

# Co- and secondary infection in COVID-19 patients within ICUs in England. A retrospective cohort study from the first wave of the pandemic

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## INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), is associated with high mortality and morbidity, and increased hospitalisation.<sup>1</sup> With severe cases of SARS-CoV-2 requiring intensive care unit (ICU) support.

Both co-infections and secondary bacterial and fungal infections with SARS-Cov-2 have been reported.<sup>2</sup> Concerns have been raised over the risk of co- or secondary infection in these cases and subsequent impacts on morbidity and mortality.<sup>3</sup>

Here we present the findings of co- and secondary infections of patients within English ICUs with SARS-CoV-2 infection from the first wave of the pandemic in England.

## METHODS

### Data collection

Laboratory confirmed SARS-CoV-2 cases in England notified to Public Health England (PHE) from 01/03/2020-30/08/2020 were linked to Blood Stream Infection (BSI) cases captured in the ICU data capture system, up to 30/09/2020, to allow a secondary BSI to have occurred.

### Definitions

Co- and secondary infections were defined as a culture positive organism, isolated  $\pm$  1 day, or +2-27 days from the SARS-COV-2 positive specimen date, respectively.

### Analysis

All descriptive data analysis were carried out using STATA<sup>TM</sup>15

Case fatality rate (CFR) analysis were age and sex adjusted to European population standards.

### Counts of cases and characteristics

A total of 698 ICU BSI were identified during the study period, 1.4% (n=10) and 33.7% (n=235), were classified as a co- or secondary infection, respectively. All co- and secondary infections were identified in adult units only (Table 1).

Median time from COVID-19 infection to ICU BSI co- or secondary infection was 13 days (IQR: 9-20 days).

A total of 112 deaths were recorded in this study population, of which 84% (n=94) had a secondary infection, and 4.5% a co-infection.

**Table 1: Characteristics of cases**

Characteristic	All ICU BSIs (%)	Secondary Infection (%) <sup>a</sup>	Co-infection (%) <sup>†</sup>
Total	640	235	10
Age	55 $\pm$ 18	59 $\pm$ 14	55 $\pm$ 13
Sex	76 (26.7)	57 (25.2)	2 (20.0)
Ethnicity			
White	160	129 (57.1)	4 (40.0)
Asian/Asian British	50	37 (16.4)	3 (30.0)
Black/Black British	42	33 (14.6)	2 (20.0)
Mixed	7	6 (2.7)	0 (0.0)
Other	24	19 (8.4)	1 (10.0)
Unknown	2	2 (1.0)	0 (0.0)
IMD Decile (1 most deprived)			
1	34	26 (11.5)	2 (20.0)
2	49	37 (16.4)	2 (20.0)
3	42	33 (14.6)	1 (10.0)
4	36	32 (14.2)	2 (20.0)
5	31	21 (9.3)	1 (10.0)
6	25	22 (9.7)	0 (0.0)
7	13	11 (4.9)	1 (10.0)
8	17	13 (5.8)	0 (0.0)
9	17	12 (5.3)	1 (10.0)
10	21	19 (8.4)	0 (0.0)
NHS Region			
East of England	33	24 (10.6)	0 (0.0)
London	112	93 (41.2)	3 (30.0)
Midlands	40	34 (15.0)	1 (10.0)
North East and Yorkshire	21	14 (6.2)	3 (30.0)
North West	38	26 (11.5)	3 (30.0)
South East	26	24 (10.6)	0 (0.0)
South West	15	11 (4.9)	0 (0.0)
Died (crude CFR)	112 (40.1) <sup>*</sup>	94 <sup>**</sup> (84.0)	5 <sup>**</sup> (4.5)

<sup>a</sup>Secondary infection, COVID-19 first positive specimen date is between 2 to 30 days of the positive BSI

<sup>†</sup>Co-infection – COVID-19 first positive specimen date within 2 days (+/-) of positive BSI case

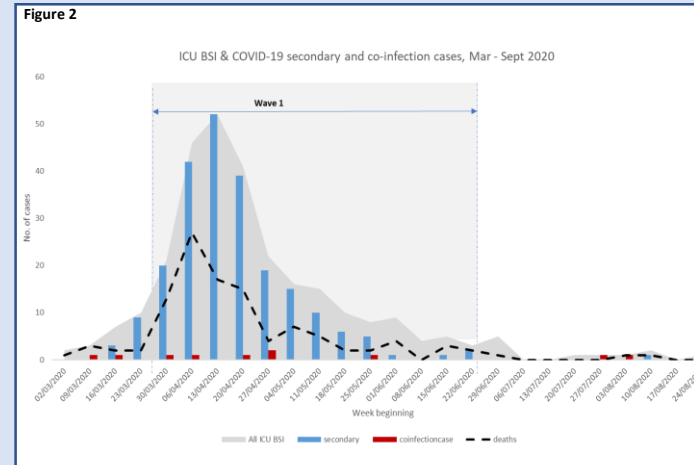
<sup>\*</sup>All deaths

<sup>\*\*</sup> Died within 60 days of COVID-19 positive specimen or COVID-19 on death certificate

## RESULTS

### Time trend

ICU BSI infections rose steeply during the first wave of the pandemic (late Mar to mid-June), secondary infections also rose during this period and accounted for 93% (n=219) of all secondary infections observed. Deaths also increased during this period (Figure 2).



### Case Fatality Rate

Age and sex adjusted case fatality rates (CFRs) were higher in ICU patients with BSI defined as co- and secondary infections compared to ICU BSI patients without COVID-19, 35.5 (95%CI: 25.5-47.0) and 2.5 (95%CI:1.2-4.3).

### Organisms

The most common BSI in the co- and secondary infection patients were from *Klebsiella pneumoniae* (40.0%). Of all the *Klebsiella pneumoniae* BSIs, 80.9% (n=38) were identified as secondary infections (Table 2).

**Table 2: Breakdown of most common organisms isolated in co- and secondary cases**

organism	All ICU BSI cases	Secondary infections (%)	Co infections (%)
<i>KLEBSIELLA PNEUMONIAE</i>	47	38 (80.9)	
<i>STAPHYLOCOCCUS SP., OTHER</i>	42	36 (85.7)	
<i>ENTEROCOCCUS FAECIUM</i>	36	26 (72.2)	
<i>STAPHYLOCOCCUS EPIDERMIDIS</i>	32	27 (84.4)	7 (21.9)
<i>ESCHERICHIA COLI</i>	31	22 (71.0)	
<i>PSEUDOMONAS AERUGINOSA</i>	23	14 (61.0)	

## DISCUSSION

Bacterial co- and secondary infections are commonly identified in severe respiratory viral infections, and are associated with an increased morbidity and mortality.<sup>4</sup>

Of patients in ICUs identified with a positive BSI, COVID-19 co- and secondary infection cases were most common during the first wave of the pandemic.

Age-sex-adjusted CFR were 14 times higher in those with COVID and a co- or secondary BSI, compared to those with just a BSI.

*Klebsiella pneumoniae* was identified as the most common secondary infection, and accounted for almost 90% of all *Klebsiella pneumoniae* ICU infections. *Staphylococcus epidermidis* accounted for 70% (n=7/10) of all the co-infections identified.

More work is needed to determine the underlying drivers of these infections but probable risks are lower staff ratios, changes to antibiotic prescribing practice and immunosuppression of patients.

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