Antibiotic prescriptions targeting bacterial respiratory infections in admitted COVID-19 patients: a prospective observational study

Supplementary material

Johan Van Laethem[1]*, Stephanie Wuyts[2,3]*, Sven Van Laere[4], Silke Dirkx[1], Lucie Seyler[1], Rembert Mertens[1], Bart Ilsen[5], Patrick Lacor[1], Denis Pierard[6] & Sabine D. Allard[1]

*: Both authors contributed equally.

Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium

[1] Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Department of Internal Medicine, Laarbeeklaan 101, 1090 Brussels, Belgium

[2] Universitair Ziekenhuis Brussel (UZ Brussel), Hospital Pharmacy, Laarbeeklaan 101, 1090 Brussels, Belgium

[3] Vrije Universiteit Brussel (VUB), Research group Clinical Pharmacology and Pharmacotherapy, Laarbeeklaan 101, 1090 Brussels, Belgium

[4] Vrije Universiteit Brussel (VUB), Interfaculty Centre Data processing and Statistics, Laarbeeklaan 101, 1090 Brussels, Belgium

[5] Universitair Ziekenhuis Brussel (UZ Brussel), Department of Medical Imaging, Laarbeeklaan 101, 1090 Brussels, Belgium

[6] Universitair Ziekenhuis Brussel (UZ Brussel), Microbiology Department, Laarbeeklaan 101, 1090 Brussels, Belgium

Corresponding author:

Johan Van Laethem, MD

E-mail: johan.vanlaethem@uzbrussel.be

Supplementary Material 1: Applied definitions in patient data collection

- Fever was defined as a tympanic temperature above 38°C.
- A respiratory sample with significant result was defined as respiratory samples with culture results positive for a respiratory tract pathogen, in the presence of leukocytes on semi-quantitative analysis and without contamination by epithelial cells.
- *Mycoplasma pneumoniae* respiratory tract super/co-infections were identified by the presence of compatible clinical signs and symptoms together with a four-fold rise in specific antibody titre or the presence of a positive PCR on sputum or oropharyngeal swab.
- Need for supplemental oxygen was documented by calculating the pulsed finger saturation to fraction of inspired oxygen ratio (SpO2/FiO2).

Supplementary Material 2: Definitions used to score appropriateness of antibiotic prescriptions

Appropriate	The use of antibiotics in the setting of an established or empirical infection that cannot be improved in one of the following categories: Indication, drug choice, drug route and drug dose.
Inappropriate	The use of antibiotics in the setting of established infection to which the pathogen is resistant, the use of antibiotics not recommended in treatment guidelines or absolute/relative contraindications (prolonged QTc, type 1 hypersensitivity, important interactions...)
Suboptimal	The use of antibiotics in the setting of established infection that can be improved in one of the following categories: drug choice, drug route and/or drug dose.
Unnecessary	The use of antibiotics for nonbacterial infections, days of therapy beyond the indicated duration of therapy without any clinical reason for lengthened course, use of redundant antimicrobial therapy, continuation of empiric broad-spectrum therapy when cultures have revealed the infecting pathogen.

From Charlson ME, Pompei P, Ales KL et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.

Supplementary Material 3: Microbiological data

Table S1. Microbiological data

	All admissions (n=281)	Confirmed COVID-19 admissions (n= 203)	Rejected COVID-19 admissions (n=78)
General data (n, % per admission)			
At least one respiratory sample	51 (18.1)	28 (13.8)	23 (29)
At least one respiratory sample with a significant result	22 (7.8)	10 (4.9)	12 (15)
At least one prescription of antibiotics for Respiratory Tract Infection	58 (21)	29 (14)	29 (37)
Bacteremia of respiratory origin	1 (0.4)	1 (0.5)	0 (0)
Mycoplasma spp Infection	0 (0)	0 (0)	0 (0)
Specification of significant respiratory samples (n,%)	**31 (100)**	**16 (100)**	**15 (100)**
Aerobic, gram positive cocci	**10 (32.3)**	**6 (37.5)**	**4 (27)**
MSSA*	5 (16.1)	4 (25.0)	1 (6.7)
MRSA**	2 (6.5)	0 (0)	2 (13)
Streptococcus pneumoniae	2 (6.5)	2 (12.5)	0 (0)
S. pyogenes	1 (3.2)	0 (0)	1 (3.7)
Aerobic, gram negative bacilli, Enterobacterales	**14 (45.2)**	**7 (43.8)**	**7 (46.7)**
ESBL[¥] or CPE[ø] in significant respiratory sample	1 (3.2)	1 (6.3)	0 (0)
Klebsiella pneumoniae	6 (19.4)	1 (6.3)	5 (33.3)
Escherichia coli	3 (9.7)	2 (12.5)	1 (3.7)
Other	4 (12.9)	3 (18.8)	1 (3.7)
Aerobic, gram negative bacilli, Non-Enterobacterales	**1 (3.2)**	**0 (0)**	**1 (3.7)**
Haemophilus influenzae	1 (3.2)	0 (0)	1 (3.7)
Aerobic, gram negative bacilli, non-fermenter	**6 (19.4)**	**3 (18.8)**	**3 (20.0)**

Pseudomonas aeruginosa	5 (16.1)	2 (12.5)	3 (20.0)
Acinetobacter spp.	1 (3.2)	1 (6.3)	0 (0)

* MSSA: methicillin-sensitive Staphylococcus aureus; ** MRSA: methicillin-resistant Staphylococcus aureus; ¥ ESBL: Extended Spectrum Beta-Lactamase; ø CPE: Carbapenemase producing Enterobacteriaceae; Influenza PCR testing was not performed, as the study took place outside the yearly influenza season.

Supplementary Material 4: Specification of 'Other' reasons of antibiotic prescribing

Table S2. 'Other' reasons of antibiotic prescribing in admissions with (suspected) bRTI

Reason	**n (7)**
Immunocompromised state*	5
Pulmonary empyema	1
Bacteraemia of respiratory origin	1

*Immunocompromised state: haematological neoplasia (n=3), kidney transplant (n=1), sickle cell crisis (n=1)