

Nosocomial transmission of COVID-19: a retrospective study of 66 hospital-acquired cases in a London teaching hospital

Hannah M Rickman¹, Tommy Rampling¹, Karen Shaw², Gema Martinez-Garcia², Leila Hail², Pietro Coen^{1,2}, Maryam Shahmanesh^{1,3,4}, Gee Yen Shin¹, Eleni Nastouli^{1,5}, Catherine F Houlihan^{1,5}

1. Department of Virology, University College London Hospitals NHS Trust, London, UK
2. Department of Infection Prevention and Control, University College London Hospitals NHS Trust, London, UK
3. Institute for Global Health, University College London, London, UK
4. Africa Health Research Institute, Durban, South Africa
5. Department of Infection and Immunity, University College London, London, UK

Contact information

Corresponding author: Dr Hannah Rickman, Department of Virology, University College London Hospital, 250 Euston Road, NW1 2BU hannahrickman1@gmail.com ; hannah.rickman1@nhs.net ; +44 7814254919

Abstract

COVID-19 can cause deadly healthcare-associated outbreaks. In a major London teaching hospital, 66/435 (15%) of COVID-19 inpatient cases between 2 March and 12 April 2020 were definitely or probably hospital-acquired, through varied transmission routes. The case fatality was 36%. Nosocomial infection rates fell following comprehensive infection prevention and control measures.

Keywords: Nosocomial, transmission, COVID-19, healthcare-associated infection; infection prevention and control

Accepted Manuscript

Background

COVID-19, caused by the novel coronavirus SARS-CoV-2, poses unique challenges for infection prevention and control (IPC) within healthcare facilities(1). Transmission may occur via droplet, fomite and (following aerosol-generating procedures) airborne routes(2–5), and from individuals who are asymptomatic or yet to develop symptoms(3,6). Healthcare users are more likely to be elderly with comorbidities, and therefore particularly vulnerable to severe COVID-19(7). Furthermore, efforts to prevent hospital-acquired infection are undertaken in a context of rapidly evolving knowledge, and unprecedented demands on healthcare services.

In most UK hospitals, initial IPC responses to COVID-19 followed paradigms established for other respiratory viruses: identification of symptomatic cases meeting a clinical case definition, SARS-CoV-2 real-time polymerase-chain reaction (RT-PCR) testing of upper respiratory samples, and isolation or cohorting with enhanced IPC precautions. Most who did not meet the case definition were managed as usual in shared bays of up to six patients. However, given the median incubation period of 5 days(8,9), and high transmissibility before and at the time of symptom onset(3,6), this strategy may be insufficient to prevent nosocomial transmission.

COVID-19 outbreaks have been reported in varied healthcare settings(6,7,10–12). Of 138 hospitalised COVID-19 cases in Wuhan, 12% were originally admitted for other reasons and were presumed to have acquired COVID-19 in hospital(13). Of these, 53% required intensive care compared to 22% in the rest of the cohort, suggesting that this group may be particularly susceptible to adverse outcomes.

In March-April 2020, our central London teaching hospital experienced many cases of COVID-19, including apparently hospital-acquired infections. We therefore performed a retrospective analysis to describe the epidemiological and clinical characteristics of hospital-acquired COVID-19, inform knowledge of transmission, and target IPC practices.

Methods

Setting and participants –The setting was University College London Hospitals NHS Trust, a tertiary centre with 1160 inpatient beds over four hospital sites. All admitted patients with a positive SARS-CoV-2 PCR test in the 6-week period 2 March–12 April 2020 were included.

Definitions – the median incubation period of COVID-19 is five days(8), with a maximum of around 14 days. Clinical notes were reviewed for documented symptom onset date, and hospital-acquired infection defined as follows: i) *Definite hospital-acquired COVID-19* – symptom onset 14 days or more after admission; ii) *Probable hospital-acquired COVID-19* – symptom onset seven or more days after admission, or symptom onset 5-6 days from admission, with preceding documented contact with a COVID-19 case in hospital.

Epidemiological analysis – For all definite or probable hospital-acquired cases, electronic hospital systems (EPIC Systems Corporation, Verona, USA) were used to identify other PCR-confirmed COVID-19 patients admitted into the same bay (room containing four to six patient beds, partitioned by curtains, generally sharing the same bathroom) or ward (department comprising of multiple bays on the same floor, opening into the same corridors, often sharing staff, equipment and other facilities). The case with the earlier symptom onset was considered the potential index case. A contact was deemed relevant if it included a time period i) where the index case was potentially infectious, defined as two days prior to seven days after their symptom onset, and ii) compatible with the incubation period of COVID-19, defined as within the 14 days prior to the secondary case's symptom onset.

Statistical analysis –Statistical analysis of anonymised data was performed using Stata version 12 (College Station, Texas, USA). Non-parametric numerical variables were compared using Wilcoxon rank-sum. Network visualisation was performed using Gephi 0.9.2(14).

IPC procedures – This period saw multiple changes in national and hospital policy (*Fig 1a*). Guided by Public Health England, local IPC approaches initially focused on prompt recognition, isolation and testing of patients according to case definitions. Before 11th March this required an epidemiological link with COVID-19; subsequently it included any admitted patient with acute respiratory distress syndrome, pneumonia or influenza-like illness. From 27th March, suspected cases were isolated or cohorted according to their risk(15). Throughout the study period, asymptomatic screening was neither part of national guidelines nor routinely practised in our hospital (though it has since been introduced). Staff personal protective equipment (PPE) consisted of a minimum of gloves, apron and surgical mask, with gowns, eye protection and Filtering Facepiece Class 3 masks for aerosol-generating procedures. PPE was initially used for suspected or confirmed cases, and extended to all patient interactions from April 1st. Progressive visitor restrictions, and training and support to all staff for measures including hand hygiene, environmental and equipment cleaning, and PPE, were implemented before and throughout this period. Where hospital-acquired cases were identified, outbreak investigations were performed and IPC measures audited and reinforced. Cases were isolated and any exposed patients were cohorted and monitored for development of symptoms.

Results

Of 435 cases of PCR-positive COVID-19 inpatients in this six-week period, 47 (11%) met the definition for definite hospital acquisition, with a further 19 (4%) probable hospital-acquired. Symptom onset for these 66 hospital-acquired cases was a median of 26 days (IQR 13-55) from admission.

The median age of hospital-acquired cases was 70 years (IQR 60-80), compared to 65 (50-79) amongst community-acquired cases ($p=0.06$.) Between 2nd-30th March, hospital-acquired cases constituted 21% of all cases; in the subsequent two weeks this fell to 7% (*Fig 1a*).

Possible sources of infection

Of 66 hospital-acquired cases, 36 (55%) were identified as having been in the same bay as a patient with PCR-confirmed COVID-19, in a timeframe compatible with possible transmission (*Fig 1b*). The median serial interval was six days (IQR 3-9, range 1-14). A further nine (14%) had no identified contacts in the same bay, but had contacts on the same ward. For the remaining 21 (32%) no clear source of infection was apparent. This included eight cases (12%) who had been accommodated in single-occupancy rooms for the majority of their admission.

Amongst the 36 cases with a possible index case in the same bay, 22 (61%) of the index infections were themselves hospital-acquired, with several possible chains of patient-to-patient in-hospital transmission. The remaining 14 (39%) were linked to six individual community-acquired putative index cases. Four index cases had no documented COVID-19 symptoms on admission but developed them following admission to a shared bay; the remaining two were admitted with symptoms which were not immediately identified as suggestive of COVID-19, or did not meet contemporaneous testing criteria.

45 (68%) of hospital-acquired COVID-19 cases were not themselves associated with any linked secondary cases on the same bay or ward, partly due to prompt identification and isolation. However, there were several community- and hospital-acquired cases associated with four or more likely secondary infections.

Outcomes

At a minimum of three weeks of follow-up, 37 (56%) of patients with hospital-acquired COVID-19 had been discharged, five (8%) remained inpatients, and 24 (36%) had died, a median of eight days (IQR 6-13) from symptom onset.

Discussion

During the March-April 2020 peak of the London COVID-19 outbreak, around 15% of inpatient cases in our hospital were hospital-acquired. This is similar to reports from other hospital settings(12,13), although lower than seen in outbreaks of SARS-CoV-1 and MERS-CoV, in which nosocomial transmission may predominate(16,17). The case fatality rate in this vulnerable cohort was 36%.

There are multiple possible routes of in-hospital COVID-19 transmission. Evidence of patient-to-patient transmission through contact in the same bay was found in 55% of hospital-acquired cases, with serial interval six days (slightly higher than the 4-5 days reported in the literature(3,9,18)). For a further 14% of patients with no contact in the same bay but cases on the same ward, cross-infection may have occurred through use of shared facilities and equipment, or staff movement(4,5,19).

For the remaining 32% of infections, no source was identified. In particular, 12% had been in single-occupancy rooms for much of their stay, with minimal patient-to-patient contact. Likely sources include asymptomatic or undiagnosed patients, visitors, or staff members. Staff illness levels were high during this period, and while symptomatic staff were advised to self-isolate at home, surveillance testing of London healthcare workers found that 27% of those infected were asymptomatic(20).

The transmission analysis has several limitations. We only identified PCR-positive symptomatic inpatients, and not patients exposed in hospital who were discharged before developing symptoms, those exposed in outpatients or other healthcare settings, those with undiagnosed COVID-19, or staff. We were only able to identify contacts between patients based on their admission location, and not with staff members or contacts in other contexts (e.g. emergency department.) Presently these epidemiological data are not supported by sequencing, so potential transmissions are inferred.

Following a comprehensive IPC response, both the numbers and proportions of hospital-acquired cases fell considerably. While it is challenging to attribute this to specific interventions, important contributors

included: expanded staff and patient testing, use of PPE for all patient contacts, enhanced IPC measures, and cohorting of suspected cases to increase capacity to isolate the most vulnerable(15), as well as the falling community incidence.

This high incidence and mortality of hospital-acquired COVID-19 demand urgent preventive actions. As lockdowns ease and community transmission may resurge, we would recommend a combination of measures including screening all patients on admission (to prevent transmission from unidentified or presymptomatic community-acquired cases), meticulous universal PPE and IPC precautions, and surveillance testing of staff and patients.

Competing interests

M.S. reports grants from USA National Institute for Health, Bill and Melinda Gates Foundation, UK Medical Research Institute, UK National Institute for Health Research, Wellcome Trust, and Unitaaid, outside the submitted work. All other authors have declared that no competing interests exist.

References

1. Islam MS, Rahman KM, Sun Y, *et al.* Current knowledge of COVID-19 and infection prevention and control strategies in healthcare settings: A global analysis. *Infect Control Hosp Epidemiol.* 2020 May 15;1–29.
2. van Doremalen N, Bushmaker T, Morris DH, *et al.* Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med.* 2020 Mar 17; 382:1564-1567
3. He X, Lau EHY, Wu P, *et al.* Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med.* 2020 Apr 15;1–4
4. Ye G, Lin H, Chen S, *et al.* Environmental contamination of SARS-CoV-2 in healthcare premises. *J Infect.* 2020 Apr 30 [ahead of print]
5. Wu S, Wang Y, Jin X, Tian J, Liu J, Mao Y. Environmental contamination by SARS-CoV-2 in a designated hospital for coronavirus disease 2019. *Am J Infect Control.* 2020 May 12 [ahead of print]
6. Arons MM, Hatfield KM, Reddy SC, *et al.* Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. *N Engl J Med.* 2020 Apr 24 [ahead of print].
7. Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020 Mar 28;395(10229):1054–62.
8. Lauer SA, Grantz KH, Bi Q, *et al.* The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med.* 2020 May 5;172(9):577-582

9. Li Q, Guan X, Wu P, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med.* 2020;382(13):1199–207.
10. Wang X, Zhou Q, He Y, *et al.* Nosocomial outbreak of COVID-19 pneumonia in Wuhan, China. *Eur Respir J.* 2020 Jun;55(6):2000544
11. Van Praet JT, Claeys B, Coene AS, Floré K, Reynders M. Prevention of nosocomial COVID-19: Another challenge of the pandemic. *Infect Control Hosp Epidemiol.* 2020 Apr 23:1-2.
12. Meredith LW, Hamilton WL, Warne B, *et al.* Rapid implementation of real-time SARS-CoV-2 sequencing to investigate healthcare-associated COVID-19 infections. *MedRxiv [preprint].* 2020 May 14 [cited 2020 Jun 9]; Available from: <https://doi.org/10.1101/2020.05.08.20095687>
13. Wang D, Hu B, Hu C, *et al.* Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *J Am Med Assoc.* 2020 Mar 17;323(11):1061–9..
14. Bastian M, Heymann S, Jacomy M. Gephi : An Open Source Software for Exploring and Manipulating Networks Visualization and Exploration of Large Graphs [Internet]. [cited 2020 May 7]. Available from: www.aiai.org
15. Patterson B, Marks M, Martinez-Garcia G, *et al.* A novel cohorting and isolation strategy for suspected COVID-19 cases during a pandemic. *J Hosp Infect.* 2020 May 30 [ahead of print]
16. Chowell G, Abdirizak F, Lee S, *et al.* Transmission characteristics of MERS and SARS in the healthcare setting: a comparative study. *BMC Med.* 2015 Dec 3;13(1):210.
17. De Wit E, Van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: Recent insights into emerging coronaviruses. *Nat Rev Microbiol.* 2016 Aug;14(8):523-34

18. Nishiura H, Linton NM, Akhmetzhanov AR. Serial interval of novel coronavirus (COVID-19) infections. *Int J Infect Dis* 2020 Apr;93:284-6.
19. Ong SWX, Tan YK, Chia PY, *et al.* Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) from a Symptomatic Patient. *J Am Med Assoc.* 2020 Mar 4;323(16):1610-2.
20. Treibel TA, Manisty C, Burton M, *et al.* COVID-19: PCR screening of asymptomatic healthcare workers at London hospitals. *Lancet.* 2020 May 7;395(10237):1608-10

Accepted Manuscript

Figure legends

Figure 1a. Numbers of community- and hospital-acquired cases admitted to hospital between 2 March and 6 April 2020, with associated timetable of local and national infection prevention and control measures implemented during this time period. “Hospital-acquired” cases include definite and probable cases.

ICU: intensive care unit. ARDS: acute respiratory distress syndrome. PPE: personal-protective equipment.

**Testing criteria prior to 11th March required an epidemiological link with a case of COVID-19 or a high-risk country; following 11th March they were extended to all admitted patients with ARDS, influenza-like illness or pneumonia.*

Figure 1b. Network representation of all definite and probable hospital-acquired cases (red), and community-acquired cases identified as potential index cases (blue) between 2 March and 6 April 2020. Black links represent a possible transmission within the same bay; grey links represent transmission in the same ward, with the earliest compatible case on the ward identified as the index case. Direction of arrow represents possible direction of transmission based on dates of symptom onset and the size of the node is proportionate to its number of identified possible secondary cases (out-degree).

Figure 1a

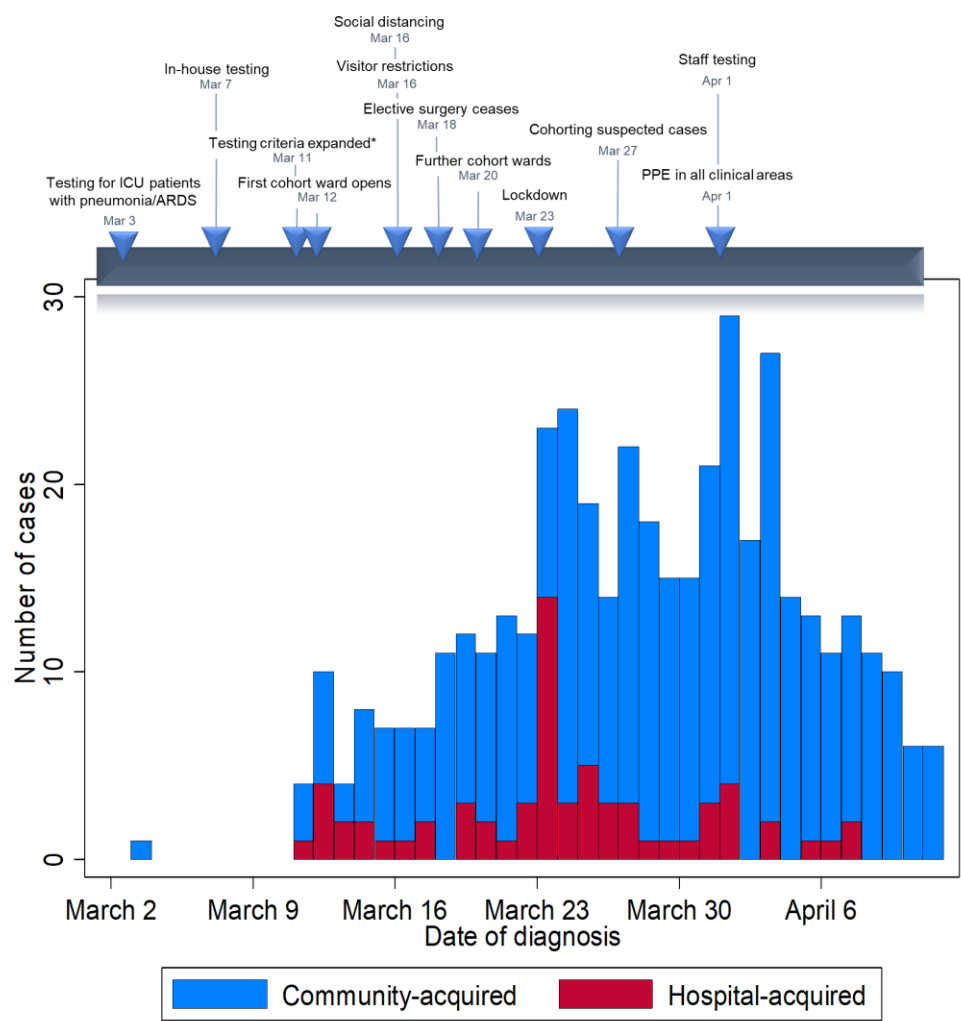


Figure 1b

