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Sixty-eight consecutive patients assessed for COVID-19 infection: Experience from a UK Regional infectious diseases Unit

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Abstract

Background: Assessment of possible infection with SARS-CoV-2, the novel coronavirus responsible for COVID-19 illness, has been a major activity of infection services since the first reports of cases in December 2019.

Objectives: We report a series of 68 patients assessed at a Regional Infection Unit in the UK.

Methods: Between 29 January 2020 and 24 February 2020, demographic, clinical, epidemiological and laboratory data were collected. We compared clinical features between patients not requiring admission for clinical reasons or antimicrobials with those assessed as needing either admission or antimicrobial treatment.

Results: Patients assessed were aged from 0 to 76 years; 36/68 were female. Peaks of clinical assessments coincided with updates to the case definition for suspected COVID-19. Microbiological diagnoses included SARS-CoV-2, mycoplasma pneumonia, influenza A, non-SARS/MERS coronaviruses and rhinovirus/enterovirus. Nine of sixty-eight received antimicrobials, 15/68 were admitted, 5 due to inability to self-isolate. Patients requiring admission on clinical grounds or antimicrobials (14/68) were more likely to have fever or raised respiratory rate compared to those not requiring admission or antimicrobials.

Conclusions: The majority of patients had mild illness, which did not require clinical intervention. This finding supports a community testing approach, supported by clinicians able to review more unwell patients. Extensions of the epidemiological criteria for the case definition of suspected COVID-19 lead to increased screening intensity; strategies must be in place to accommodate this in time for forthcoming changes as the epidemic develops.

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KEYWORDS
community assessment, COVID-19, respiratory infection, SARS-CoV-2

1 | INTRODUCTION

SARS-CoV-2 is a recently named novel coronavirus responsible for the outbreak of respiratory disease named COVID-19, arose in Wuhan, China, in December 2019.1-3 At the time of writing (27 February 2020), the overwhelming majority of cases have been reported from inside China; however, single or small numbers of cases have been confirmed in 46 other countries. Transmission has occurred in some countries outside China,4,5 including the UK.6

In the UK, public health and clinical services have been working to identify suspected cases according to a national case definition and to arrange testing, predominantly by real-time PCR of nose and throat swabs. Since testing began, local procedures and national guidelines have changed in response to changing understanding of the disease and demand for testing. On the evening of 06 February 2020, the UK definition of a suspected case was extended to include people presenting with respiratory illness (defined as cough, shortness of breath or fever with or without other symptoms) returning from or transiting through China including Hong Kong and Macau, Japan, Malaysia, South Korea, Singapore, Taiwan or Thailand within the last 14 days, with the case definition subsequently changing further on 25 February 2020 to include northern Italy, Iran and further countries in SE Asia. As of 27 February 2020, 7690 tests have been performed nationally, of which 15 were positive (0.2%). Initially, testing has been led by clinicians, predominantly by infectious diseases or emergency department physicians, although there are plans to move to a community testing model led by other groups of healthcare professionals, and some regions have already done so. Patients are instructed to self-isolate while results are pending and until their symptoms have resolved, with possible financial and health implications for the 99.8% so far in the UK who have an illness other than COVID-19. During the 2009 H1N1 influenza pandemic when a syndromic management strategy with presumptive treatment and self-isolation was used, initial clinical diagnoses of influenza were reported to delay diagnoses of a number of diseases including primary HIV infection7 and *Plasmodium falciparum* malaria,8 and although scoring systems were developed, it remains difficult to distinguish between viral and bacterial pneumonia on clinical grounds.9 In addition, many mild respiratory viral infections were managed as influenza,10 with significant resource implications, both for healthcare services and for patients.

Here, we describe our experience of the first 68 patients we have tested for SARS-CoV-2 at a Regional infectious diseases Unit (RIDU) in the UK. We present the spectrum of illness, alternative diagnoses made and management provided. This is of particular interest at this stage of the epidemic, where many individuals meeting the definition of a suspected case are returning travellers, where the differential diagnosis of respiratory or undifferentiated febrile illness may be broad.11 These findings have implications for the clinical and logistical support that may be required for roll-out of community testing to be a safe and effective replacement for the current predominantly hospital-based, physician-led system.

2 | METHODS

2.1 | Patients

The RIDU at Hull University Teaching Hospitals NHS Trust is based at Castle Hill Hospital, East Yorkshire, UK, and serves a population of 1.2 million people. Patients were predominately referred following telephone assessment by the national NHS 111 service, using Public Health England (PHE) case definitions. Patients were assessed by an infection clinician either in the infectious diseases ward, the ambulance or the patient's car that had transferred them to the unit, and in one instance in the emergency department of the trust. The first 68 consecutive cases are presented here.

2.2 | Clinical assessment and testing

All patients had symptoms recorded, together with a travel and exposure history for at least the 14 days preceding symptom onset. Due to the use of personal protective equipment and in some cases assessment in the patient's car, clinical examination and observations varied between cases. Patients were managed as outpatients if clinically stable and able to self-isolate. All cases were tested for SARS2-CoV using a combined throat and nasopharyngeal (NP) swab, which were processed at the designated public health laboratory. A separate NP swab was tested locally using the BioFire Film Array Respiratory Panel 2 plus (BioMérieux) which can detect 21 targets (17 viral and 4 bacterial). Blood samples were only performed on patients being admitted or where another serious diagnosis was being considered.

2.3 | Data collection, analysis and governance approval

Data were entered directly from clinical notes into a centrally held password-protected spreadsheet, to facilitate patient follow-up and data analysis. Clinical features, observations, investigations, management and outcomes are presented with descriptive statistics where relevant. Local clinical governance approval was granted to record the data as an ongoing service evaluation. As all care delivered to patients was routine, no ethical approval is necessary in keeping with UK national guidance that this is an evaluation of a current NHS service.

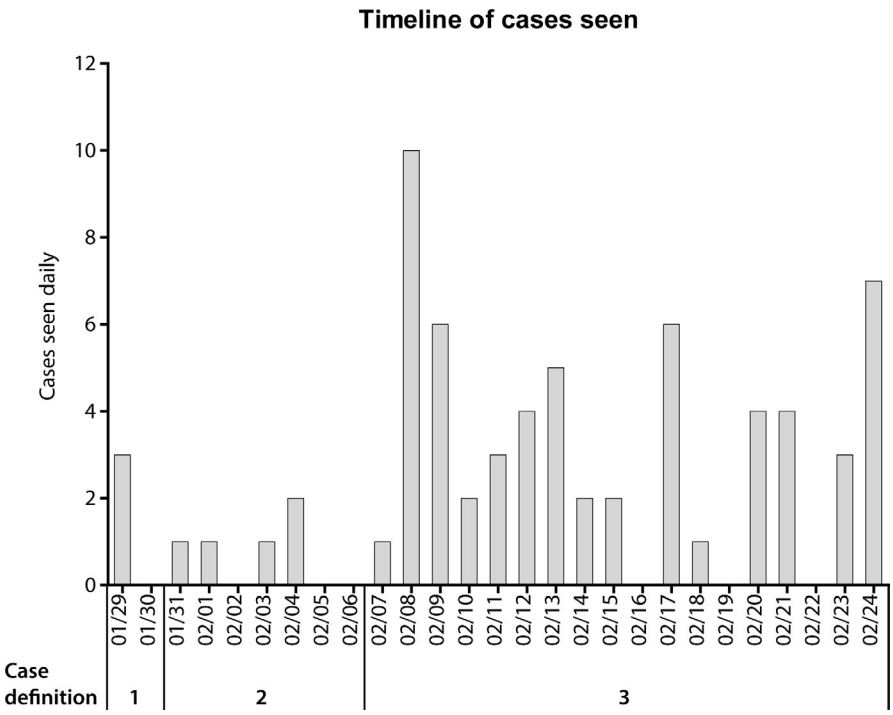

FIGURE 1 Daily cases seen showing changes in case definition for suspected COVID-19. Epidemiological criteria for case definitions: 1. Hubei Province, 2. Mainland China, 3 China, Taiwan, Hong Kong, Macau, Thailand, Japan, Singapore, Malaysia, Republic of Korea

TABLE 1 Presenting features of cases

Clinical Feature (n = 68)	Present (%)
Self-reported fever	27 (40)
Cough	53 (78)
Sore throat	39 (57)
Shortness of breath	17 (25)
Chest pain/discomfort	9 (13)
Myalgia/arthralgia	11 (16)
Nasal symptoms	20 (29)

TABLE 2 Observations of cases (excluding two children assessed)

Observation	Mean	Range
Temperature (°C) (n = 58)	36.4	33.5-38.8
Respiratory rate (/min) (n = 57)	17	14-24
Oxygen saturations on air (%) (n = 56)	97.6	94-100
Pulse (/min) (n = 58)	83.2	52-125
Systolic blood pressure (mm Hg) (n = 45)	125	96-180

3 | RESULTS

3.1 | Timeline of cases, countries visited and location of management

The timeline of cases seen is shown in Figure 1. With the change in case definition to include those returning from SE Asia, the number of cases markedly increased from an initial mean of 0.9 cases/d to 3.3/d. Fifteen of sixty-eight patients (23%) were admitted to the unit, with the remaining patients being managed in an ambulatory manner. Of those admitted, six were only admitted as they could not effectively self-isolate pending results. Mean length of hospital stay in those admitted was 2.4 days (range 1-10 days). Ten patients (15%) had returned from China in the 14 days prior to onset of symptoms, with 26 of the cases (38%) having visited the most common country of travel, Thailand. Eight patients had not left the UK in the preceding 14 days and were seen as contacts of confirmed or suspected cases.

3.2 | Clinical features, patient demographics, antimicrobial usage/management and discharge diagnoses

Of the 68 patients seen, 36 were female (53%), with a mean age of 42.5 years (range 0.5-76). Table 1 shows the presenting features of the cases seen. In addition to the symptoms shown in the table, three cases (4%) had headache, three (4%) had ear pain, and nine (13%) had diarrhoea (two with vomiting as well). Table 2 shows the baseline physical observations, with seven patients (10%) having a temperature of 37.5° or greater on assessment. Antimicrobial therapy was prescribed to nine patients (1.3%), with doxycycline given to five patients (78%), moxifloxacin to three (4%) and oseltamivir to one confirmed influenza A case (1%).

Clinical diagnoses in this cohort included upper respiratory tract infection in 50 patients (74%), exacerbations of airway disease in five patients (7%), lower respiratory tract infections in four patients (6%), gastroenteritis in three (4%), influenza-like illness in two patients

TABLE 3 Results of multiplex PCR of nasopharyngeal swabs

Pathogen detected on local testing	Number detected (total tested n = 67)
No pathogen detected	42 (60.9%)
Rhinovirus/enterovirus	12 (17.9%)
Non-SARS/MERS coronavirus*	10 (14.9%)
Influenza A	3 (4.4%)
Mycoplasma	1 (1.5%)
Respiratory syncytial virus (RSV)	1 (1.5%)
Adenovirus	1 (1.5%)
Human metapneumo virus	1 (1.5%)

*6 coronavirus OC43, 2 coronavirus 229E, 1 coronavirus NL63, 1 coronavirus HKU1.

(3%) and with one patient (1%) each diagnosed with the following: otitis media, a well contact, inebriation and community-acquired pneumonia.

3.3 | Laboratory investigations

Table 3 shows the results of both virological sampling for standard respiratory pathogens in 49 (98%) of the cases assessed. In addition to the virological sampling of NP swabs, four patients (6%) had sputum tested using the BioFire pneumonia panel, with one patient (2%) found to have *Staphylococcus aureus* (MSSA), one patient with *E coli* and *Haemophilus influenzae*, one patient with *Haemophilus influenzae* and seasonal coronavirus co-infection and one with *Haemophilus influenzae* mono-infection. Malaria films were performed and were negative in four patients (6%), while blood cultures were negative in all 14 patients (28%) they were performed on. Standard clinical chemistry and haematology tests were performed in 20 patients (29%). Five patients (7%) had elevated total white cell counts (highest recorded 15.3×10^9/L) with one patient having mild thrombocytopaenia (92×10^9/L). No patients had abnormal serum creatinine or electrolytes, with two (4%) having mildly elevated serum alanine transaminase levels (highest level 63 IU/L). C-reactive protein (CRP) levels were within the normal range in 12 out of 19 cases tested (63%), with the highest recorded level being 73 mg/L.

3.4 | Comparison of clinically well patients with those requiring antimicrobials/clinical need for admission

Table 4 shows the physiological and demographic features of those patients who were prescribed antimicrobial therapy or admitted for clinical reasons (as a group that represents those patients requiring medical input) compared to the other patients seen who were either managed as outpatients, or admitted due to being unable to self-isolate. Fever ≥ 37.5° and shortness of breath as a symptom were the only predictors of requiring antimicrobials or admission for a clinical need.

4 | DISCUSSION

We have presented our experience of testing for SARS-CoV-2 at a UK University Teaching Hospital. Sixty-eight individuals, including 2 children, were tested over 26 days. The majority were ambulant and able to self-isolate and had features consistent with an upper respiratory tract viral infection, or common cold. After the first 10 cases, 6/58 (10.3%) were admitted, at least three of whom only because they lived in shared accommodation where self-isolation was unrealistic, rather than on clinical grounds. This observation supports a community testing approach for the majority. Five of fifty individuals were prescribed antimicrobials without being admitted, emphasising the importance of the availability of clinical decision-makers and prescribers for more unwell patients. None of our cases had severe respiratory illness requiring non-invasive or mechanical ventilation, suggesting it will be rare that patients meeting the definition of a suspected case will require enhanced care, at least while COVID-19 itself remains rare in the UK. Some COVID-19 case series have suggested up to 20% of cases may require respiratory support,2,12 although this figure may be influenced by ascertainment bias. If more generalised outbreaks occur outside China, we may start to see severe COVID-19 presenting to UK healthcare services.

Specialist infectious diseases consultant-delivered assessment of a group of patients who predominantly have mild illness is unlikely to be sustainable, especially as the case definition broadens to include a wider geographical area and/or COVID-19 patients requiring inpatient care becomes more common in the UK. There was

TABLE 4 Differences between patients requiring medical admission and antimicrobials

	Antimicrobial/medical admission group (n = 14)	Remaining patients (n = 52)	*P* value (Fisher's exact test/*t* test)
Age (y)	42.2	42.6	.949
Temperature ≥ 37.5°	5/14	2/46	.0057
Pulse (/min)	88.6	81.8	.225
Respiratory rate	17.9	16.7	.0316
Reported shortness of breath	6/14	11/54	.0968
Cough	9/14	44/54	.2753

Note: Physiological parameters did not include the two children assessed.

a step-change in the number of suspected cases seen after the introduction of the third case definition on the evening of 6 February 2020 as a high number of people with respiratory symptoms and recent travel suddenly became suspected of having COVID-19. As there is further spread in the coming weeks, as is the case in Italy and Iran, and the epidemiological criteria of the case definition are notably extended again, infectious diseases clinicians will be unable to sustain a hospital-based screening service. The NHS is responding to this challenge by moving to a community provider screening model, which will deliver the majority of testing in the home.

Specialist input and assessment, supported by appropriate laboratory investigations, must be easily accessible to a COVID-19 testing service, especially if delivered by health care workers other than infectious diseases physicians. This is important for patients in the self-isolation periods both before and after receiving a test result as these individuals will not readily be able to access the usual healthcare services. This may apply particularly to patients with pre-existing lung disease, where respiratory viral illness, caused by SARS-CoV-2 or otherwise, may trigger clinical deterioration that could ordinarily be managed by early community intervention. Infectious diseases physicians may be the group best placed to support patients in this situation for the short period of self-isolation,13 especially given the need for ongoing personal protective equipment use.14 Although we did not observe any imported "tropical" infections such as dengue, malaria, typhoid, rickettsiosis or leptospirosis, these remain important differential diagnoses in returning travellers from some areas of South-East Asia and may be life-threatening if missed.8,15 These diagnoses may become more common in this group now that the definition of a suspected case has been expanded to include other countries in South or South-East Asia such as Vietnam. Individuals receiving testing for COVID-19 should be signposted to an accessible clinical service with an understanding of this differential diagnosis in case of worsening illness.

Our data from the routine virological testing performed are in keeping with community-based results, showing that symptoms and viral detection do not always go together16 and show a different spectrum to those patients admitted and tested using the same assay,17 with fewer influenza diagnoses and a greater proportion of rhinovirus/ enterovirus as well as seasonal coronaviruses cases. A recent report from Italy,18 immediately before the recent increase in SARS-CoV-2 detection, showed a greater proportion of influenza B than in our cohort, which may be explainable by the differing geographical exposures between the two groups.

Admitting individuals to a secondary care facility, even for short periods of assessment, may have other drawbacks. Travellers to South-East Asia, particularly those who received antibiotics or were admitted to healthcare facilities, can potentially carry and transmit carbapenem-producing enterobacteriaceae. Additionally, because these patients need to be more pragmatically managed than patients not suspected of COVID-19, they may be more likely to be exposed to antimicrobial therapy. There are also significant resource implications not just in terms of PPE use but predominantly in terms of the time required to don and doff PPE for every care interaction from bringing food to routine observations to clinical review. This burden can be at least partially alleviated through a home testing approach.

Infection clinician time is another important resource that may not be best used in managing mild respiratory illness that meets the suspected COVID-19 case definition. In recent years, many studies have demonstrated the benefit of ID physician review in terms of clinical outcome and resource utilisation in infections such as *Staphylococcus aureus* bacteraemia19,20 and resistant Gram-negative infections.21 Our findings support the assessment of, and testing for, possible COVID-19 by other cadres of healthcare workers, outside the secondary care setting, but supported by specialist physicians and hospital-based further diagnostics where needed. The optimum configuration for such a service remains unclear and is likely to vary depending on local constraints, but during the containment phase of the epidemic response there may be time to pilot and compare a range of models before we are forced to move to delay and possibly mitigation strategies.

AUTHOR CONTRIBUTIONS

Nicholas Easom: Conceptualization (equal); data curation (equal); investigation (equal); methodology (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal). **Peter Moss**: Data curation (supporting); investigation (equal); project administration (supporting); Writing – review and editing (supporting). **Gavin Barlow**: Conceptualization (equal); data curation (supporting); investigation (equal); writing – review and editing (equal); **Anda Samson**: Conceptualization (supporting), data curation (equal); investigation (equal); writing – review and editing (equal). **Thomas Taynton**: Data curation (supporting); investigation (supporting); project administration (supporting); writing – review and editing (supporting). **Kate Adams**: Data curation (equal); investigation (equal); writing and review and editing (supporting). **Monica Ivan**: Data curation (equal); investigation (equal); writing – review and editing (Supporting). **Phillipa Burns**: Data curation (equal); investigation (equal); writing – review and editing (equal). **Kavitha Gajee**: Data curation (equal); investigation (supporting); writing – review and editing (supporting); **Kirstine Eastick**: Data curation (supporting); investigation (supporting); writing – review and editing (supporting). **Patrick J. Lillie**: Conceptualization (equal); data curation (lead); formal analysis (lead); investigation (equal); methodology (equal); project administration (equal); supervision (equal); writing – original draft (equal).

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