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▶ **To cite this version:**

Alexandre Elabbadi, Matthieu Turpin, Grigoris T Gerotziafas, Marion Teulier, Guillaume Voiriot, et al.. Bacterial coinfection in critically ill COVID-19 patients with severe pneumonia. Infection, 2021, 49 (3), pp.559 - 562. 10.1007/s15010-020-01553-x . hal-03254023

HAL Id: hal-03254023

https://hal.sorbonne-universite.fr/hal-03254023v1

Submitted on 8 Jun 2021

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Infection (2021) 49:559–562
https://doi.org/10.1007/s15010-020-01553-x

CORRESPONDENCE

Bacterial coinfection in critically ill COVID-19 patients with severe pneumonia

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Received: 24 August 2020 / Accepted: 3 November 2020 / Published online: 3 January 2021
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Abstract

Severe 2019 novel coronavirus infectious disease (COVID-19) with pneumonia is associated with high rates of admission to the intensive care unit (ICU). Bacterial coinfection has been reported to be rare. We aimed at describing the rate of bacterial coinfection in critically ill adult patients with severe COVID-19 pneumonia. All the patients with laboratory-confirmed severe COVID-19 pneumonia admitted to the ICU of Tenon University-teaching hospital, from February 22 to May 7th, 2020 were included. Respiratory tract specimens were obtained within the first 48 h of ICU admission. During the study period, 101 patients were referred to the ICU for COVID-19 with severe pneumonia. Most patients ($n = 83$; 82.2%) were intubated and mechanically ventilated on ICU admission. Overall, 20 (19.8%) respiratory tract specimens obtained within the first 48 h. *Staphylococcus aureus* was the main pathogen identified, accounting for almost half of the early-onset bacterial etiologies. We found a high prevalence of early-onset bacterial coinfection during severe COVID-19 pneumonia, with a high proportion of S. aureus. Our data support the current WHO guidelines for the management of severe COVID-19 patients, in whom antibiotic therapy directed to respiratory pathogens is recommended.

Keywords Coronavirus disease 2019 · Bacterial coinfection · *Staphylococcus aureus* · Intensive care unit · Pneumonia

Abbreviations

COVID 19	Coronavirus infectious disease
ICU	Intensive care unit
SAPSII	Simplified acute physiology score
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SOFA	Sequential Organ Failure Assessment

Introduction

Severe 2019 novel coronavirus infectious disease (COVID-19) with pneumonia is associated with high rates of admission to the intensive care unit (ICU) and in-hospital mortality [1]. Information about the rates of coinfection with SARS-CoV-2 and one or more additional microorganisms are conflicting. Bacterial coinfection has been reported to be rare [1], while viral coinfection has been recently reported to be as high as 20.7%, using a panel of non-SARS-CoV-2 respiratory pathogens, mainly respiratory viruses [2].

We aimed at describing the rate of bacterial coinfection in critically ill adult patients with severe COVID-19 pneumonia.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s15010-020-01553-x) contains supplementary material, which is available to authorized users.

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Methods

All the patients with laboratory-confirmed severe COVID-19 pneumonia admitted to the 42-bed ICU of Tenon University-teaching hospital, from February 22 to May 7th, 2020 were included. Respiratory tract specimens were obtained within the first 48 h of ICU admission. Direct examination and quantitative cultures were performed on usual media for sputum, tracheal aspirate, plugged telescoping catheter, or bronchoalveolar lavage, considering the respective positivity thresholds: 10^6 cfu/ml, 10^5 cfu/ml, 10^3 cfu/ml and 10^4 cfu/ml. Empirical antimicrobial therapy combined broad-spectrum antibiotics (a third-generation cephalosporin plus a macrolide), and oseltamivir along the Flu season.

Results

During the study period, 101 patients were referred to the ICU for COVID-19 with severe pneumonia after 8 (5.5–11) days of symptoms onset, and 1 (0–2) day of hospitalization in the wards. They were 79 men (78.2%), aged 61 (53–69) years, with moderate overweight [body mass index 27.6 (24.5–31)] and frequent comorbid conditions, mainly arterial hypertension ($n=66$; 65.3%) and diabetes ($n=33$; 32.7%). Most patients ($n=83$; 82.2%) were intubated and mechanically ventilated on ICU admission. The SAPSII score and SOFA score were 27 (22–37) and 3 (2–5), respectively. By the end of the study period, 21 patients (21%) had died, 12 (11.9%) were still hospitalized in the ICU, while 51 (50.4%) and 17 (16.8%) had been discharged to conventional wards or long-term rehabilitation care units, respectively.

Overall, 20 (19.8%) respiratory tract specimens obtained within the first 48 h of ICU admission yielded positive culture at or above the thresholds for at least one pathogen ($n=12$), and below the thresholds ($n=8$, including 6 with prior antibiotic therapy before ICU admission, and 1 associated with pneumococcal bacteremia) (Table 1 and Table S1). *Staphylococcus aureus* was the main microorganism identified, accounting for almost half of the early-onset bacterial etiologies (Table 2). Late-onset bacterial superinfections were diagnosed after 7.5 days (4–11) in 48 patients, and were mainly related to *Pseudomonas aeruginosa*. There was no difference in comorbidities or admission clinical and laboratory characteristics between patients with or without early bacterial coinfection, except a trend towards a more pronounced lymphopenia (Table 1).

Discussion

We found a high prevalence of early bacterial coinfection during severe COVID-19 pneumonia, with a high proportion of *S. aureus*. Data from China and South-east Asia pointed to a low prevalence of bacterial coinfection in patients with COVID-19 pneumonia [3]. In one cohort in which this information was reported in detail, including 201 patients hospitalized for COVID-19 pneumonia [of whom 53 (26%) were admitted to the ICU], none had documented bacterial co-infection[2]. If the high rate of coinfection with *S. aureus* has been well described in Flu [4], first reported cohorts do not mention bacterial co-infection as a common feature of COVID-19 with pneumonia [5]. Our findings are consistent with those of two recent series which focused on the early bacterial coinfection associated with SARS-CoV-2 pneumonia, and highlighted that *S. aureus* was one of the main identified microorganism, using molecular diagnostic tests alone or in association with conventional tests [6, 7]. Interestingly, procalcitonin level did not differ between the patients with and without associated bacterial coinfection, as already reported by Kreitmann et al. [7] raising the question of the usefulness of this biomarker to help for identifying early bacterial coinfection during COVID-19 pneumonia.

Our findings support the current WHO guidelines for the management of severe COVID-19 patients, in whom antibiotic therapy directed to respiratory pathogens is recommended [8].

This is a single-center study, so our findings should be extrapolated with caution. However, clinicians should be alert of the high proportion of *S. aureus* co-infection during COVID-19 pneumonia.

Table 1 Baseline characteristics, management and outcomes of the COVID19 cohort

	All patients ($n=101$)	Early bacterial coinfection ($n=20$)	No early bacterial coinfection ($n=81$)	*P* Value
Age (year)	61 [53–69]	60 [53.8–63.5]	63 [53–71]	0.24
Sex male	79 (78.2)	17 (85)	62 (76.5)	0.55
Current smoking	4 (4)	1 (5.3)	3 (3.7)	0.57
Body-mass index (kg/m^2)	27.6 [24.5–31]	26.5 [24.4–29.8]	27.7 [24.8–31]	0.76
Comorbid conditions				
None	14 (13.9)	2 (10)	12 (14.8)	0.73
Arterial hypertension	66 (65.3)	14 (70)	52 (64.2)	0.63
Coronary heart disease	14 (13.9)	1 (5)	13 (16)	0.29
Cerebrovascular disease	7 (6.9)	1 (5)	6 (7.4)	0.99
Peripheral artery disease	4 (4)	0	4 (4.9)	0.58
Previous venous thromboembolism	3 (3)	0	3 (3.7)	0.99
Diabetes	33 (32.7)	6 (30)	27 (33.3)	0.78
Chronic pulmonary disease	7 (6.9)	1 (5)	6 (7.4)	0.99
Cancer or hematologic malignancy	4 (4)	0	4 (4.9)	0.58
Chronic kidney disease	21 (20.8)	4 (20)	17 (21)	0.99
Chronic dialysis	9 (8.9)	0	9 (11.1)	0.20
Long-term antiplatelet treatment	23 (22.8)	2 (10)	21 (25.9)	0.15
Long-term anticoagulation	4 (4)	0	4 (4.9)	0.58
Long-term corticosteroids	9 (8.9)	1 (5)	8 (9.9)	0.68
Medication before ICU admission				
NSAIDs	0	0	0	*NA*
Corticosteroids	1 (9.9)	0	1 (1.2)	0.99
Immunomodulatory therapy[†]	11 (10.9)	3 (15)	8 (9.9)	0.45
Antibiotics	58 (57.4)	10 (50)	48 (59.3)	0.45
Time between symptoms onset and ICU admission (days)	8 [5.5–11]	8 [5.5–10]	8 [5.8–11.3]	0.68
Time between ward admission and ICU referral (days)	1 [0–2]	1 [0–2.3]	1 [0–2]	0.44
SOFA score	3 [2–5]	4 [2.8–6.3]	3 [2–5]	0.10
SAPSII score	27 [22–37]	26.5 [19–41]	27 [24–37]	0.92
Biological parameters, day 1				
WBC, G/L	7.5 [6.1–10.5]	7 [6–11.4]	7.5 [6.1–10]	0.76
Neutrophil, G/L	6.3 [4.9–8.9]	6.2 [4.8–10.1]	6.3 [4.9–8]	0.94
Lymphocyte, G/L	0.75 [0.5–1.1]	0.58 [0.4–0.8]	0.76 [0.52–1.1]	0.08
Platelet, G/L	211 [151–262]	192 [145–255]	214 [155–262]	0.39
CRP, mg/L	184 [119–271]	177 [87–274]	189 [126–266]	0.44
Procalcitonin, µg/L	0.73 [0.3–2.07]	0.73 [0.48–1.52]	0.73 [0.3–2.61]	0.91
Organ support during ICU stay				
Mechanical ventilation	83 (82.2)	19 (95)	64 (79)	0.11
Vasopressor	54 (53.5)	11 (55)	43 (53.1)	0.88
ECMO	5 (5)	0	5 (6.2)	0.58
Renal replacement therapy	26 (25.7)	5 (25)	21 (25.9)	0.93
Outcomes				
Died	21 (21)	4 (20)	17 (21)	0.99
Discharged from ICU to conventional wards	51 (50.4)	11 (55)	40 (49.4)	0.65
Long term acute care units	17 (16.8)	5 (25)	12 (14.8)	0.32
Still in the ICU	12 (11.9)	0	12 (14.8)	0.12
ICU length of stay (days)	14 [6–26]	14 [8.8–23]	14 [5–27]	0.98

Data are reported using frequencies and percentages or median and interquartile ranges [IQRs], unless otherwise stated

ECMO extracorporeal membrane oxygenation

[†]Immunomodulatory therapy administered were Anakinra ($n=1$) and Tocilizumab ($n=10$)

Table 2 Bacterial microorganism(s) identified in severe COVID-19 pneumonia

Microorganism, *n*	Early Bacterial Coinfection[†]
Gram-positive cocci	12
Staphylococcus aureus	11
MSSA	9
MRSA[a]	2
Streptococcus pneumoniae	1
Enterococcus sp.	0
Gram-negative bacilli	13
Enterobacteriaceae	
E. coli	2
Klebsiella spp.	2
Enterobacter, Citrobacter, Hafnia spp.	4
Serratia	0
Non-fermenting GNB	
Pseudomonas spp.	2
Others	0
Other GNB	
H. influenza	2
M. catarrhalis	1
Other	
Intracellular pathogen	0

[a]*MRSA* methicillin-resistant *S. aureus* (MRSA), in one renal transplant recipient, and one patient without identified risk factor

[†]defined as microorganism(s) identified within the first 48 h of ICU admission. More than one bacterium was identified in 5 patients

Author contributions MF, AE, MT collected, analyzed, and interpreted the data. AE and MF drafted the manuscript. The authors read and approved the final manuscript.

Funding The authors declare that they have no funding source.

Availability of data and materials The datasets and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Competing interest The authors have no conflict of interest to declare.

Ethics approval and consent to participate This is a non-interventional data-based research, using the care data collected during patients stay, involving all the consecutive critically ill COVID-19 patients with severe pneumonia admitted to the ICU in Tenon Hospital during the pandemic. There is no processing of indirectly identifiable data, or chaining with data from other sources, or long-term patient follow-up for this research. Patients and proxies were informed, written consent was waived.

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