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TITLE: EVALUATION AND ANALYSIS OF RATES OF BACTERIAL CO-INFECTIONS AND ANTIMICROBIAL USAGE IN COVID-19 PATIENTS: A RETROSPECTIVE COHORT ANALYSIS

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Abstract

Background: The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread over the world. Although there are minimal microbiological and antibiotic data on COVID-19, bacterial co-infections have been related to poor outcomes in respiratory viralinfections. Adequate antibiotic use in conformity withantibiotic stewardship (ABS) recommendations is necessary during the pandemic.

Material and procedure: We conducted a retrospective single-center cohort analysis of 140 adulthospitalised patients (ages 17–99) with confirmed COVID-19 who were admitted between February 16, 2021, and April 22, 2021, and who were discharged onMay 6, 2021. From 140 COVID-19 participants, the following clinical data was gathered: Men made up 63.5 percent of the participants, with a median age of
63.5 years (range 17–99).

Results: According to local ABS recommendations, the most commonly administered antibiotic regimen was ampicillin/sulbactam (41.5 percent) with a median length of 6 (range 1–13) days. Urine antigen testing for Legionella pneumophila and Streptococcus peumoniaewas negative in all of the patients. In critically ill patients hospitalised to intensive care units (n = 50), co-infections with Enterobacterales (34.0%) and Aspergillus fumigatus (18.0%) were discovered. Blood cultures obtained at admission had a diagnostic yield of 4.2 percent.

Conclusion: While bacterial and fungal co-infections are rare in COVID-19 patients, they are widespread in critically ill individuals. More investigation into the impact of antimicrobial therapy on therapeutic success in COVID-19 patients is essential to prevent antibiotic abuse.COVID-19 management might be improved with the aid of ABS standards. It's also necessary to look at the microbiological patterns of infectious consequences in COVID-19 individuals who are severely unwell.

Keywords COVID-19, Antibiotic stewardship, Bacterialco-infections, Diagnostic stewardship

Introduction

In December 2019, patients in Wuhan, China, were diagnosed with respiratory tract illnesses caused by an unknown microbial pathogen. A novel beta-coronavirusknown as severe acute respiratory syndrome coronavirus2 was eventually identified as the cause (SARS-CoV-2).The ensuing sickness has been dubbed coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) [1, 2]. A pandemic arose from the emergence of SARS-CoV-2, which is more infectious than SARS-CoV. As of May 5, 2020, COVID-19 had been connected to more than 3 million illnesses and 200,000 deaths worldwide. Although the majority of people have a mild or easy illness, a tiny minority of people acquire a serious illness that requires hospitalisation[3]. In extreme cases, complications such as acute respiratory distress syndrome (ARDS), sepsis, and multi-organ failure can occur, necessitating treatment. [4,5]

Clinicians are advised to collect blood cultures (BCs) as well as respiratory samples from the upper respiratorytract for bacterial cultures, and to commence empirical antibiotic therapy only in severe instances, according to WHO guidelines for the clinical management ofCOVID-19 [4].

Although the symptoms, clinical history, and risk factors for disease severity associated with COVID-19 have been studied [6,] there is little information on bacterial or fungal co-infections in COVID-19. In general, respiratory viral

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infections are associated withbacterial co-infections, which worsen illness severity and death. Sepsis and ventilator-associated pneumonia have been identified as a common consequence in COVID-19 patients [7-10]. Antimicrobial coverage was observed in the majority of COVID-19 patients. Bacterial and fungal co-infection rates are typically low in COVID-19 patients, with higher rates in critically sick ICU-patients. Most studies do not describe or detect co-infections in COVID-19 cases. Microbiological diagnosis of co-infection is challenging, and data on microorganisms causing such infections in COVID-19 patients is scarce. In case series published in the literature, gram-negative pathogens and Aspergillus spp. caused bacterial and fungal co-infections in COVID-19 patients. The lack of data on bacterial and fungal cultures could be due to a lack of routine microbiological workup, as health care workers who collect respiratory samples and laboratory technicians who process these samples are at risk of exposure. Notably, the rate of antibiotic usage in COVID-19 patients was much greater than the prevalence of confirmed secondary infections.

A bacterial or fungal co-infection incidence of 8% in COVID-19 patients was estimated based on just a few studies with no defined sampling procedures, but 72 percent of all COVID-19 patients treated with (empiric broad-spectrum) antibiotic treatment.

Antimicrobial overuse raises the likelihood of nosocomial secondary infections, which are linked to poor clinical outcomes. As a result, the use of empiricalantibiotic coverage in COVID-19 patients should becarefully scrutinised.

Antibiotic stewardship (ABS) programmes aim to optimise antimicrobial usage while lowering the risk of antimicrobial resistance, adverse effects, and pharmaceutical costs. National and international recommendations advise hospitals to use local ABS standards to optimise treatment and de-escalation techniques. COVID-19-specific ABS actions have beenrare thus far, despite their enormous potential for good in the future.

The goal of this study was to examine the microbiological results and antibiotic therapy used in our cohort in order to add to our understanding of bacterial co-infections and antibiotic regimens for COVID-19.

Materials and methods

We conducted a retrospective single-center cohort study of 140 hospitalised adult patients (ages 17–99) with confirmed COVID-19 who were admitted betweenFebruary 16, 2021, and April 22, 2021,until May 6, 2021. Medical records were reviewed, including clinicalcharts and nursing records; only the in-hospital patient course was examined; no further outcome data wasprovided. The first emergency department (ED) care provided to patients who were to be admitted to the hospital was also considered part of the in-hospital patient course. Patient demographics, comorbidities, clinical characteristics, laboratory results, microbiological analysis, inpatient care, hospital stay, and outcome, as well as antibiotic regimen, were all collected. The following procedures were used to gather data from laboratory-confirmed COVID-19 individuals:

Two medical students identified important factors, abstracted them, and extracted them from electronic data. An infectious diseases specialist and a clinical microbiologist provided training, as well as monitoring data extraction performance and being available for questions. Inter-rater agreement was not verified, and chart reviewers were not blinded. Due to the retrospective nature of the investigation, missing patient data for laboratory values and antibiotic prescriptions was accepted.

This ABS guideline contains a diagnostic algorithm based on clinical, laboratory, and chest CT results, as well as recommendations for microbiological and virological diagnostics and empirical antibiotic treatment. Only in situations of clinically suspected infection and high inflammatory markers should antibiotic treatment be started, according to the SOP. The doctors have the final say on whether or not to initiate or adjust antimicrobial treatment. Because laboratory COVID-19 test results were only accessible with a delay, initial diagnosis in the emergency room was based on clinical condition and chest CT scans that were instantly available and sent. Biomarkers were readily available in the ED, allowing physicians to tailor antibiotic therapy based on laboratory findings. Laboratory test results are available prior to the start of antibiotic therapy in the standard ED workflow.However, in our retrospective study, we have no way of knowing if laboratory parameters were actually noticed before the antibiotic was administered.

Statistics

The median (range) of continuous data is used to represent categorical data, whereas absolute and relative frequencies are used to describe categorical data. The statistical significance of the link between carbapenem treatment and superinfection detection was established using a two-tailed Fisher's exact test with a significance level of P 0.05. Microsoft Excel 2013 and IBM SPSS Statistics Version 25.0 were used to conduct statistical analyses (IBM Corp, Armonk, NY).

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Results

140 confirmed COVID-19 patients were assessed during the study period. On the last day of the study, 27 patients (19%) remained inpatient (13 in general wards and 14 in ICU), 18 patients (13%) died (6 in general wards and 12 in ICU), and 95 patients (68%) were discharged.

COVID-19 was detected by PCR in 126 patients (90.0%) and by serology in 14 cases. Patients who were given ampicillin/sulbactam had a lower chest CT than those who were not given antibiotics. Initial laboratory findings for CRP and PCT were increased in cases where piperacillin/tazobactam was given. In patients with an initial median PCT of 0.1 ng/dL, only 5.4 percent (3/56) died, indicating that increased PCT on admission is associated with a negative outcome (i.e. death).

In 57 COVID-19 patients, changes in antibiotic medication occurred during hospitalisation; 14 patients were moderate instances, and 43 patients were severe cases. Changes in antimicrobial treatment are shown inSupplementary Table 2. Antimicrobial alterations are computed using these 57 cases as a reference. Antibiotic de-escalation in accordance with ABS principles was not reported in our sample, however medication was terminated in 11 patients within three days of arrival due to critical reassessment. Changes tobroad-spectrum ureidopenicillins and carbapenems with or without glycopeptides/oxazolidinones were characterised as escalation. Additionally, the inclusion of antifungal medication was investigated. Other antimicrobials, such as azithromycin, ceftazidime, ceftriaxone, cefepime, tobramycin, or tigecycline, were added in a few instances. Piperacillin/tazobactam treatment was used for escalation in 17 patients (29.8%), and these instances were more common in intermediate cases (n = 9, 64.3%) than severe cases (n = 8, 18.6%).

In our dataset, escalation to meropenem was observed in 9 (15.8%) COVID-19 patients, with almost equal percentages of more severe and mild instances. Surprisingly, escalation to piperacillin/tazobactam plus vancomycin or linezolid was uncommon (n = 1, 1.8 percent), whereas the majority of escalations to combination-regimens involved meropenem + vancomycin or linezolid (n = 20, 35.1 percent), whichafflicted particularly severe cases (n = 19, 44.2 percent).

Antimycotic medication was only used in the most severe instances; echinocandins were used in 5 (8.8%), voriconazole in 4 (7.0%), fluconazole in 6 (10.5%), andliposomal amphotericin-B was used in 8 (14.0%) COVID-19 patients.

According to local SOP, the majority of patients had a microbiological workup upon admission to the hospital. BCs were taken from 118 patients (84.3%), and BCs were found to be positive in ten of them (7.1 percent). Only 5 instances of true bacteraemia with proven bloodstream infection were found, yielding a 4.2 percent BC diagnostic yield. In 50 percent of all positive BCs, pathogens deemed contaminants were the only source of bacteremia. PCT on admission was significantly greaterin cases of genuine bacteremia than in sterile BCs or contamination, underscoring PCT's diagnostic utility inidentifying bloodstream infections.

Follow-up BCs were collected for 57 COVID-19 patients (40.7%), notably in more severe cases, and relevant pathogens were found in 11 instances (7.9 percent). In our dataset, 114 individuals (81.4%) had scan findingsthat were compatible with COVID-19 symptoms. In sixcases, CT results were unspecific, and in another six cases,a chest CT scan was not conducted.

The complete cohort's patient characteristics, laboratory results, microbiological workup, and antibiotic usage were studied. Furthermore, depending on clinical outcome, the cohort was separated into two subgroups: Only patients admitted to the general ward were included in subgroupone (n = 84: moderate cases). Patients admitted to the ICU and all patients who died during their hospital stay, regardless of whether they died in the ICU or on the generalward (n = 56: severe cases) were included in the secondgrouping. The cohort's median age was 63.5 (17–99) years, and90 (64.3%) of the patients were men. The median age and the number of men were both greater in severe cases. In 75.7 percent of patients, at least one underlyingco-morbidity was present, with arterial hypertensionbeing the most common; a higher frequency was reported in more severe cases. The severity of the condition was linked to the median length of hospital stay. The average length of stay in the ICU was 11 days.Twenty-two patients (15.7 percent) were admitted to theICU immediately, and 41 patients (73.2 percent) required invasive mechanical breathing.

On admission, severe COVID-19 patients had greater C-reactive protein (CRP), leukocyte count, and procalcitonin (PCT) levels than moderate COVID-19 patients. Table 1 shows the demographic and laboratorydata in detail.

To avoid the spread of the disease, all patients were treated in proper isolation units while in the hospital. Antibiotic

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medication information was unavailable for five individuals who were all treated on general wards. The majority of the other 135 patients (n = 109, or 80.7 percent) received antimicrobial therapy within 24 hours of admission (n = 109, or 80.7 percent): antimicrobial medication was started in the ED in 113 patients, and therapy was started on the ICU in 22 patients (in cases of direct admittance to ICU). During their stay in the hospital, only 19 patients (14.1%) were not given any antimicrobial medication. Ampicillin/sulbactam with or without azithromycin (41.5 percent) with a me- dian duration of 6 (1–13) days was the most often used antibiotic regimen, followed by piperacillin/tazobactam with or without azithromycin (19.3 percent) with a median duration of 10 (3–26) days. Ampicillin/sulbactam is used empirically in accordancewith local ABS recommendations.

Surprisingly, laboratory data on admission appear to differ between antibiotic regimens, indicating that elevated inflammatory markers impacted the physician's choice of antimicrobial to begin. Table 2 provides detailed information on beginning empirical antibiotic treatment, including length of medication. Individuals with high CRP or PCT levels were more likely to get (broad-spectrum) antibiotics: CRP on arrival was greater in these patients. For 111 (79.3%) and 107 (76.4%) patients, respectively, urine antigen tests for Legionella pneumophila and Streptococcus pneumoniae were done, and the findings were all negative.

Only a subgroup of patients (17.9%) on arrival had respiratory samples taken for microbiological investigations, all of whom had severe COVID-19 disease. The majority of cultures, on the other hand, remained sterile or revealed the presence of normal oral flora. Only three instances were found to have relevant pathogens, including growth of Escherichia coli (n = 1),Staphylococcus aureus (n = 1), and Klebsiellaoxytoca (n = 1).

Patients hospitalised to the ICU (n = 50) provided themajority of respiratory samples for follow-up microbiological examinations. Only one respiratory sample was taken from a non-ICU patient, and it revealed the presence of Klebsiella aerogenes.Respiratory samples were obtained from 38 (76.0%) ICU patients for follow-up microbiological investigations, and relevant infections were found in 23 (46.0%) instances, with Enterobacterales and Aspergillus fumigatus predominating. Enterobacter cloacae was the pathogen found in the samples.

The patients with superinfection with Enterobacterales did not get carbapenem-based therapy since neither a multidrug-resistant gram- negative pathogen nor a methicillin-resistant Staphylococcus aureus (MRSA) was present, according to the German national classification. Only two patients (22.2 percent) who had not had carbapenem medication had Aspergillus fumigatus in their respiratory samples, presumably demonstrating the negative antibacterial impact of a broad-spectrum antimicrobial in terms of increased sensitivity to fungal colonisation . Because of the small number of patients, the link between carbapenem usage and the identification of Aspergillus fumigatus was not statistically significant (p = 0.427). Also, usage of carbapenems may merely indicate more severe instances with Aspergillus fumigatus as a bystander, thus this data should be read with caution.

Discussion

This descriptive study of COVID-19 patients'microbiological testing results revealed that, while bacteraemia and L. pneumophila or S. pneumoniae infection were uncommon at the time of admission, 46.0 percent of severely ill patients admitted to the ICU developed bacterial and fungal co-infections, particularly due to Enterobacterales and A. fumigatus.

Even if a causal microorganism cannot be identified definitively, empirical antibiotic treatment should be started as soon as possible in patients with clinically suspected bacterial infection or pneumonia, and frequently before the findings of microbiological tests are available. Antimicrobial therapy may help to avoid subsequent infections and minimise the number of complications. Only pathogen identification and susceptibility testing, on the other hand, allow for the de-escalation of empirical antimicrobial therapy and improve our understanding of the bacterial spectrum and antimicrobial resistance, which is a crucial pillar ofABS. Diagnostic stewardship is an essential componentand the foundation for ABS intervention when it is necessary.

Diagnostic stewardship is a critical component of ABS intervention, since the use of microbiological diagnostics leads to a more nuanced diagnosis and, as a result, better patient care. As part of an ABS programme, multidisciplinary methods to diagnostic stewardship involve the creation of local sample collecting guidelines. Diagnostic bundles have been proven to improve sepsis diagnosis, which is critical for effective patient care since mortality is lowered when the proper antibiotic medication is begun immediately based on local resistance knowledge.

It's worth noting that some COVID-19 patients who arrive to the ED at the same time have other illnesses such urinary

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tract infections or skin and soft tissue infections. This must be taken into account while beginning proper diagnoses and empirical treatment. Asa result, antimicrobial therapy requirements in our sample cannot be solely attributable to COVID-19, andmust be considered when assessing antibiotic usage.

There is a scarcity of data on bacterial and/or fungal co-infections, and research differ in their sampling methodologies. Three hundred and ninety-three COVID-19 individuals were found to have a 6% risk of bacteraemia at hospital admission. These findings should be taken with caution since, as in ourinvestigation, there may be a high rate ofcontamination, possibly due to the use of cumbersomepersonal protective equipment. In keeping with our findings, only two occurrences of culture (gram- negative and fungal) development were detected in a study on the microbiological investigation of lung samples from 99 COVID-19 patients [9, 12]. In COVID-19 patients, widespread antimicrobial usage is prevalent, with quinolones being the most often used antimicrobials, followed by carbapenems and cephalosporins. The use of broad-spectrum antimicrobials is even recommended in certain national recommendations.

During the 2003 SARS-CoV-1 epidemic, there was an increase in MRSA rates among ICU patients, which was ascribed to the widespread use of broad-spectrum antimicrobials, particularly cefepime, carbapenems, and fluoroquinolones.

ABS is difficult during COVID-19 because of biosafety concerns for medical and laboratoryprofessionals. To limit the misuse of antibiotics and combat developing resistance and antimicrobial side effects, guidelines should focus on sufficient sampling procedures prior to antibiotic treatment and focused antimicrobial therapy. The concepts of ABS might be quite useful in the treatment of COVID-19 patients. For suspected COVID-19 patients, we implemented local ABS recommendations for diagnostic and treatment measures. In terms of diagnostics, adherence to the guidelines was > 75%, however the extensive usage of macrolide antibiotics identified was not supported by the local ABS guideline. It's possible that this finding is related to the overlap.[7-10]

Because of the small cohort size, the results of this studyshould be regarded with care. However, given the large number of patients involved in the research, we feel thatthis COVID-19 cohort is typical of Germany. To further understand the prevalence, clinical course, and prognosticaspects of bacterial co-infections in COVID-19, larger clinical investigations are needed. Due to the nature of thestudy, only the in-hospital patient course was examined; no further follow-up data was available, and some patientswere still in the hospital and receiving antibiotic therapy atthe time of analysis, so the final clinical result could not bedetermined. Due to safety concerns, breathing sampleswere not collected from all patients due to the retrospectivenature of this investigation. More research on themicrobiological results in COVID-19 patients is required.

Conclusion

To conclude, there is a scarcity of information onbacterial co-infections in COVID-19 patients. We discovered that antimicrobials were being given out at ahigh rate, but that the number of confirmed bacterial infections was low in this research. Patients with severe COVID-19 who were admitted to the ICU had a greater risk of lung enterobacterial and Aspergillus infections than those who had less severe forms of the illness. The impact of ABS measures and antibiotic usage in COVID-19 should be carefully examined in future investigations, especially given the low verified prevalence of bacterial infection.

Table 1: shows the demographic and laboratory data in detail.

Mean age Male sex Comorbidities	**63.5(17–99)** **90(64.3%)**	**68.5(26–99)** **40(71.4%)**	**63(17–95)** **50(59.5%)**
Presence of any comorbidity as	106 (75.7%)	43 (76.8%)	**63 (75.0%)**
listed below*			
- Obesity	23 (16.4%)	12 (21.4%)	**11 (13.1%)**
- Arterial hypertension	68 (48.6%)	30 (53.6%)	**38 (45.2%)**
- Diabetes	30 (21.4%)	16 (28.6%)	**14 (16.7%)**
- Coronary heart disease	26 (18.6%)	12 (21.4%)	**14 (16.7%)**

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- Congestive heart failure	12 (8.6%)	5 (8.9%)	**7 (8.3%)**
- COPD	7 (5.0%)	6 (10.7%)	**1 (1.2%)**
- Bronchial asthma	15 (10.7%)	2 (3.6%)	**13 (15.5%)**
- Chronic kidney disease	16 (11.4%)	10 (17.9%)	**6 (7.1%)**
- Cancer	29 (20.7%)	15 (26.8%)	**14 (16.7%)**
- HIV	5 (3.6%)	1 (1.8%)	**4 (4.8%)**
- Any medical	15 (10.7%)	7 (12.5%)	**8 (9.5%)**
immunosuppression			
- Chronic liver disease	7 (5.0%)	4 (7.1%)	**3 (3.6%)**
Duration of hospital stay (days)	12 (1–47)	19 (1–47)	**10 (1–46)**
Duration of ICU stay (days)		11 (1–38)	
Interval from hospital admission to ICU admission (days)		1.0 (0–23)	
Laboratory findings on admission			
- CRP (mg/dL)	6.1 (0.1–35)	9.9 (0.3–35.0)	**4.7 (0.1–26.6)**
- Leukocyte (G/L)	6.4 (1.4–26.3)	7.2 (1.6–22.4)	**6.1 (1.4–26.3)**
- PCT (ng/mL)	0.1 (0.1–18.7)	0.3 (0.1–18.7)	**0.1 (0.1–5.9)**
Laboratory findings on day of highest CRP value			
- CRP (mg/dL)	14.8 (0.1–50.6)	27.6 (1.5–50.6)	**8.8 (0.1–33.5)**
- Leukocyte (G/L)	10.2 (1.8–56.6)	16.1 (5.9–56.6)	**7.8 (1.8–37.4)**
- PCT (ng/mL)	**0.2 (0.1–175.5)**	**1.8 (0.1–175.5)**	**0.1 (0.1–138.4)**

Moxifloxacin	**4 (3.0%)**	**2 (3.6%)**	**2 (2.5%)**	**Leukocytecount8.2(6.3–11.1)G/L**
Duration of therapy (days)	4 (2–8)	5 (2–8)	4 (3–5)	**CRP 9.0 (6.1–18.1) mg/dL**

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				PCT 0.1 (0.1–0.2) ng/mL
Azithromycin	2 (1.5%)	0	2 (2.5%)	**Leukocytecount2.6(1.4–3.7)G/L**
Duration of therapy (days)	3	-	3	**CRP 2.9 (1.2–4.5) mg/dL**
				PCT 0.1 (0.1–0.1) ng/mL
Cephalosporin (cefuroxime,	3 (2.2%)	2 (3.6%)	1 (1.3%)	**Leukocytecount7.9(7.5–8.8.)G/L**
ceftazidime, ceftriaxone)				**CRP 8.2 (5.2–35) mg/dL**
Duration of therapy (days)	7 (3–20)	13.5 (7–20)	3	**PCT 0.2 (0.2–0.3 ng/mL**
Initial combination therapy of	7 (5.2%)	6 (10.7%)	1 (1.3%)	**Leukocytecount8.8(6.8–14.9)G/L**
beta-lactam antibiotic				**CRP 18.2 (0.8–35.0) mg/dL**
(+/− azithromycin) with				**PCT 0.3 (0.1–4.9) ng/mL**
vancomycin or linezolid				
Duration of therapy (days)	**14 (4– 25)]**	**10.5 (4– 25)]**	**18**	

Table 2: Most commonly used initial empirical antibiotic therapy

Ampicillin/sulbactam	**41 (30.4%)**	**8 (14.3%)**	**33 (41.8%)**
Duration of therapy (days)	7 (1–13)	6 (3–9)	**7 (1–13)**
Ampicillin/sulbactam + azithromycin*	15 (11.1%)	9 (16.1%)	**6 (7.6%)**
Duration of therapy	4 (1–10)	6 (4–10)	**4 (1–7)**
Piperacillin/tazobactam	10 (7.4%)	5 (8.9%)	**5 (6.3%)**
Duration of therapy (days)	9 (5–20)	9 (6–20)	**8 (5–15)**
Piperacillin/tazobactam +	16 (11.9%)	10 (17.9%)	**6 (7.6%)**
azithromycin*			
Duration of therapy (days)	10 (3–26)	11.5 (3–26)	**10 (7–17)**
Meropenem	1 (0.7%)	1 (1.8%)	**0**
Duration of therapy (days)	10	10	
Meropenem + azithromycin*	5 (3.7%)	2 (3.6%)	**3 (3.8%)**
Duration of therapy (days)	**10 (5–25)**	**18.5 (12–25)**	**7.5 (5–10)**

Table 3 Results of microbiologic diagnostics on admission and further relevant microbiological findings during hospitalisation

	FullCOVID-19cohort(*n*=140)	**Severe COVID-19 patients (*n* = 56)**	**Moderate COVID-19 patients (*n* =84)**
BC collected	118 (84.31%)	52 (92.91%)	**66 (78.61%)**
BC positive	10 (7.1)	5 (8.9%)	**5 (6.0%)**
Contamination only	5 (3.64%)	1 (1.81%)	**4 (4.8%)**
BC pathogen in confirmed, true bacteraemia		*E. coli* (*n* = 1), *S. aureus* (*n* = 1), *S. epidermidis* (*n* = 2)	***E. coli* (*n* = 1)**
PCT on admission in true bacteraemia	5.3 (0.8–18.78)	5.55 (0.8–18.51)	**5.9**

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PCT on admission in sterile	0.1 (0.1–15.12)	0.2 (0.1–15.12)	**0.1 (0.1–4.5)**
BC or contamination only			
Follow-up BC diagnostic	57 (40.7%)	45 (80.4%)	**12 (14.3%)**
Cases with positive follow-up BC	11 (7.9%)	10 (17.9%)	**1 (1.2%)**
Pathogens in positive follow-up BC		***K. oxytoca*(*n* = 1), *K. pneumoniae* (*n* = 1), *P. aeruginosa* (*n* = 1), *S. epidermidis***	***S. aureus* (*n* = 1)**

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