

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.¹ 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.² Concerns have been raised over the risk of co- or secondary infection in these cases and subsequent impacts on morbidity and mortality.³

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 STATATM15

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 (%) ^a	Co-infection (%) [†]
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) [*]	94 ^{**} (84.0)	5 ^{**} (4.5)

^aSecondary infection, COVID-19 first positive specimen date is between 2 to 30 days of the positive BSI

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

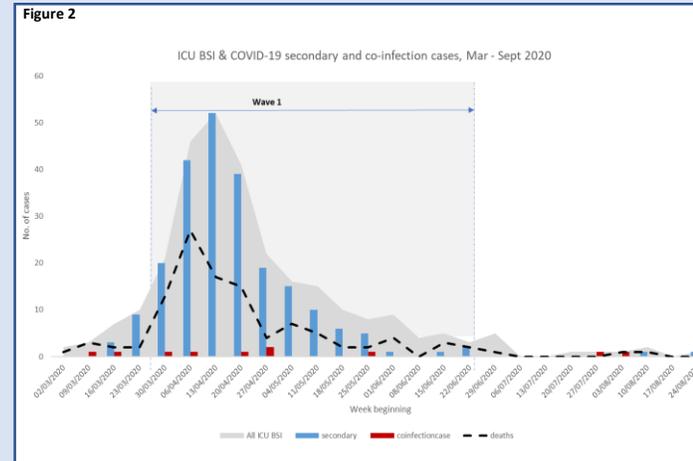
^{*}All deaths

^{**} 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.⁴

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.

ACKNOWLEDGEMENTS

We are very grateful to all the participating units for providing data to the ICCQIP surveillance programme. We also thank the ICCQIP board members for their continued support.

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