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COVID-19 patients at risk of fatal co-infection during ICU stays

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By [Sally Robertson, B.Sc. \(/medical/authors/sally-robertson\)](#)

Oct 29 2020

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Researchers in the UK have conducted a study showing that a high proportion of patients admitted to intensive care units (ICU) with coronavirus disease 2019 (COVID-19) acquire a secondary bacterial co-infection during their hospital stay.

The retrospective cohort study of patients admitted to ICUs in England up to May 18th, 2020 found that the longer the ICU stay, the more significant the proportion of patients who developed nosocomial (hospital-acquired) infections.

While bacterial co-infection within 48 hours of ICU admission was uncommon, the proportion of pathogens detected started to increase after 48 hours. The pathogens mostly consisted of Gram-negative bacteria, particularly *Klebsiella pneumoniae* and *Escherichia coli*.

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It is possible that reducing unnecessary exposure to such antibiotics could lower the risk of patients later acquiring Gram-negative infections that are potentially resistant to antibiotics, they add.

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Gram-positive bacteria are more susceptible to treatment with antibiotics than Gram-negative bacteria since they have a single-layered cell wall that is more easily penetrated than the double-layered cell wall of Gram-negative bacteria.

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The team recommends that a high level of microbiological vigilance is maintained when managing patients hospitalized with COVID-19.

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A pre-print version of the paper is available on the server *medRxiv* (<https://www.medrxiv.org/content/10.1101/2020.10.27.20219097v1>)*, while the article undergoes peer review.

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The contribution of co-pathogens to illness during viral pandemic is not well understood

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Co-infection with other pathogens during viral pandemics has been reported previously.

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During the 1918 influenza pandemic, for example, reports estimated that almost all (95%) of severe infections and death had been complicated by bacterial co-infection, predominantly co-infection with *Streptococcus pneumoniae* and *Staphylococcus aureus*.

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Following SARS-CoV-2 infection, the immune response includes an increase in the proinflammatory cytokine interleukin 6 and the inflammation marker C-reactive protein, with levels increasing the more severe the disease.

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However, the role that co-pathogens play during SARS-CoV-2 infection is not well understood, say Baskaran and colleagues.

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Furthermore, the lack of effective antiviral treatments for SARS-CoV-2, as well as the difficulty distinguishing between secondary bacterial co-infection and severe COVID-19 alone, has led to the widespread use of empirical antibiotics as a first-line treatment approach for hospitalized COVID-19 patients.

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“Over the long course of the pandemic, 83.1% of hospitalized patients in the UK received empirical antibiotic treatment,” say the researchers. “A better understanding of the incidence of co-infection in patients with COVID-19 infection and the pathogens involved is necessary for effective antimicrobial stewardship.”

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Investigating bacterial co-infection in severely ill COVID-19 patients

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To determine the incidence and nature of co-infection among critically ill COVID-19 patients in England, the team conducted a retrospective study of 254 patients who had completed ICU stays at seven acute hospitals across England.

Patients (aged 16 years or older) with COVID-19 pneumonia who had been receiving treatment from the point of disease emergence up to May 18th, 2020, had either died while in ICU or had been discharged from hospital.

The proportion of co-infection was determined at three-time points: on ICU admission, within 48 hours of admission and beyond 48 hours of admission, to distinguish between patients with community- versus hospital-acquired co-infection.

The researchers identified 139 clinically significant pathogens among 83 (32.7%) of the 254 patients studied.

Bacterial co-infection within 48 hours of hospital admission was uncommon, occurring in 4 (1.6%) of the patients on admission and 14 (5.5%) of the patients within 48 hours of admission.

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The most common pathogens identified in the first 48 hours of admission were the Gram-positive bacteria *Staphylococcus aureus* and *Staphylococcus pneumoniae*.

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The proportion of co-pathogens started to increase after 48 hours in ICU

Beyond 48 hours of ICU admission, the proportion of co-pathogens detected increased until the end of the stay (either death or hospital discharge).

Aside from two fungal organisms, all of the co-pathogens identified were Gram-negative bacteria, predominantly *Klebsiella pneumoniae*, and *Escherichia coli*.

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"These pathogens are commonly associated with hospital and ventilator-acquired pneumonia and have been reported as common co-pathogens in COVID-19 infections, particularly in ICU patients," say Baskaran and colleagues.

"The predominance of Gram-negative bacteria in these studies likely reflects nosocomial infection following prolonged ICU stay and empirical antibiotic use," they write.

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Univariate analyses showed that patients aged 50-64 years were more likely to have a bacterial co-infection than those aged 18-49 years.

Patients with these co-infections were also at a significant 78% greater likelihood of dying in the ICU than patients who did not have a bacterial co-infection.

Care should be taken over administering antibiotics



"Our data indicate that early in hospitalization, bacterial co-infection in COVID-19 is very uncommon and that the use of empirical antibiotics should not be started routinely in primary care or at the point of hospital admission without clinical suspicion of bacterial infection," say the researchers.

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The high rate of co-infection at a later stage during hospitalization and involving nosocomial pathogens is concerning, they add.

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"It is plausible that reducing unnecessary early antibiotic exposure in patients with COVID-19 could reduce their risk of late, Gram-negative, potentially antibiotic-resistant infections," write Baskaran and colleagues.

"In the setting of serious infectious diseases pathogens, ongoing surveillance for co-infections in patients hospitalized with COVID-19, ideally through prospective studies with standardized sampling protocols, is advised," they conclude.

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Sally has a Bachelor's Degree in Biomedical Sciences (B.Sc.). She is a specialist in reviewing and summarising the latest findings across all areas of medicine covered in major, high-impact, world-leading international medical journals, international press conferences and bulletins from governmental agencies and regulatory bodies. At News Medical, Sally generates daily news features, life science articles and interview coverage.

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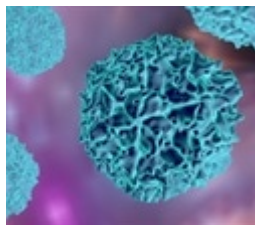
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