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International Journal of Infectious Diseases



INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

journal homepage: www.elsevier.com/locate/ijid

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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ARTICLE INFO

Article history: Received 16 September 2020 Received in revised form 10 November 2020 Accepted 12 November 2020

Keywords: COVID-19 SARS-CoV-2 Clinical findings Screening Score Prediction

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 \geq 14 should undergo SARS-CoV-2 PCR testing. A patient with a score \geq 30 should be considered at high risk of COVID-19 and should undergo testing but also needs prompt isolation and contact tracing. © 2020 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.

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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

E-mail address: raberahona@gmail.com (M. Raberahona). ¹ Equal contribution. 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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https://doi.org/10.1016/j.ijid.2020.11.151

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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 \geq 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 \geq 14 should undergo SARS-CoV-2 PCR testing. A patient with a score \geq 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.

$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	Variables	Total	Negative	Positive	p-value ^a
Overall CHURB n = 1364 2795 n = 1660 1105 n = 1288 1060 Age in pears (median, IQR) 3295 1660 115 Age in pears (median, IQR) 3203 3203 3203 15-29 970 (3.1) 630 (3.3) 357 (27.7) 30-44 970 (3.1) 630 (3.3) 362 (25.3) 30-44 530 (5.1) 172 (3.4) 300 (25.6) 260 305 (9.7) 133 (7.1) 172 (3.4) Age in pears (median, IQR) 627 (21.3) 342 (18.3) 300 (25.6) 260 305 (9.7) 133 (7.1) 172 (13.4) 400 (8.5) Symptomatic 1579 (50.1) 953 (51.1) 62 (48.6) 0.713 Symptomatic 177 (48.6) 500 (49.2) 547 (48) 0.558 Symptom sorst between 3 and 14 days 107 (48.6) 560 (49.2) 547 (48) 0.503 Symptom sorst between 3 and 14 days 136 (25.9) 31 (234) 90 (7.53) -0.001 Symptom sorst between 3 and 14 days 136 (55.9) 596 (58.4) 477 (48) 0.203		n (%)	n (%)	n (%)	
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Age stat223 (5.8)36 (5.3)163 (10.2)<0001Anosmia374 (16.4)63 (5.5)311 (27.3)<0.001		22 (1)	13 (1.3)	195 (16 2)	<0.091
AndianaJF4 (10.4)O (3.3)JF1 (27.5)(0.001Nasal obstruction76 (3.3)42 (3.7)34 (3)0.347Abdominal pain58 (2.5)26 (2.3)32 (2.8)0.429Wheezing39 (1.7)29 (2.5)10 (0.9)0.002Chest pain296 (13)178 (15.6)118 (10.4)<0.001	Anosmia	374(164)	63 (5.5)	311 (273)	<0.001
Nation $76 (3.7)$ $72 (3.7)$ $54 (3.7)$ $54 (3.7)$ $54 (3.7)$ $54 (3.7)$ 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	Nasal obstruction	76 (3 3)	42 (3.7)	34 (3)	0.347
Advordinary Wheezing $30 (2.5)$ $20 (2.5)$ $22 (2.5)$ 0.022 Wheezing $39 (1.7)$ $29 (2.5)$ $10 (0.9)$ 0.022 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	Abdominal nain	58 (2.5)	$\frac{1}{2}(3.7)$	32 (28)	0.120
KitchingDS (17)DS (213)H (0.5)H (0.5)Obde(Chest pain296 (13)178 (15.6)118 (10.4)<0.001	Wheezing	39 (17)	20 (2.5)	10(0.9)	0.425
InstructionInstructionInstructionInstructionInstructionMyalgia/Arthralgia638 (20.2)240 (12.9)388 (30.9)<0.001	Chest nain	296 (13)	178 (15.6)	118(10.4)	<0.002
Malaise/Fatigue 506 (31) 506 (31) 506 (35.4) <0.001	Myalgia/Arthralgia	638 (20.2)	240 (12.9)	398 (30.9)	<0.001
Initial product100 (17)100 (17)100 (17)100 (17)Dyspnoea456 (20)257 (22.6)199 (17.5)0.002Headache634 (27.8)276 (24.3)358 (31.4)<0.001	Malaise/Fatigue	706 (31)	303 (26.6)	403 (354)	<0.001
by protect 100 (22) 100 (12) 100 (12) 100 (12) Headache 634 (27.8) 276 (24.3) 358 (31.4) <0.001	Dysphoea	456 (20)	257 (22.6)	199 (175)	0.002
Nausea/vomiting 107 (4.7) 54 (4.8) 53 (5.1) 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	Headache	634 (278)	276 (24 3)	358 (314)	<0.002
Initial planthoea10 (4.8)31 (13)31 (13)31 (13)Diarthoea110 (4.8)49 (4.3)61 (5.4)0.245Signs of pneumonia316 (13.9)150 (13.2)166 (14.6)0.341Acute respiratory distress68 (3)38 (3.3)30 (2.6)0.321Self-reported contact with confirmed cases379 (76.7)212 (76.3)167 (77.3)0.783Household cluster529 (23.2)226 (19.9)303 (26.6)<0.001	Nausea/vomiting	107(47)	54 (4 8)	53 (47)	0.914
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	Diarrhoea	110(4.8)	49 (4 3)	61 (5.4)	0.245
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	Signs of pneumonia	316 (13.9)	150 (13.2)	166 (14.6)	0.341
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	Acute respiratory distress	68 (3)	38 (3.3)	30 (2.6)	0.321
Household cluster 529 (23.2) 226 (19.9) 303 (26.6) <0.001 Neighbourhood 1429 (62.7) 615 (54) 814 (71.4) <0.001	Self-reported contact with confirmed cases	379 (76.7)	212 (76.3)	167 (77.3)	0.783
Neighbourhood 1429 (62.7) 615 (54) 814 (71.4) <0.001 Concurrent conditions 512 (22.5) 256 (22.5) 256 (22.5) 0.982	Household cluster	529 (23.2)	226 (19.9)	303 (26.6)	< 0.001
Concurrent conditions 512 (22.5) 256 (22.5) 256 (22.5) 0982	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.

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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.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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 $N^\circ 144/$ MSANP/CERBM).

Acknowledgment

The authors would like to thank the Ministry of Public Health and the medical staff that has been involved in the screening of COVID-19 patients at the Centre Hospitalier Universitaire Joseph Raseta Befelatanana, Antananarivo, the Centre Hospitalier Universitaire Tambohobe, Fianarantsoa, and the Centre Hospitalier Universitaire Andrainjarto. We also thank the laboratories that have performed PCR for SARS-CoV-2 (Centre d'Infectiologie Charles Mérieux Antananarivo, Laboratoire d'Analyse Médicale Malagasy, Institut Pasteur de Madagascar, Centre Hospitalier Universitaire Joseph Ravoahangy Andrianavalona).

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