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.

International Journal of Antimicrobial Agents 56 (2020) 106100

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

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

Letter to the Editor

No evidence of SARS-CoV-2 circulation before identification of the first Swiss SARS-CoV-2 case

Dear Editor,

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) global pandemic spread from China in a very short period of time. Undetected infectious individuals shed the virus in populations and substantially contributed to its dissemination [1]. Rapid identification and isolation of cases, and contact tracing are part of the World Health Organization's recommendations to fight the outbreak.

We read with interest the paper by Deslandes et al. [2] reporting a case of retrospectively diagnosed SARS-CoV-2 infection among 14 selected patients admitted to the intensive care unit (ICU) of a single French hospital for an influenza-like illness with pulmonary ground-glass opacity. The infected patient was admitted a month before the first reported cases in France.

This description raised questions on the early dynamics of the SARS-CoV-2 pandemic and the adequacy of testing strategies. Switzerland faced one of the sharpest initial cumulated infection prevalence in the world; this dynamic suggests the presence of unidentified infectious individuals before the first reported case of SARS-CoV-2 (26 February 2020 in Switzerland and 02 March 2020 in Western Switzerland). During this period, testing recommendations for Switzerland were limited to patients with a suggestive clinical picture and a documented epidemiological exposure to SARS-CoV-2.

We aimed to retrospectively identify undetected SARS-CoV-2 infection in patients who presented to their general practitioners or an emergency department (ED) with a suggestive clinical picture (acute respiratory tract infection) in the months preceding the first case detection in Switzerland. During this period, patients with an acute lower respiratory tract infection were prospectively included in two studies: (1) a cluster-randomized clinical trial conducted in 60 primary care practices in Western and Central-Western Switzerland [3]; and (2) a cohort study conducted in the ED of Lausanne University Hospital (Western Switzerland).

Using previously described methods [4,5], SARS-CoV-2 RT-PCR was retrospectively performed using the COBAS SARS-CoV-2 test (Roche) on nasopharyngeal swabs prospectively collected following a standardized procedure and stored at −80°C. We included 144 patients from primary care and 30 patients from the ED who attended care between November and February 2020. Table 1 summarises the patients' characteristics. Mean age was 49 years (SD 17) in primary care and 74 years (SD 15) in ED. Most patients included in primary care were female, while most patients in ED were male. While 23% of patients had a chest X-ray in primary care, almost all had an X-ray in ED and a third of them had lung infiltrates. None of the nasopharyngeal samples tested positive for SARS-CoV-2 (95% CI 0.0–2.5%).

The characteristics of patients included in the ED in the period before the first Swiss positive SARS-CoV-2 patient and during the outbreak were compared to ensure that the inclusion criteria would capture COVID-19 patients. Of note, we stopped recruiting patients in primary care for ethical reasons after the first Swiss case. During the Swiss outbreak period, 134 additional patients were included in the ED cohort and routinely tested for SARS-CoV-2 (Table 1). Of them, 87 (65%) tested positive for SARS-CoV-2 between March and May 2020. Patients included in the ED during the outbreak were significantly younger (mean age 64 years, SD 18) compared with patients included before the outbreak (mean age 74 years, SD 15; $P < 0.001$). Sex distribution and duration of symptoms were similar between the two groups, while patients included during the outbreak more often had fever (72% vs. 43%; $P = 0.001$) and infiltrates on chest X-ray (69% vs. 38%; $P = 0.019$). The same differences were identified when comparing SARS-CoV-2 infected patients with patients included in the ED before the first case.

Patients were included in this study using a clinical syndromic approach (acute respiratory tract infection) and with less severe disease, compared with the French study which included patients with influenza-like illness and radiologic abnormalities in the ICU [2]. Although, the pre-test probability for COVID-19 was possibly lower in our study population, we identified SARS-CoV-2 infected patients (87 of 134, 65%) using the same inclusion criteria in the ED during the outbreak, suggesting that appropriate patients were targeted. Unfortunately, we could not include patients in primary care during the outbreak and could not prove that the inclusion criteria were optimal. A higher proportion of females was seen in the primary care cohort, whereas a higher representation of males is expected in SARS-CoV-2 infected patients.

Although these results were subject to selection bias, the fact that cases were not retrospectively identified suggests that there was no or only limited ongoing human transmission of SARS-CoV-2 in Western Switzerland before 02 March 2020.

Acknowledgements

We thank all the patients who agreed to participate and make this study possible. We thank all healthcare workers of the emergency department, internal medicine ward, infectious disease service and ICU of the University Hospital of Lausanne, who managed COVID-19 patients. We thank all general practitioners and their medical assistants who participated in the primary care study. We thank Hélène Donnet and Marie-Josée Vez for helping in sample collection at the emergency department. We are grateful to Martin Delaloye who helped us with sample storage and triage. We thank

https://doi.org/10.1016/j.ijantimicag.2020.106100

Table 1
Characteristics of patients included in primary care and emergency departments before the first detected Swiss SARS-CoV-2 case and during the outbreak.

	Before the first detected Swiss SARS-CoV-2 case		During the Swiss SARS-CoV-2 outbreak
	Primary care	Emergency department	Emergency department
Number of samples, n	146	30	134
November 2019, n	30	0	0
December 2019, n	28	0	0
January 2020, n	50	0	0
February 2020, n	38	30	5
March 2020, n	0	0	107
April 2020, n	0	0	21
May 2020, n	0	0	1
SARS-CoV-2 infection*	0	0	87 (64.9)
Female, n (%)	86 (59)	13 (43)	60 (44.8)
Age in years, mean (SD)	49 (17)	74 (15)	64 (18)
Duration of symptoms in days, median (IQR)	6 (4–10)	7 (3–8)	7 (4–10)
Presenting complaints			
Cough, n (%)	146 (100)	26 (87)	117 (87)
Fever, n (%)	101 (69)	13 (43)	96 (72)
Dyspnoea, n (%)	94 (65)	24 (80)	99 (74)
Abnormal auscultation, n (%)	67 (46)	19 (63)	79 (59)
Chest X-Ray performed, n (%)	34 (23)	29 (97)	113 (84)
Lung infiltrates, n (%)	12/34 (35)	11/29 (38)	78/113 (69)

* Before the first Swiss detected SARS-CoV-2 case, patients were retrospectively tested for SARS-CoV-2 using stored nasopharyngeal swabs.

Marie-Anne Page and the team of molecular microbiology for their support in running SARS-CoV-2 PCR.

Declaration of Competing Interest

None declared.

Funding

None.

Ethical Approval

Not required.

References

[1] Li R, Pei S, Chen B, Song Y, Zhang T, Yang W, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). Science 2020;368(6490):489–93.
[2] Deslandes A, Berti V, Tandjaoui-Lambotte Y, Alloui C, Carbonnelle E, Zahar JR, et al. SARS-CoV-2 was already spreading in France in late December 2019. Int J Antimicrob Agents 2020;55(6):106006.
[3] Lhopitallier L, Kronenberg A, Meuwly JY, Locatelli I, Dubois J, Marti J, et al. Procalcitonin and lung ultrasonography point-of-care testing to decide on antibiotic prescription in patients with lower respiratory tract infection in primary care: protocol of a pragmatic cluster randomized trial. BMC Pulm Med 2019;19(1):143.
[4] Opota O, Brouillet R, Greub G, Jaton K. Comparison of SARS-CoV-2 RT-PCR on a high-throughput molecular diagnostic platform and the cobas SARS-CoV-2 test for the diagnostic of COVID-19 on various clinical samples. in preparation 2020.
[5] Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill 2020;25(3).

Loïc Lhopitallier[1]
Thomas Brahier[1]
Onya Opota
Andreas Kronenberg
Yolanda Mueller
Olivier Hügli
Katia Jaton[2]
Noémie Boillat-Blanco[2]
Switzerland
E-mail address: loic.lhopitallier@chuv.ch (L. Lhopitallier)
[1] equal contribution to this work.
[2] equal contribution to this work.