

# Bacterial and fungal co-infections, antimicrobial treatment and clinical outcome in COVID-19 patients in an acute Irish hospital

Amro Ahmed Omar (✉ [dramr\\_1232002@yahoo.com](mailto:dramr_1232002@yahoo.com))

Cork University Hospital, Cork, County Cork, Ireland

Shianna Malika Cudeshia Williams

University Hospital Kerry, Tralee, County Kerry, Ireland

Jack Patrick Finn

University Hospital Kerry, Tralee, County Kerry, Ireland

Siddig Omer Eltayeb

University Hospital Kerry, Tralee, County Kerry, Ireland

Gabriela Dornikova

University Hospital Kerry, Tralee, County Kerry, Ireland

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## Research Article

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## Abstract

**Background** Serious bacterial infections may be missed when all attention focuses on COVID-19. It is therefore important to consider bacterial infection when assessing the febrile patient.

**Aims** The aim of the study was to look at the bacterial and fungal co-infections, antimicrobial treatment and clinical outcome in COVID-19 patients in an acute Irish hospital.

**Methods** A retrospective study of all laboratory confirmed COVID-19 cases admitted to a secondary care university hospital was performed, and clinical, radiology and laboratory data was extracted and analysed.

**Results** 42 patients met eligibility criteria for the study inclusion. Male/female ratio was 22/20 (52.4%/47.6%), median age of the patients was 64 years and the median duration of hospital stay was 11 day. In-hospital mortality rate was 3 (7.1%). Four laboratory confirmed co-infections were identified in 3 (7.1%) patients. All 3 patients were discharged home. Out of 42 patients, 12 (28.6%) patients received specific antiviral treatment. 34 (85.0%) patients were prescribed antimicrobials with antibacterial effect and 3 (7.5%) antimicrobials with antifungal effect.

**Conclusions** We found a low frequency of bacterial and fungal co-infections in confirmed COVID-19 cases. Further prospective data are needed to be collected in relation to the co-infections in COVID-19.

## Introduction

The COVID-19 pandemic challenges all aspects of healthcare including recognition and management of serious acute bacterial co-infection and effective delivery of antimicrobial stewardship. Serious bacterial infections may be missed when all attention focuses on COVID-19. It is therefore important to consider, investigate and empirically treat bacterial infection when assessing the febrile patient. Many studies of hospitalised patients with COVID-19 note the empiric use of antibiotics in a majority of patients [1].

A limited number of publications have been available to date in the peer reviewed medical journals, as well as limited clinical guidelines for COVID-19 management and treatment.

We performed a retrospective review of 42 patients, admitted to the University Hospital Kerry (UHK) for COVID-19 treatment in period from 12<sup>th</sup> March 2020 when the first case was admitted via Emergency department (ED) until 15<sup>th</sup> May 2020, when the last confirmed case of the first wave was discharged.

## Methods

A retrospective study of all laboratory confirmed COVID-19 cases admitted to UHK was performed, and clinical, radiology and laboratory data was extracted and analysed.

For COVID-19, case definition by the Health protection surveillance centre (HPSC) criteria was followed. The definition included *clinical criteria*: A patient with acute respiratory infection or sudden onset of anosmia, ageusia and dysgeusia, or a patient with severe acute respiratory infection requiring hospitalisation and with no other aetiology that fully explains the clinical presentation. *Epidemiological criteria*: At least one of the following two epidemiological links: Close contact with a confirmed COVID-19 case in the last 14 days prior to onset of symptoms, or having been a resident or staff member, in the 14 days prior to onset of symptoms, in a residential institution for vulnerable people, where on-going COVID-19 transmission has been confirmed. *Diagnostic imaging* criteria: Radiological evidence showing lesions compatible with COVID-19. *Laboratory criteria*: Detection of SARS-CoV-2 nucleic acid in a clinical specimen.

Co-infection was defined as a viral, bacterial or fungal infection in COVID-19 patient that was laboratory confirmed by a positive blood culture or by other positive culture or molecular test in a specimen valid to the site of infection.

The molecular tests for detection of SARS-CoV-2, as well as the bacteriology studies were performed in the UHK Microbiology Department. For detection of coronavirus were used either, Genexpert or RespiBio molecular tests. In the beginning of the pandemic, prior to introduction of molecular tests in the UHK, the specimens were tested in the regional laboratory, or in the national viral reference laboratory.

The UHK is a secondary care university hospital, providing care to the catchment area of 147 707 (2016 census) population in county Kerry, as well as to the residents of North Cork and West Limerick. It provides care for the patients in medical and surgical specialities, paediatrics, gynaecology-obstetrics, as well as psychiatry.

## Results

### Demographic data and symptoms

42 patients met eligibility criteria for the study inclusion. They were admitted to the hospital between 12<sup>th</sup> March 2020 and 2<sup>nd</sup> May 2020. Male/female ratio was 22/20 (52.4%/47.6%). Median age of the patients was 64 years with range from 1 to 97 years. In-hospital mortality rate was 3 (7.1%). The median age of deceased patients was 72 years.

The median duration of hospital stay was 11 day, ranging from 2 to 112 days.

The prevalent symptom on admission was cough (31 cases, 73.8%), followed by shortness of breath (SOB) (28 cases, 63.7%), fever (22 cases, 52.4%), hypothermia (3 cases, 7.1%), fatigue (8 cases, 19.0%), diarrhoea (8 cases, 19.0%), vomiting (6 cases, 14.3%), chills (5 cases, 11.9%) and sore throat (4 cases, 9.5%). The further breakdown showed that in those who presented with cough, dry cough was prevalent (38.7%), followed by productive cough (19.4%). Non-specified cough occurred in 41.9%. Myocarditis occurred in 1 case (2.4%).

The most frequent comorbidity was hypertension (HTN) – in 15 cases (35.7%), followed by atrial fibrillation in 10 (23.8%), type 2 diabetes mellitus (T2DM) in 8 (19.0%), hyperlipidaemia in 6 (14.3%), asthma in 4 (9.5%), gout in 4 (9.5%), chronic obstructive pulmonary disease (COPD), ischaemic heart disease (IHD), chronic cardiac failure (CCF), chronic kidney disease (CKD), each in 3 cases (7.1%).

6 (14.3%) patients were admitted to ICU. The median length of ICU stay was 18 days range from 11 to 88 days. All 6 patients were ventilated - median duration of mechanical ventilation was 14.5 days, range 1 – 78 days.

### Co-infections and microbiology

Four (laboratory confirmed co-infections were identified in 3 (7.1%) patients , one case of pneumonia due to *Candida albicans*, one urinary tract infection (UTI) due to *Klebsiella pneumoniae* and 2 cases of central line associated bloodstream infection, one due to *Enterococcus faecalis* and one due to *Enterococcus faecium*. All 4 co-infections occurred more than 48 hours after admission.

### Radiology

Total of 38 (90.5%) patients had chest X ray (CXR). In 27 (71.0%) cases a significant consolidation was reported and in 9 (23.7%) cases no acute changes were seen. Pleural effusion was identified in 4 (10.5%) cases. Pericardial effusion was found in 2 (5.3%) cases of COVID-19.

CT was performed in 8 (19.0%) patients only. It showed peripheral ground glass opacities (GGO) in 4 (50.0%) cases, significant bilateral consolidation in one case (12.5%) and both features, (GGO and consolidation) in 2 (25.0%) patients. No acute changes were reported in 1 (12.5%) case.

### Scores and biomarkers

Scoring system was not consistent across the hospital. National Early Warning Score (NEWS) was assessed in 39 (92.8%) patients and was ranging from 0 to 10, median 2. Glasgow coma score (GCS) was evaluated in 26 (61.9%) patients, scoring from 3 to 15, median 15. COVID-19 score was only assessed in 5 (11.9%) patients. It was ranging from 0 to 10, median 3.

We assessed the biomarkers on admission. White blood cell count (WBC) median was  $6.6 \times 10^9/L$  (range  $2.8-18.5 \times 10^9/L$ ), neutrophils  $4.5 \times 10^9/L$  (range  $1.7-14.6 \times 10^9/L$ ), lymphocytes median was  $1.1 \times 10^9/L$  (range  $0.3-2.8 \times 10^9/L$ ), CRP 57.8 mg/L (range 0.3 – 356.0 mg/L), CK 596 U/L (70-8835 U/L) serum ferritin 650 ng/ml (range (106-14 783 ng/ml), LDH 586 U/L (range (306-1 545 U/L), D-dimers 0.7 mg/L (range 0.2 – 31.2 mg/L) and troponin I 10 ng/L (range 3-7142 ng/L).

### **Antimicrobial treatment**

Out of 42 patients, 12 (28.6%) patients received specific antiviral treatment. 34 (85.0%) patients were prescribed antimicrobials with antibacterial effect and 3 (7.5%) patients antimicrobials with antifungal effect. In total, antimicrobials accounted for 141 prescriptions, including antiviral, antibacterial and antifungal treatment. Antiviral treatment accounted for 14 (9.9%) prescriptions as follows: hydrochloroquine (n=11, 7.8%) lopinavir/ritonavir (n=2, 1.4%) and remdesivir (n=1, 0.7%). Antibiotic treatment included 121 (85.8%) antimicrobials with antibacterial effect and 6 (4.3%) with antifungal effect. The most frequently prescribed antimicrobials were as follows: ceftriaxone (n=24; 17.0%), clarithromycin (n=20; 14.2%), co-amoxiclav (n=16; 11.3%), piperacillin-tazobactam (n=15; 10.6%), azithromycin (n=15; 10.6%), linezolid (n=6; 4.3%), meropenem (n=4; 2.8%). Anidulafungin was the most frequently used antifungal (n=2; 1.4%).

5 (11.9%) patients did not receive any antimicrobials.

### **Limitations**

The limitation of the study was a short follow-up of the patients, as well as a retrospective design of the study that reduced control over data collection. Respiratory samples were not available for all patients; many of them were unable to produce sputum during their admission, and invasive respiratory sampling was restricted in order to minimize aerosol-generating procedures.

## **Discussion**

In our retrospective study were reviewed 42 cases of laboratory confirmed COVID-19. Mortality rate was 3 (7.1%). 6 (14.3%) patients were admitted to ICU. Four laboratory confirmed co-infections were identified in 3 (7.1%) patients as follows: one case of pneumonia due to *Candida albicans* (day 11), one urinary tract infection (UTI) due to *Klebsiella pneumoniae* (day 47) and 2 cases of central line associated bloodstream infection, one due to *Enterococcus faecalis* (day 60) and one due to *Enterococcus faecium* (day 3). Out of 42 patients, 12 (28.6%) patients received specific antiviral treatment, 34 (85.0%) patients were prescribed antimicrobials with antibacterial effect and 3 (7.5%) antimicrobials with antifungal effect. In total, antimicrobials accounted for 141 prescriptions.

Similar results were published recently [1 - 4], showing in general low rates of bacterial and fungal co-infections and a widespread antibiotic use in patients with confirmed COVID-19. In one study only, a high incidence of bacterial and fungal co-infections was presented [5].

Recently issued Irish national guideline on Antimicrobial Stewardship in COVID-19 suggests that secondary bacterial infection appears uncommon in COVID-19 patients [6]. However, the fact remains that the serious bacterial infections may be missed when all attention focuses on COVID-19. It is therefore important to consider (investigate and empirically treat) bacterial infection when assessing a febrile patient. Antibiotics have unintended consequences for each individual patient and so prudent use is vital. Inappropriate use may cause significant side effects in the individual patient, reduce availability if used indiscriminately, and broad-spectrum antibiotics in particular may lead to *Clostridioides difficile* infection. Frail elderly patients are at greater risk of complication and death from all infections. Although there may be a lower threshold for prescribing antibiotics, older patients are also at greater risk of harm from antibiotics. Currently antivirals or agents with antiviral properties

for COVID-19 remain experimental; their use is restricted to hospitalised patients for treatment only, and ideally as per a clinical trial. These agents should not be prescribed in the community for treatment or prophylaxis.

## Conclusion

In conclusion, our study showed low rates of bacterial and fungal co-infections and a widespread antibiotic use in patients with confirmed COVID-19.

42 COVID-19 patients were reviewed retrospectively. Four cases of infection in 3 patients were confirmed laboratory, one case of pneumonia, one UTI and 2 cases of central line associated bloodstream infection. All 4 co-infections occurred more than 48 hours after admission.

Antimicrobial treatment was prescribed in 37 (88.1%) patients, 5 (11.9%) patients did not receive any antimicrobials. 12 (28.6%) patients received specific antiviral treatment, 34 (85.0%) patients were prescribed antimicrobials with antibacterial effect and 3 (7.5%) antimicrobials with antifungal effect.

Further prospective data are needed to be published in relation to co-infections in COVID-19.

## Declarations

Funding: None

Conflicts of interest/Competing interests: Nothing to declare

Availability of data and material: The data that support the findings of this study are available from the corresponding author, [AAO] upon a reasonable request.

Code availability: Not applicable

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study formal consent is not required.

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