Comparing dynamics and determinants of SARS-CoV-2 transmissions among health care workers of adult and pediatric settings in central Paris

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Key points:

- Compliance to control measures allowed containment of the outbreak in HCW.
- Medical masks in most situations and N95/FFP2 in aerosol-generating procedures largely protect HCW against SARS-CoV-2.
- Small-sized childcare facilities may be acceptable to help HCW stay at work.

Abstract

Background: Health-care workers (HCW) have paid a heavy toll to the coronavirus disease-19 (COVID-19) outbreak. Routes of transmission remain to be fully understood.

Methods: This prospective study compared a 1,500-bed adult and a 600-bed pediatric setting of a tertiary-care university hospital located in central Paris. From February 24th until April 10th, 2020, all symptomatic HCW were screened for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) on a nasopharyngeal swab. HCW screened positive were questioned on their profession, symptoms, occupational and non-occupational exposures to SARS-CoV-2.

Results: Among 1344 HCW tested, 373 were positive (28%) and 336 (90%) corresponding questionnaires were completed. Three hospitalizations and no death were reported. Most HCW (70%) had patient-facing occupational activities (22% in COVID-19 dedicated units). The total number of HCW cases peaked on March 23rd, then decreased slowly, concomitantly with a continuous increase of compliance to preventive measures (including universal medical masking and personal protective equipment (PPE) for direct care to COVID-19 patients). Attack rates were of 3.2% and 2.3% in the adult and pediatric setting, respectively (p=0.0022). In the adult setting, HCW more frequently reported exposure to COVID-19 patients without PPE (25% versus 15%, p=0.046). Report of contacts with children attending out-of-home care facilities dramatically decreased over the study period.

Conclusion: Universal masking, reinforcement of hand hygiene, and PPE with medical masks for patients' care allowed protection of HCW and containment of the outbreak. Residual transmissions were related to persistent exposures with undiagnosed patients or colleagues and not to contacts with children attending out-of-home care facilities.

Key words: COVID-19, SARS-CoV-2, Health Care Workers, Dynamics, Determinants

Introduction

From the start of the pandemic, health-care workers (HCW) have been particularly exposed to nosocomial transmissions of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). As of February 11th, 2020, China reported more than 1,700 infected HCW in Hubei alone[1], contributing to 3.8% of total coronavirus disease-19 (COVID-19) cases, and at least 23 had died[2]. Occupational transmission of SARS-CoV-2 to HCW was lately reported in other countries as in the United-Kingdom [3,4] and the United States (US)[5].

Front-line HCW paid a heavy price to previous Coronavirus outbreaks. During the 2003-SARS epidemic in Singapore, the index patient started off a chain of nosocomial cases resulting in transmission to 60 HCW, with attack rates of up to 32% for ward-based staff[6]. Nosocomial transmissions have been recognized as an important amplifier in Coronavirus epidemics. Cross-transmissions both drive a shortage of HCW and raise anxiety and fear among hospital staff. This cascading effect further contributes to saturation of the health-care system.

Protection of HCW is therefore a key concern. As the pandemic declared then accelerated, knowledge on ways of transmission of SARS-CoV-2 also advanced. Epidemiological data and temporal patterns of viral shedding now suggest that infectiousness starts from two days before symptom onset and declines within seven days in most cases[7]. Patients with severe or critical COVID-19 or with immunosuppressive conditions may shed infectious virus for longer periods of time compared to what has been reported in patients with mild illness[8,9]. The virus mainly spreads by droplets transmission and may survive on surfaces up to 72 hours[9]. Most guidelines recommend that HCW in contact with COVID-19 patients should wear personal protective equipment (PPE) including gowns, gloves, eye protections, medical masks for standard care and FFP2 during aerosol-generating procedures[10–14].

In France, the first imported case of COVID-19 was detected on January 24th, 2020 in a 31-year-old Chinese male tourist from Wuhan[15]. By February 29th, a total of 100 COVID-19 cases had been confirmed (https://www.santepubliquefrance.fr). Two administrative regions (Ile-de-France, including Paris, and Grand-Est) were most rapidly and severely affected. Social distancing strategies were successively implemented by the French Government by mid-March 2020. In health-care settings, in addition to PPE for direct care of COVID-19 patients, symptomatic staff were recommended

systematic screening for SARS-CoV-2 and prompted to stay isolated when positive. Nevertheless, as of April 20th, 4,180 professionals were infected in the Assistance Publique-Hôpitaux de Paris (AP-HP, the largest French hospital institution, accounting for about 100,000 employees [http://www.aphp.fr]), raising questions on persistent routes of transmission and on the respective role of in-hospital and out-hospital exposures. Here, we describe the spread of the COVID-19 outbreak among HCW of two settings of the AP-HP (one mainly caring for children and the other adults) and compared their occupational and non-occupational exposures to SARS-CoV-2.

Material and method

Setting

The study was conducted in two settings of a 2,100-bed tertiary-care university hospital (AP-HP.Centre, Université de Paris) located in central Paris, France. Cochin-Broca ("Adult setting") is a 1,500-bed healthcare setting mainly caring for adult patients, except for a neonatology unit (63 beds). Necker ("Children setting") is mainly dedicated to children care (436 beds), and additionally includes five wards (150 beds) caring for immunocompromised adults (hematology, infectious diseases and nephrology-kidney-transplantation) along with an obstetrical unit and an intensive care unit. As of March 10th, 2020, 7,916 and 5,362 employees were regularly working in the Adult and Children setting respectively. Triage and management of COVID-19 patients were comparable in both settings for the entire time period. Briefly, all patients with a suspected SARS-CoV-2 infection were screened on a nasopharyngeal swab or a respiratory invasive sample on admission. Patients screened positive were referred to dedicated wards with dedicated personnel.

Participants and interventions

Social distancing strategies were successively implemented by the French Government on March 12th (school closure) and March 17th (widespread closures, restriction of business and transport). Of note, schools and nurseries remained opened for children of hospital staff all along the epidemic period.

In health-care settings, from the start of the epidemic in February 2020, PPE was recommended for HCW caring for suspected or confirmed COVID-19 patients. In brief, PPE consisted in gowns, gloves, eye protections and either medical masks for standard care or FFP2 masks during airway aerosol-generating procedures. In addition to specific precautions for patients' care, social distancing and universal masking with medical masks was advised for all hospital employees from March 16th in the AP-HP. All employees were encouraged to wear a face mask as often as possible in hospital (particularly in the presence of other persons), to wash/disinfect their hands regularly (and after every contact with other persons), to stay at least 2 meters away from others, to cover their mouth and nose with a tissue or sleeve when coughing or sneezing, to put used tissues in the bin immediately and wash hands afterwards, to avoid touching eyes, mouth. Educational messages were released on the internal website and on posters placed in all hospital premises. Testing for SARS-CoV-2 of symptomatic staff started on February 24th in the Adult setting, and on March 5th in the children setting. Hospital employees presenting either with fever (reported or measured >37.8°C), cough, rhinorrhea, muscle pain, shivers, loss of smell or taste, unusual persistent headaches or severe asthenia, were referred to the two on-site screening pods. Trained medical doctors or nurses collected a nasopharyngeal swab for each symptomatic staff member. Test results were communicated within 24 hours via a secured email or by phone. If they felt well enough to do so, HCW with pending tests were allowed to continue working, on condition to strictly comply with the hygiene protocol (careful hand hygiene and mask wearing at any time) while waiting for the results. HCW with positive results were sent home and able to return to work after seven days (including two days after resolution of any symptoms).

Data

Shortly thereafter, HCW with positive results were prospectively contacted by phone and invited to participate. After three unsuccessful attempts, they were considered unreachable. Data were collected on a standardized questionnaire on age, gender, profession, date of symptoms onset, and exposure to SARS-CoV-2 in the 10 preceding days. For confidentiality reasons, we did not collect data on past medical history and comorbidities. Exposures were classified as: in-hospital related to patients' care (average number of close contacts per day with COVID-19 index patients with and without PPE, compliance to infection prevention and control [IPC] protocols), in-hospital related to other activities (contacts with colleagues during meal breaks, meetings, etc.) and out-hospital (frequentation of public transports, contacts with household members, especially children kept outside the household). Index cases were patients with COVID-19 infection, either probable (compatible clinical signs and radiographic evidence of pneumonia on thoracic computed tomography scan) or confirmed (detection of SARS-CoV-2 RNA in a clinical specimen using rt-PCR). A contact at a distance <2 meters for >10 minutes was defined as close contact[15].

Virology methods

SARS-CoV-2 was detected by amplification of E, RdRp and N genes using the Allplex Eurobio® reagent or the RealStar® rtPCR kit, a triplex PCR amplifying the viral genome in the E and S genes and an internal control. The result was considered positive if three out of the three targets were amplified. A control sample was requested if only one or two target genes were amplified.

Statistical methods

The number of cases was computed on a daily basis. Continuous variables are presented as medians (interquartile ranges, IQR) and categorical variables as numbers (percentages). Fischer's exact tests were used for comparisons of qualitative variables and Mann Whitney's tests for quantitative variables. All tests were two-sided with a 0.05 value for significance. Mobile means were calculated and displayed on the graphs. Statistical analyses were performed using the R software (3.3.2, R Foundation for Statistical Computing, Vienna, Austria).

Ethics

This study was approved by the Ethical Review Committee for publications of the Cochin university Hospital (CLEP) (N°: AAA-2020-08012). According to French policy, a non-opposition statement was obtained for all participants, meaning that all had received written detailed information on the objectives of the study and were free to request withdrawal of their data at any time.

Results

From February 24th until April 10th, 1,344 symptomatic HCW were tested for SARS-CoV-2 over a total of 13,278 employees (10%, Adult setting [866/7916, 10.9%], Children setting [478/5,362, 8.9%]). Overall, 373/1,344 (28%) tested positive (Adult setting [251/866, 29%], Children setting [122/478, 26%]), leading to an overall attack rate of 2.8% (Adult setting [251/7,916, 3.2%], Children setting [122/5,362, 2.3%] p=0.0022). Figure 1 details daily breakdown of SARS-CoV-2 testing in the Adult (Figure 1A) and the Children setting (Figure 1B). The total number of cases peaked on March 23rd then decreased slowly until April 10th. The outbreak appeared to be more intense in the Adult setting, particularly in the early phase of the epidemic. A residual number of cases was observed in both settings after the peak. The crude number of daily consultations in emergency departments for suspected or confirmed COVID-19 in Paris during the study period peaked on March 31st (Figure 1C). Overall, 336/373 hospital personnel (90%) answered to the phone interview, two refused and 35 were unreachable. Main characteristics of the participating HCW and their symptoms are presented in Table 1. In both centers, the large majority were women (265/336, 79%), with direct patient-facing activities (234/336, 70%). Most were posted outside COVID-19 dedicated wards (261/336, 78%). Employees were younger in the Children setting. The most frequently reported symptoms were asthenia and headaches and 118/336 (35%) did not report any fever. Patients reporting measured or subjective fever had a median temperature of 38.5°C (minimal 36.2°C, maximal 41.0°C). Three staff members were hospitalized. No death was reported.

Exposures reported by participants are presented in Table 2. The majority recalled a contact without PPE with an index case. Iterative contacts with patients without PPE were more frequently reported

by hospital staff from the Adult setting (56/227 [25%] versus 16/109 [15%] in Children setting, p=0.046), whereas contact with index cases in the household or with colleagues were more frequent in the Children setting. Most employees declared wearing a mask always/most of the time at hospital, but 65/336 (19%) admitted removing masks during breaks in the presence of other colleagues (204/336, 61% during lunch breaks). More than half (201/336, 60%) reported using public transportation, including 112/201 (56%) over one hour per day, but less than 25% (82/334) wore mask outside home. Forty-seven (14%) had children aged 0-4 years and 78 (23%) aged 5-15 years in the household. Sixty (18%) reported having children kept outside the family home: 42 at school (70%), 18 at nursery (30%), and 9 (15%) by other persons (grandparents, neighbors). The large majority (54/60, 92%) were in childcare facilities welcoming more than five children simultaneously.

A second analysis focused on HCW with direct patient-facing activities (n=234), comparing those caring for adults to those caring for children, regardless of the geographic location. Overall, 169 HCW were posted in adult units (either from the Adult setting [n=160] or from the Children setting [n=9]) and 65 in pediatric units (1 from the neonatology ward of the Adult setting and 64 from the Children setting). Results are detailed in the Supplementary Appendix. The proportion of HCW reporting contacts with COVID-19 patients without PPE was even higher in Adult units (35% in adult staff versus 13% in pediatric staff, p=0.00060).

Figure 2 presents the dynamics of various exposures reported by positive HCW over time. Exposure to COVID-19 patients with PPE increased (Figure 2A), concomitantly to the rise of COVID-19 patients' admissions. The rate of HCW reporting contact with COVID-19 patients without PPE was relatively stable around 20% over the study period (Figure 2B). The number of patients' admissions was higher in the Adult setting, consistent with the number of cases reported in adults compared to children in the general French population (Supplementary Figure). Concomitantly, compliance with mask wearing increased (Figure 2C-D): the proportion of employees who declared wearing a mask always/most of the time at hospital increased from 17% (3/18) to 66% (206/312) after implementation of the universal masking policy on March 16th. However, at the end of the study period, a residual proportion of staff still reported contacts without PPE with COVID-19 patients and with colleagues without masks. This was more marked in the Adult setting, where between April 3-10, eight personnel

reported contacts with COVID-19 patients, including four in the same geriatric ward. Mask wearing outside home increased but capped around 60% as of April 10th (Figure 2E). Conversely, the proportion reporting childcare outside home fell dramatically over the study period (Figure 2F).

Discussion

This prospective, implemented in real-time study gives new insights on the dynamics and occupational exposures to SARS-CoV-2 in HCW. Most cases were reported at the very early phase of the French epidemic. Rapidly after implementation of control measures, in both hospitals, new infections in HCW decreased, while the epidemics was still progressing in the community. A residual number of contaminations were reported as of April 1st, mainly driven by contacts with undiagnosed patients or colleagues without protection. Conversely, HCW infected during this late phase of the epidemic marginally reported contacts with children attending community childcare facilities.

Compared to previous studies and national surveillance data on SARS-CoV-2 infections in HCW[1,3–5], we systematically investigated all staff members infected with COVID-19 and confronted an adult and a pediatric setting. Our data collected from the start of the French epidemics give an unprecedentedly reported landscape of HCW infection with COVID-19.

Preventive measures including universal masking, reinforcement of hands hygiene and social distancing were applied from mid-March in our two settings. One week later, the epidemic curve flattened, although HCW were increasingly exposed to COVID-19 patients and the outbreak was concomitantly peaking in the region Ile-de-France. This shift is consistent with the SARS-CoV-2 incubation interval[7] and data reported elsewhere[3]. Our results support that current adopted practices (medical masks in most patients and N95/FFP2 in aerosol generating procedures)[11,14] can largely protect HCW against contaminations. This observation, in real-life conditions, further suggests that SARS-CoV-2 is primarily transmitted via droplets, despite discussion on the possibility of airborne transmission, raised by experimental studies[9]. Lack of compliance to mask wearing reported during breaks, and recent data evidencing viral shedding occurring before symptoms

onset[7], also underscore the importance of maintaining physical distancing rules between hospital employees during out-of-duty activities.

The attack rate was significantly lower in the Children setting, possibly related to a lower number of COVID-19 patients admitted in this setting, and to higher awareness and compliance to IPC measures. Indeed, in pediatric settings, gowns and droplet precautions are routinely recommended even out of a pandemic context[16], and compliance to hands hygiene is reported to be higher[17].

Children have been initially suspected to play a central role in transmission of SARS-CoV-2. However, recent data have been more balanced[18–20]. Attack rates in children may be lower than in adults[21,22]. Moreover, in a French cluster of 12 COVID-19 cases, the only child involved did not cause any documented secondary case despite multiple contacts while symptomatic[23]. In France, the majority of schools and childcare facilities closed on March 12th, but few remained open to welcome HCWs' children in small groups. This choice raised questions on the risk of maintaining virus circulation among children of HCW, thus exposing them to the infection. Interestingly in our cohort, the proportion of infected HCW reporting a child in an out-of-home care service dramatically decreased all over the epidemic period. Although many confounding factors were not taken into account in the analysis, this observation is reinsuring regarding the decision to keep childcare facilities accessible to children of HCW during the epidemic period. This suggests that in case of second wave of the COVID-19 outbreak, keeping children services available for HCW may be acceptable to help asymptomatic hospital staff stay at work. However, access to these collective structures were restricted to HCW and limited to a very small number of children. Thus, this does not presume on the impact of wide reopening of schools and nurseries after the lift of containment measures.

The main limitation of our study is the lack of a control group (i.e. HCW that were not infected by SARS-CoV-2). This limitation in study design prevents from adequately adjusting for potential confounding variables and accounting for effect modification, and deserves cautious interpretation of

the results. Identification of negative controls is nevertheless difficult. Indeed, sensitivity of the rt-PCR on nasopharyngeal swabs is imperfect[24]. Serologic assessment may contribute to definitively rule out the diagnosis of COVID-19. However, serological assays for SARS-CoV-2 are still under investigation before large implementation among French HCW. We chose to rapidly communicate timely data in order to guide decisions in view of the soon upcoming lift of containment measures. Further investigations are planned to identify negative controls and formally compare their exposures to HCW of our cohort. Our study also only captured symptomatic infections; we were then unable to assess exposures in the whole cohort of HCW who developed COVID-19 (particularly in those who remained asymptomatic), and potentially missed additional routes of acquisition. Another limitation is the recall bias which is inherent to the use of questionnaires in epidemiological studies, however infected HCW were interrogated prospectively and shortly after PCR assessment. Last, exposures were self-reported. We did not perform a formal phylogenetic viral analysis that could have allowed definitive confirmation of the true source of infections.

Several conclusions can be drawn from our results: (i) HCW are exposed to emerging viral diseases, particularly at the early phase of the epidemic; (ii) compliance to control measures increased over the study period, concomitantly with containment of the outbreak among hospital staff ; (iii) incidence was lower in HCW of the Children setting, likely related to a better adherence to IPC measures by the pediatric staff and (iv) residual transmissions observed at the late phase of the epidemic among HCW were related to persistent exposures with undiagnosed patients or colleagues and not to contacts with children attending out-of-home care facilities.

Authors' Contributions

AC, JL, OL and SK designed the study and drafted the paper. AC, JL, ML, FR, OL and SK contributed to data analysis and interpretation. All authors critically revised the manuscript for important intellectual content and gave final approval for the version to be published. OL and SK had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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This study had no funding source or sponsor implicated in the study design, in the collection, analysis, and interpretation of data, in the writing of the report, and in the decision to submit the article for publication.

Declaration of interests

AC reports personal fees and non-financial support from Janssen Cilag, outside the submitted work. RG reports personal fees and other from Sanofi, personal fees from MSD, personal fees from Eumedica, personal fees from Pfizer, personal fees from Frezenius, personal fees from Cubist, personal fees from Correvio, personal fees from Astellas, outside the submitted work. PF reports personal fees and non-financial support from MSD France, personal fees from ViiV Healthcare, non-financial support from Gilead Science, personal fees and non-financial support from Janssen Cilag, personal fees from Medtronic SAS, non-financial support from Astellas, non-financial support from

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Tables and figures

Table 1: Study population characteristics

Results are presented as n (%) or median [Q1-Q3]

	Overall cohort (n=336)	Adult setting (n=227)	Children setting (n=109)	p-value
Age, years	40 [30-53]	42 [31-53]	37 [29-50]	< 0.0001
Sex (female)	265 (79)	180 (79)	85 (78)	0.78
Professional category				
Physicians	91 (27)	64 (28)	27 (25)	0.21
Paramedic staff (nurses, care assistants...)	205 (61)	132 (58)	73 (67)	
Administrative staff	28 (8)	20 (9)	8 (7)	
Other employees (kitchen, child carriers...)	12 (4)	11 (5)	1 (1)	
Occupational activities with direct patient facing	234 (70)	161 (71)	73 (67)	0.53
Symptoms				0.17
Asthenia	272 (81)	176 (78)	96 (88)	
Headaches	262 (78)	172 (76)	90 (83)	
Fever (measured or reported)	246 (73)	169 (74)	77 (71)	
Cough	227 (68)	143 (63)	85 (77)	
Anosmia	229 (68)	146 (64)	83 (76)	
Muscle pain	220 (66)	145 (64)	75 (69)	
Ageusia	215 (64)	134 (59)	81 (74)	
Rhinorrhea	171 (51)	118 (52)	51 (49)	
Diarrhea	129 (38)	88 (39)	41 (37)	
Dyspnea	126 (37)	80 (33)	46 (42)	
Median time from symptom onset to screening	3 [1-4]	3 [1-4]	2 [1-4]	0.59

Table 2: Exposures reported by 336 HCW tested positive for SARS Cov2, in the 10 days preceding symptoms onset

Results are presented as n (%).

***** distance <2 meters for >10 minutes; †PPE: Personal Protective Equipment

	Adult setting (n=227)	Children setting (n=109)	p-value
At least one close contact* with an index case without PPE†	141 (62)	76 (70)	
Patient	57 (25)	23 (21)	0.49
Household member	35 (15)	31 (28)	0.0079
Children <15 years	7 (3)	9 (8)	
Colleague	81 (36)	52 (49)	0.043
Exposure to patients			
Regularly posted in a unit caring for COVID19-patients	50 (22)	25 (23)	0.89
Has ≥1/day close contact with suspected or confirmed COVID19 patients without PPE†	56 (25)	16 (15)	0.046
Exposure to colleagues			
Wears a medical mask always/most of the time at hospital	141 (63)	68 (64)	0.90
Spends on average >1 hour/day with colleagues without mask	78 (35)	33 (33)	0.80
Has on average >4 close contacts/day with colleagues without mask	118 (52)	63 (59)	0.28
Out-of-hospital exposure			
Uses public transports	134 (59)	67 (62)	0.72
Wears a mask always/most of the time outside home	61 (27)	21 (19)	0.14
Leaves home on average more than once a week	191 (84)	99 (91)	0.13
Lives with ≥ 2 additional household members	117 (52)	55 (51)	0.91
Has ≥1 child kept outside the household (school, nursery)	38 (17)	22 (21)	0.36

Figure 1: Epidemic curves

A: epidemic curve in the Adult setting. B: epidemic curve in the Children setting. C: Number of daily hospitalizations for COVID-19 in the hospitals of Paris area. Red bars represent the COVID-19 positive cases among hospital staff ; green bars represent the hospital personnel tested negative for COVID-19 ; blue bars represent the crude number of daily consultations in emergency departments for suspected or confirmed COVID-19 in central Paris (data provided by https://geodes.santepubliquefrance.fr/).

Figure 2: Evolution of exposures reported by positive hospital personnel over time.

Grey bars represent the number of COVID-19 cases among hospital staff in the two settings (left y-axis). The grey line represents the crude daily proportion of positive HCW reporting the exposure and the blue line its 7-days mobile mean (right y-axis).

A: HCW reporting close contact with a COVID-19 patient with PPE ; B: HCW reporting close contact with a COVID-19 patient without PPE ; C: HCW reporting wearing mask most of the time or always at hospital ; D: HCW reporting close contact with colleagues without masks for more than one hour per day; E: HCW reporting childcare out of the household ; F: HCW reporting wearing mask out of hospital.

Figure 1

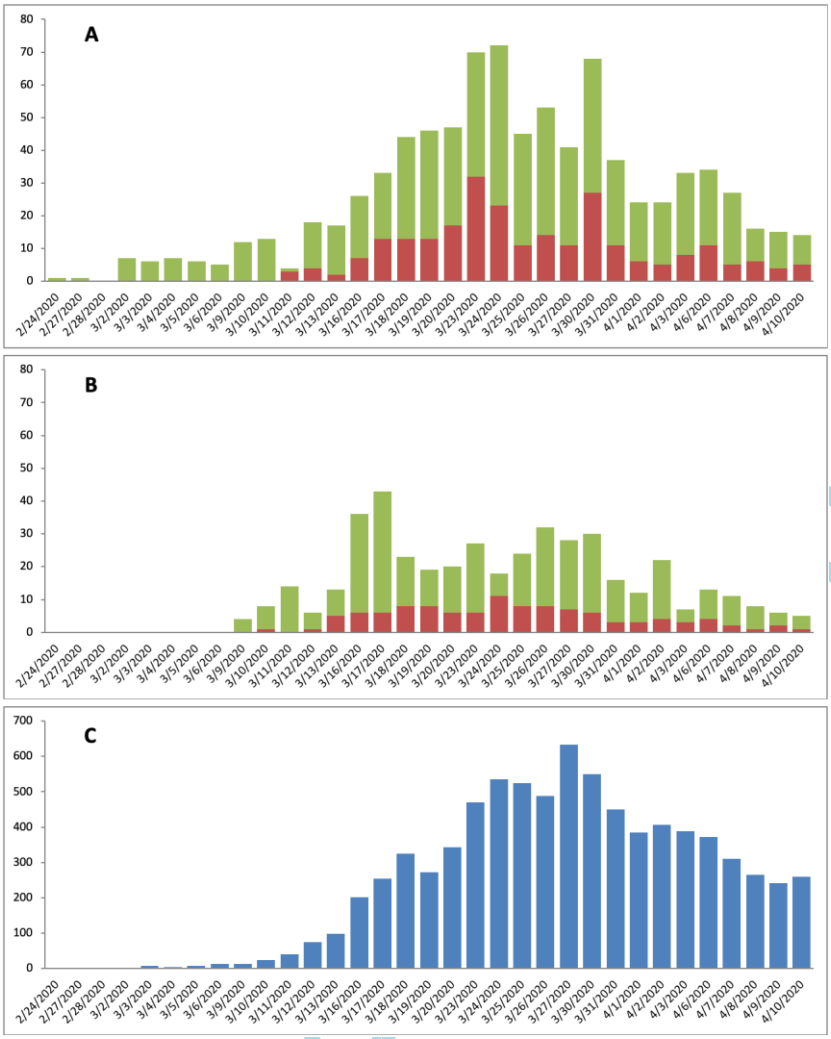

Figure 2