (aOR:2.24, 95%CI:1.42–3.54, p = 0.001), anosmia (aOR:6.04, 95%CI:4.19–8.69, p < 0.001), chest pain (aOR:0.63, 95%CI:0.47–0.85, p = 0.003), myalgia and/or arthralgia (aOR:1.64, 95% CI:1.31–2.04, p < 0.001), household cluster (aOR:1.49, 95%CI:1.17–1.91, p = 0.001) and evidence of confirmed cases in the neighbourhood (aOR:1.92, 95%CI:1.56–2.37, p < 0.001) could help discriminate COVID-19 patients from SARS-CoV-2 negative. A screening score derived from multivariate logistic regression was developed to assess the probability of COVID-19 in patients. We suggest that a patient with a score ≥14 should undergo SARS-CoV-2 PCR testing. A patient with a score ≥30 should be considered at high risk of COVID-19 and should undergo testing but also needs prompt isolation and contact tracing.

Prompt detection, contact tracing and quarantine of cases are estimated to be highly effective in controlling the transmission and reducing mortality from COVID-19 (Kretzschmar et al., 2020; Nussbaumer-Streit et al., 2020). Therefore, screening based on clinical features is critical at the community level especially in a context of local transmission of the virus. We aimed to assess whether some symptoms and a combination of several of them could help discriminate COVID-19 infections among patients visiting 2 screening centres.

We included in this analysis routinely collected data on patients visiting the screening centre at the Centre Hospitalier Universitaire Joseph Raseta Befelatanana (CHUJRB), Antananarivo, from May, 6 to July, 1 and on those visiting the screening centre at the Centre Hospitalier Universitaire Tambohobe (CHUT), Fianarantsoa, from July, 4 to August, 14. We excluded patients with unknown or inconclusive PCR results. We have also investigated whether the patient lives in a neighbourhood or an area where COVID-19 patients were previously confirmed (neighbourhood) and whether

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other people living in the same dwelling are symptomatic (household cluster).

We compared clinical and epidemiological features of confirmed cases with those with negative test for SARS-CoV-2 by univariate and multivariate analysis by logistic regression model. We used β-coefficient multiplied by 10 and rounded to the nearest multiple of 2 derived from the logistic regression model to generate a screening score to ascertain the probability of COVID-19 in patients aged ≥15 years considering a combination of clinical signs and epidemiological features. The performance of the model was assessed by ROC curve. The sensitivity (Se), specificity (Sp), positive likelihood ratio (LR+) and negative likelihood ratio (LR−) were estimated for each cut-off. Statistical analysis was performed with Stata 14.0 (StataCorp, LP). We collected data on 3154 patients. Overall characteristics and comparison between patients with negative and positive PCR results among those symptomatic are detailed in Table 1. The screening score derived from the β-coefficient of the logistic regression model is detailed in Table 2. The ROC curve analysis suggested that a cut-off point of 10, 12, 14, 16, 18 and 20 will provide a Se/Sp/LR+/LR− respectively of 0.963/0.221/1.24/0.17, 0.945/0.328/1.40/0.17, 0.907/0.421/1.57/0.22, 0.856/0.516/1.77/0.28, 0.795/0.604/2.00/0.34 and 0.729/0.679/2.27/0.40. An Sp >90% can be obtained with a cut-off point of 30 but with a Se of 34.4%. A cut-off of 34 will provide an LR+ of at least 5 which can be considered a red flag according to the commonly arbitrary definition (Struyf et al., 2020). The area under the ROC curve was 0.7723 (95%CI: 0.75–0.79). The internal validation using 1000 bootstrap samples from the original dataset found an ROC curve area of 0.7614.

We suggest that a patient with a score ≥14 should undergo SARS-CoV-2 PCR testing. A patient with a score ≥30 should be considered at high risk of COVID-19 and should undergo testing but also needs prompt isolation and contact tracing. A previous study has shown that prediction models that include routine blood tests

Table 1
Comparison of clinical findings and epidemiological features between COVID-19 confirmed cases and SARS-CoV-2 negative patients.

Variables	Total n (%)	Negative n (%)	Positive n (%)	p-value[a]
Overall	n = 3154	n = 1866	n = 1288	
CHUJRB	2795	1680	1115	
CHUT	359	186	173	
Age in years (median, IQR)	34 (24–48)	32 (23–45)	38 (26–52)	<0.001
<15	262 (8.3)	197 (10.6)	65 (5.1)	<0.001
15–29	987 (31.3)	630 (33.8)	357 (27.7)	
30–44	928 (29.4)	564 (30.2)	364 (28.3)	
45–59	672 (21.3)	342 (18.3)	330 (25.6)	
≥60	305 (9.7)	133 (7.1)	172 (13.4)	
Male	1579 (50.1)	953 (51.1)	626 (48.6)	0.173
Asymptomatic	876 (27.8)	728 (39)	148 (11.5)	<0.001
Symptomatic	2278 (72.2)	1138 (61)	1140 (88.5)	
Self-reported contact with identified confirmed cases	778 (76)	521 (73.8)	257 (80.8)	0.015
Symptomatic (n = 2278)				
Male	1107 (48.6)	560 (49.2)	547 (48)	0.558
Age in years (median, IQR)	36 (25–50)	31 (23–45)	39 (27–53)	<0.001
Symptoms onset (days) (median, IQR) (n = 2118)	4 (2–7)	4 (2–7)	5 (3–7)	0.018
Symptoms onset between 3 and 14 days	1396 (65.9)	596 (58.4)	800 (72.9)	<0.001
Fever or history of fever	1238 (54.6)	543 (47.7)	695 (61)	<0.001
Cough	1545 (67.8)	719 (63.2)	826 (72.5)	<0.001
Haemoptysis	42 (1.8)	26 (2.3)	16 (1.4)	0.123
Sore throat	377 (16.6)	215 (18.9)	162 (14.2)	0.003
Rhinorrhoea	777 (34.1)	377 (33.1)	400 (35.1)	0.324
Otalgia	22 (1)	15 (1.3)	7 (0.6)	0.091
Ageusia	223 (9.8)	38 (3.3)	185 (16.2)	<0.001
Anosmia	374 (16.4)	63 (5.5)	311 (27.3)	<0.001
Nasal obstruction	76 (3.3)	42 (3.7)	34 (3)	0.347
Abdominal pain	58 (2.5)	26 (2.3)	32 (2.8)	0.429
Wheezing	39 (1.7)	29 (2.5)	10 (0.9)	0.002
Chest pain	296 (13)	178 (15.6)	118 (10.4)	<0.001
Myalgia/Arthralgia	638 (20.2)	240 (12.9)	398 (30.9)	<0.001
Malaise/Fatigue	706 (31)	303 (26.6)	403 (35.4)	<0.001
Dyspnoea	456 (20)	257 (22.6)	199 (17.5)	0.002
Headache	634 (27.8)	276 (24.3)	358 (31.4)	<0.001
Nausea/vomiting	107 (4.7)	54 (4.8)	53 (4.7)	0.914
Diarrhoea	110 (4.8)	49 (4.3)	61 (5.4)	0.245
Signs of pneumonia	316 (13.9)	150 (13.2)	166 (14.6)	0.341
Acute respiratory distress	68 (3)	38 (3.3)	30 (2.6)	0.321
Self-reported contact with confirmed cases	379 (76.7)	212 (76.3)	167 (77.3)	0.783
Household cluster	529 (23.2)	226 (19.9)	303 (26.6)	<0.001
Neighbourhood	1429 (62.7)	615 (54)	814 (71.4)	<0.001
Concurrent conditions	512 (22.5)	256 (22.5)	256 (22.5)	0.982

[a] χ^2 test or Fischer's exact test for categorical variables, Wilcoxon-Mann-Whitney test for continuous variables.

Table 2
Multivariate analysis of clinical signs and epidemiological features associated with COVID-19 and derived screening score.

Variables	β-coefficient	Adjusted odds ratio (95% CI)	p-value	Score
Age	0.024	1.02 (1.02–1.03)	<0.001	**2**[a]
Symptoms onset between 3 and 14 days	0.301	1.35 (1.09–1.68)	0.006	**4**
Fever or history of fever	0.560	1.75 (1.42–2.14)	<0.001	**6**
Cough	0.491	1.63 (1.31–2.04)	<0.001	**4**
Sore throat	−0.428	0.65 (0.49–0.85)	0.002	**−4**
Ageusia	0.806	2.24 (1.42–3.54)	0.001	**8**
Anosmia	1.799	6.04 (4.19–8.69)	<0.001	**18**
Chest pain	−0.459	0.63 (0.47–0.85)	0.003	**−4**
Myalgia/arthralgia	0.491	1.64 (1.31–2.04)	<0.001	**4**
Household cluster	0.399	1.49 (1.17–1.91)	0.001	**4**
Neighbourhood	0.655	1.92 (1.56–2.37)	<0.001	**6**

[a] 2 points for every 10 years above the age of 15 years (i.e., 25–34 = 2; 35–44 = 4; 45–54 = 6; 55–64 = 8; 65–74 = 10; 75–84 = 12)).

in addition to clinical findings are efficient to assess the probability of COVID-19 (Sun et al., 2020). However, availability, access and affordability of blood tests limit their use in resource-limited settings. A trade-off between sensitivity and specificity is challenging when considering screening tool for suspected cases. Nevertheless, a more sensitive tool is often needed and preferred in an ongoing outbreak. A recent systematic review of signs and symptoms in COVID-19 showed low sensitivity of these signs when taken separately (Struyf et al., 2020). A recent study in Somalia showed that the current WHO case definition for COVID-19 had only 32.7% (95%CI: 20–48) sensitivity that could be slightly improved when integrating anosmia in the case definition (Ahmed et al., 2020). Anosmia and ageusia are highly specific of COVID-19 and have the highest scores in the model even if they were present in only 27.3% and 16.2% of patients (La Torre et al., 2020; Liou et al., 2020). Surprisingly, dyspnoea was not associated with positive SARS-CoV-2 test and was associated with negative test in univariate analysis. Similarly, self-reported contact with a confirmed case did not help discriminate SARS-CoV-2 positive patients. Patients may have exaggerated when reporting symptoms like dyspnoea and other subjective signs or contact with confirmed cases because of panic and fear. The same situation was observed during a previous outbreak in Madagascar (Salam et al., 2020). In addition, an epidemiological link is difficult to identify when community transmission occurs. More objective signs like respiratory rate or measure of Sp02 by simple pulse oximetry that may be helpful in detecting silent hypoxia in COVID-19 were more reliable (Dhont et al., 2020; Jouffroy et al., 2020).

It is also anticipated that considering neighbourhood as a criterion for screening will be less relevant as the epidemic progresses in the community.

This study had several limitations. We could not assess other types of cluster that may be relevant like occupational clusters. Using level of transmission for each neighbourhood or area by considering attack rate would have been more accurate. Finally, a prospective external validation of the score is needed.

A screening score based on combination of clinical and epidemiological features could help front-line healthcare workers classify patients according to their probability of COVID-19.

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Conflict of interest

The authors declare no conflicts of interest.

Ethical approval

The ethics approval was waived as the study was based on routinely collected data and notification forms (letter N°144/MSANP/CERBM).

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