Outbreak report

Investigation and management of an outbreak of COVID-19 infection in an acute admission unit in a District General Hospital: lessons learnt

Chiranthi Iresha Kannangara*, Prema Seetulsingh, Jiovanna Foley, Glynis Bennett, Tracey Carter

Department of Microbiology, Infection Control and Executive Watford General Hospital, West Hertfordshire Hospital NHS Trust, United Kingdom

SUMMARY

Background: SARS-CoV-2 outbreaks are difficult to recognise and control due to its high infectivity and the wide range of clinical manifestations of the infection. An outbreak at Watford general hospital provided an opportunity to recognise the complexity involved in a COVID-19 outbreak investigation.

Methods: An outbreak control team (OCT) was convened. The terms outbreak, a case and a significant exposure were defined as per Public Health England (PHE) Guidance and in the context of the local outbreak. Root cause analyses (RCAs) were carried out on cases to identify possible causes, possible route of transmission and any learning points. All contact patients and staff were screened with RT PCR and genomic sequencing was performed on a set of positive specimens.

In addition to active contact tracing, screening and cohorting of patients and staff, standard and transmission-based precautions were reinforced to control the outbreak.

Findings: Fifteen patients and four staff members were identified in this outbreak investigation. With contact tracing, screening and through strict infection control measures the outbreak was brought under control.

Conclusion: We could successfully contain the spread of this outbreak following PHE outbreak control guidelines and our local guidelines. We recognised several challenges in investigating a COVID-19 outbreak in a hospital setting. Problems arising from variable sensitivity of the tests, difficulty in differentiating COVID-19 related symptoms from underlying diseases, problems related to establishing the route of transmission, issues with contact tracing are discussed. Additionally, the importance and limitations of genomic studies in COVID-19 are discussed.

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Introduction

World Health Organization declared COVID-19 as a “public-health emergency of international concern” on 30 January 2020. As of 1st June 2020, there were 6 million cases and 371166 deaths reported globally. [1].

Rapid detection, and suppression of local (community and healthcare associated) outbreaks is important to prevent wider spread of infection. In principle there are three types of measures to prevent an infectious epidemic: controlling the source of infection, breaking the cycle of transmission, and protecting the susceptible populations. With COVID-19, transmission is primarily through droplets, indirect transmission via contact with environmental surfaces and, also thought to be airborne. Isolation of patients with suspected disease, early detection, appropriate use of personal protective equipment (PPE), contact tracing and environmental decontamination, are important in preventing outbreaks in health care facilities.

Despite these precautions a significant number of patients have acquired COVID-19 in healthcare settings. [2,3] Here we report the investigation and management of an outbreak in an acute admission unit in a District General Hospital.

Background

Watford General Hospital is a 521-bed acute district General Hospital situated in West Hertfordshire. After the first wave of COVID-19 (2020), the hospital commenced its routine activity in May. All acute admissions were screened for COVID-19 by a PCR test on day zero and day five-seven. Patients undergoing elective procedures were screened three days prior to their admission. [4].

The outbreak happened in a 60-bed acute admission ward (ward X in this article). This ward is divided into four zones (coded Zone X1, X2, X3 and X4). (Figure 1).

Zone X1 and X2 are used to admit patients under cardiac and respiratory teams and received patients from other wards. Zone X3 and X4 are holding bays when the capacity in the acute admission unit for emergency patients is exceeded. Current PHE guidance on reducing the risk of transmission of COVID-19 in the hospital setting is followed in this unit. [5] There was no concurrent outbreak of COVID-19 in the hospital.

Methods

Description of the outbreak

Patient X1A was admitted to X1 zone with clinical and radiological evidence of pneumonia. His PCR for SARS-CoV-2 was negative on admission and on day 2 but became positive on day 9. He was considered as a “hospital-onset probable healthcare-associated infection” (first positive specimen date 8–14 days after admission) according to the PHE definitions.

A cohort, contact tracing and screening exercise was undertaken which resulted in the recognition of the outbreak. Our paper describes 15 patients who were identified during outbreak period from mid-June to early July 2020, three of whom were symptomatic, and the rest identified on screening (Table I).

The objectives of this investigation were, firstly, to understand the extent of the spread of SARS-CoV-2 in our healthcare facility and secondly, to conduct a root cause analysis to identify lapses in current infection control practices.

Initial response

Considering the nature and the number of exposures to the “index patient” and as more patients were positive in the same unit during a 3-day period (Day -3 to Day 0) an outbreak was declared in mid-June 2020 (Day 0) as per PHE definition. [6] An Outbreak control team was convened.
The OCT consisted of the Head of Microbiology department, also Infection Control Doctor, Director Infection Prevention and Control (also an executive Director), Microbiology consultants, operational manager, head of emergency planning, matron (medicine), deputy head of nursing (medicine), Infection Prevention and Control (IPC) personal assistant, IPC senior nurse, head of IPC Clinical Commissioning Group (CCG), senior Health Protection Practitioners from PHE, members of the Serious Incident Team and consultants from cardiology and respiratory medicine.

**Outbreak control team (OCT)**

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**Outbreak investigation**

**Definitions**

The first step was to agree on the definitions for an outbreak, a case, and significant exposure.

Public Health England defines an outbreak as “two or more confirmed cases of COVID-19 or clinically suspected cases of COVID-19 among individuals associated with a specific setting with onset dates 8–14 days after admission within the same ward or wing of a hospital”.

A **significant exposure** is defined as an Individual who has had close face-to-face contact with a COVID-19 patient within 2 metres for more than 15 minutes. A Health care worker providing direct care for a COVID-19 case, without recommended personal protective equipment (PPE) or with a possible breach of PPE is also considered a significant exposure. [7].

A **case** was defined as an individual (patient or staff) who stayed or worked in ward X from Day-3 until outbreak is declared over and have developed symptoms and radiological findings compatible with COVID-19 in the presence of a positive PCR test result.

**Epidemiological method**

We collected and analysed data from root cause analyses (RCAs) carried out on all 15 patients (such as patient movement and illness timeline (Figure 2). All staff members who had significant exposure were identified, contacted, and screened.
**PCR testing of samples.** Nose, throat, and nasopharyngeal swabs were tested by the Cepheid, ePlex and SAMBA II commercial PCR assays or sent to the Source Bioscience lab in Nottingham. Cepheid GeneXpert assay is an automated multiplex real-time, reverse transcriptase polymerase chain reaction (RT-PCR) assay intended for the qualitative detection of SARS-CoV-2. The procedure includes sample preparation, nucleic acid extraction, amplification and detection of the target sequence by real-time PCR.

The ePlex Panel is an automated qualitative nucleic acid multiplex diagnostic test, which automates all aspects of nucleic acid testing including extraction, amplification, and detection. The SAMBA II instrument system is an automated system. The SAMBA II Assay Module performs sample extraction for nucleic acid amplification and detection.

**Genomic sequencing.** Available specimens were transferred to the Clinical Microbiology and Public Health Laboratory (CMPHL) in Cambridge for whole genomic sequencing. The primary samples received at the CMPHL were extracted and tested for SARS-CoV-2 by a validated in-house RT-qPCR assay. [8] Samples that passed an amplicon yield threshold (>5ng/ul) were sequenced by Nanopore. Sequencing took place in the Division of Virology, Department of Pathology at the University of Cambridge via Nanopore technology, following the ARTIC version 2 protocol with version 3 primer set. [8–10] The genomes were aligned using MAFFT v7.467 with default settings and SNP differences were defined from the alignment using the snpdb package v 0.7.0. [11,12].

**Environmental screening and interventions**

It was decided not to undertake environmental sampling as the outbreak appeared to be controllable at the initial stage. However, environmental screening would be carried out if measures implemented failed to control the outbreak and if an environmental source was suspected.

**Assessment and strengthening of standard precautions and transmission based precautions**

Audits. Ward X nursing staff and infection control team carried out hand hygiene and Code of Practice (COP) audits. The COP Audit (based and adapted from the Health and Social Care Act 2008 code of practice) included general cleaning, cleaning of equipment and the environment, hand hygiene and PPE compliance.

Equipment and environment decontamination. This included enhanced cleaning in addition to the routine cleaning of frequently touched surfaces (bed tables, bed rails, arms of chairs, sinks, call bells and door handles) by increasing the frequency of cleaning (2–3 times per day) between patients and on every shift using a chlorine containing solution. Responsibilities of staff members in cleaning of the phones, workstations, computers, and other equipment were reiterated.

**Infection control interventions**

Patient movement and placement. Ward X was closed for admissions for 28 days from declaration of the outbreak and remaining patients were kept under review. Two symptomatic
patients were managed in isolation rooms and the remaining positive patients were cohorted in Zones and monitored. Privacy curtains were placed between the beds to minimise contact and further transmission. Discharged patient contacts were advised to self-isolate for 14 days.

**Staff cohorting.** To restrict the staff cross over, separate staff teams were assigned to each area.

**Staff screening.** Staff members who had significant exposure were swabbed and advised to self-isolate for 14 days from the exposure. All other staff members who worked in the unit (doctors, nurses, physiotherapists, phlebotomists, ward clerks and the housekeeping staff) were screened but allowed to continue to work pending the swab results.

**Awareness of appropriate personal protective equipment (PPE).** PPE training was undertaken across the floor. Majority of staff were found to have already undergone training, but refresher training was completed according to the updated PPE recommendation of NHS England. [13].

Visitors: No visitors were allowed as per National Guidance.

**Ventilation requirements.** The design for this ward (X 1–4) building ventilation is based on the "mixed mode" model. This means that instead of fulfilling the six air changes per hour requirement (6 ACH) for a general inpatient ward via mechanical ventilation alone, the availability of natural ventilation is assessed at design stage and is then used to theoretically make up the difference. For instance, the design flows for this ward would only achieve 2 ACH which leaves the remaining 4 ACH to be made up by natural ventilation.

**Results**

**Outbreak patient assessment**

Following recognition of the first three patients, 43 contact patients were screened with PCR assays which identified 12 further infected patients. The 15 patients identified in this outbreak investigation were in 4 different zones (X1-3 patients, X2-6 patients, X3-5 patients and X4-1 patient). Mean age of the patients was 78 years. The characteristics of the patients are summarized in Table 1. Individual case assessments revealed several factors (multiple comorbidities in 14 out of 15 patients and advanced age) that may have contributed to the increased vulnerability and the outbreak situation.

**Genomic sequencing**

Fourteen specimens belonging to 13 patients were available for genomic sequencing. This comprised 8 primary samples and 6 RNA extract samples.

Six out of fourteen samples passed an amplicon yield threshold (>5ng/ul) and were sequenced by Nanopore. The low pass rate is likely due to RNA degradation between sampling, extraction and sequencing which happened over a month after the samples were collected. Those six samples were from five patients. All six samples passed quality control filtering (>90% coverage). Four of those six specimens had the same genomic sequencing profiles and were from three patients from unit X2 and one patient from unit X 1 consistent with transmission of the same viral lineages either directly or within one or two intermediate hosts, between units X1 and X2. The remaining two samples were from one patient on unit X3 and had a distinct sequencing profile indicating that direct transmission was unlikely to have occurred from X1 or X2 to X3.

**Staff screening**

Nineteen staff members (five doctors and 14 nurses) who had contact with the index symptomatic patient were classified as high-risk exposure and they were swabbed and advised to self-isolate for 14 days after the last exposure.

A further 141 staff members (permanent staff in unit and visiting staff) were screened and four were identified as positive by PCR and were asymptomatic; they were advised to self-isolate for seven days from the date of the test as this was the PHE guidance at the time. If they developed any symptoms during their self-isolation, they were advised to self-isolate for a further 7 days from the date of onset of their symptoms in line with the PHE guidance at the time (which was revised later).

**Results of audits**

Hand hygiene audit revealed 100% compliance for doctors and nurses and 93% compliance was noted for the Code of Practice audit.

**End of outbreak**

The interventions implemented from mid-June to end of June led to a decline in the number of cases detected and no new cases were identified during the following 28 days after first week of July. The outbreak investigation was officially brought to closure on the fourth week of July.

**Discussion**

Our actions were in accordance with the PHE guidelines on outbreak management. [14,15] This outbreak investigation and management met with several key challenges.

Firstly, differentiating nosocomial cases from community acquired infections is difficult. The uncertainty is mainly fuelled by the variable sensitivity of the currently available test. Currently different studies have given different sensitivities for the PCR tests. According to one study the sensitivity of RT-PCR was lowest in pharyngeal swabs (32%) followed by nasal swabs (63%), while bronchoalveolar lavage has the highest sensitivity of 93%. [16] Overall sensitivity of the test has been suggested to be between 71% to 98%, and one systematic review reported that up to 54% of COVID-19 patients may have an initial false-negative RT-PCR. [17,18]. Patients identified in this outbreak had initial negative PCR and a subsequent positive test. Of these 15 patients there were a total of 28 initial negative PCR tests. Of these, 21 (75 %) were nasal and throat swabs. On this background we cannot rule out the possibility that some of the patients may have had or acquired the infection in the community and incubating it at the time they were admitted.

In addition, X4-A was positive on admission. However, he was again positive on day 19. The patient had multiple comorbidities and was immunocompromised. It was difficult to
determine whether X4-A is a persistent viral shedder or got reinfected during the outbreak, hence he was included in the outbreak investigation. The other possibility is persistence of viral RNA from the previous initial episode of infection in which case the patient may not have had ongoing infection and unlikely to be infectious.

Secondly, there were difficulties in determining the exact time of acquisition of infection, hence in the detection of hospital acquired cases due to an overlap and similarity of symptoms with some of the patients’ underlying cardiac or non-infective respiratory clinical condition and COVID-19 related symptoms. Some cases had shortness of breath, but detailed clinical evaluation pointed to the possible cardiac origin for their symptoms though it could also have been attributed to COVID-19. This overlap in symptomatology is also described with influenza in elderly patients who may instead present with a worsening of their underlying condition such as chronic obstructive pulmonary disease or congestive cardiac failure [19].

It was also challenging to establish a possible route of spread with a degree of certainty. Although patient X1-A was considered to be the index case in the outbreak (as X1-A was symptomatic and was on non-invasive ventilation and required more direct care resulting in multiple contacts), the first patient to be positive in this cluster was X2-E who did not have respiratory symptoms during admission. There was no patient link to explain direct transmission from X1-A in unit X1 to the X2 or X3 clusters or the case on X4. On the other hand, if we consider X2-E as the initial source, transmission to the X3 unit can be explained through X3-E though we still cannot determine a patient link to zones X1 and X4. Another possible explanation of the route of transmission is through staff working across the various areas or through contact with patients who were not initially detected due to a false negative PCR result but could still have been potentially infectious. This difficulty in identifying the source of infection is also documented in influenza outbreaks where routes of transmission are difficult to track and describe with precision limiting better understanding of disease dynamics. [20].

Thirdly, contact tracing also had potential issues. Due to the social and financial impact of being identified as a high-risk exposure and need for mandatory isolation for 14 days from the last exposure, there is a possibility for contacts to not volunteer for screening. As a result, we screened the entire staff who worked in the unit during the period of the outbreak.

Furthermore, at the time of the outbreak our standard operating procedures on SARS-CoV-2 specimens did not specify post testing storage of samples for future genomic analysis. As a result, we were only able to send specimens on 13 patients. Through genomic analysis we were able to establish that the same viral lineage was possibly spreading in zones X1 and X2 but not X3 indicating a possible mixed outbreak. However, we could not establish the link to unit X4 through genomic analysis as the RNA had degraded in the specimen. However, based on the facts that the X4-A had been previously and persistently positive and had been in a side-room during their entire stay, the lack of further cases being identified on unit X-4 and the location of this unit (Figure 1), it would indicate that the case on X-4 may be a separate and unrelated occurrence to the outbreak further supporting the mixed picture. Genomic studies were not performed on specimens from staff members due to unavailability of specimens and this was a caveat in establishing the other possible route of transmission between units. In addition, due to lack of diversity of the whole genomic profile, the genomic linkage data established through this analysis needs to be viewed in the epidemiological context.

Due to the infectious nature of SARS-CoV-2 and contribution of asymptomatic staff carriers to outbreaks described elsewhere the number of staff identified as possible contacts was high [21] though the number identified as positive was proportionately low (four staff) which can also lead to impact on the workforce and challenges in continuation of care.

Regarding environmental aspects, the lay out of the ward X consisted of 6 bedded bays with shared bathroom facilities and only a limited set of side rooms which lends itself to more patient movement and more potential for transmission to occur.

With regards to ventilation, we know that it is not practical to keep windows open all year round so there may well be instances when the remaining 4 air changes per hour (ACH) cannot be made up by natural ventilation on that ward to achieve compliance all year round. This is particularly relevant as there is now more evidence in support of air borne transmission of SARS-CoV-2 and the requirement for optimal ventilation.

Limitations

We were able to perform whole genome sequencing of six samples from five patients only. This may have been due to the degradation of RNA as a result of delay in analysis. Furthermore, staff samples that tested positive were also not available for genomic sequencing as they were processed in an off-site lab. It is also important to recognise the role of genomic sequencing in this situation. Sequencing is a useful tool to “rule-out direct transmission” if there are significant differences. However, if the genomes are identical, it gives a clue of the possibility of transmission either directly or within 1 or 2 intermediate hosts, but it does not prove transmission.

Conclusion

We could successfully contain the spread of this outbreak following PHE outbreak control guidelines and our local guidelines. We recognised several challenges in the investigation of a COVID-19 outbreak, including the sensitivity of the PCR assay, the limited understanding of the transmission dynamics, time of acquisition of the infection, the number of confounding factors (such as overlapping clinical features between COVID 19 and other respiratory and cardiac conditions), the role of staff as asymptomatic carriers all adding to a layer of complexity in the final interpretation of data. Introduction of lateral flow antigen testing for routine screening of asymptomatic staff will identify positive staff at an early stage and will limit transmission and the role of health care workers in outbreaks in the future [22] as will vaccination of both health care workers and patients.

Early recognition, prompt interventions and good communication were the key points in controlling this outbreak. We
believe that this is the first report of the investigation and management of a COVID-19 outbreak in the UK highlighting the key messages above.

**Ethical approval**

This is a report of an investigation that was conducted as a routine procedure following an outbreak and no ethical approval was sought prior to the investigation. Informed consent was not gained from patients involved in this outbreak. All patients were treated according to clinical judgement and infection control practices in order to treat them and control the outbreak according to local guidelines. Patients did not undergo randomisation or intervention for the purpose of this report. Data has been analysed and presented anonymously.

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**Conflict of interest statement**

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