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Increase in the frequency of catheter-related bloodstream infections during the COVID-19 pandemic: a plea for control

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SUMMARY

Background: The incidence of nosocomial infections including ventilator-associated pneumonia and bacteraemia has been described during the COVID-19 pandemic. However, information regarding the impact of COVID-19 on the incidence of catheter-related bloodstream infections (CR-BSIs) is very limited.

Aim: To evaluate the impact of the COVID-19 pandemic in the evolution of CR-BSIs in a large hospital.

Methods: This was a retrospective study comparing the incidence, aetiology and outcome of CR-BSIs during the months of March to May 2019 (pre-pandemic) and 2020 (during the pandemic).

Findings: The number of patients with one or more CR-BSIs in 2019 and 2020 were 23 and 58, respectively (1.89 vs 5.53/1000 admissions); $P < 0.001$. Median time from catheter implantation to demonstration of CR-BSI was 27.5 days (range 11.75–126.00 days) in the 2019 cases and 16.0 days (range 11.00–23.50 days) in the 2020 population ($P = 0.032$).

Conclusions: A dramatic increase of CR-BSIs was found during the COVID-19 pandemic. Reinforcement of classic and new preventive measures is necessary.

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Introduction

Catheter-related infection is one of the leading causes of bacteraemia and sepsis in developed countries and its

adequate control by multi-disciplinary teams represents one of the best-quality indicators of an institution. The incidence can range from 0.8 to 18 episodes/1000 days of catheter exposure, depending on the type of patient, the type of catheter and the care provided during implantation and follow-up [1–5].

The COVID-19 pandemic has led to a huge increase in the workload of hospitals around the world and many patients have required long hospital stays including extended admissions to intensive care units (ICUs) [6–8].

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Care for these patients has been provided under strenuous circumstances, not only because of the increased workload but also because sometimes there was a need to implicate staff with a sub-optimal degree of training with ICU patients [9–11].

Under these conditions, it is not surprising that an increased incidence of nosocomially acquired infections, including ventilator-associated pneumonia and bacteraemia, has been described in some centres [12–14]. Surprisingly, information regarding the impact of COVID-19 on the incidence of catheter-related bloodstream infections (CR-BSIs) is thus far limited.

Our aim was to evaluate the impact of the COVID-19 pandemic in the evolution of CR-BSIs in a large hospital, including incidence, aetiology and outcome.

Material and methods

Setting

Our institution is a general reference hospital, located in Madrid, Spain, with 1350 beds and approximately 55,000 admissions/year. The number of ICU beds is normally 70, but was expanded to 140 during the study period.

Study design

We performed a retrospective study in which we compared the incidence, aetiology, and outcome of CR-BSIs during the months of March to May in 2019 and 2020 (before and during the COVID-19 pandemic).

Ethics approval and consent to participate

The Ethics of Hospital General Universitario Gregorio Marañón approved the study. The need for informed consent for this study was waived by Ethics Committee MICRO.HGUGM.2020-030 of Hospital General Universitario Gregorio Marañón. All procedures were carried out in accordance with relevant guidelines and regulations.

Endpoints

The primary endpoint was the incidence of CR-BSI episodes before and during the pandemic. The secondary endpoints were the aetiology and consequences of CR-BSI during the first wave of the pandemic.

Definitions

CR-BSI

Presence of bacteraemia or fungaemia in a patient with clinical manifestations of infection and no other apparent source of bloodstream infection (with the exception of the catheter). A catheter-tip culture, quantitative or semi-quantitative, positive for the same micro-organism was also required [5,15].

Non-CR-BSI

In the present study, episodes of bacteraemia with a non-documented catheter origin.

Attributable mortality

In the present study, death occurring within 7 days after confirmation of CR-BSI in the absence of an alternative evident cause was considered as attributable.

Statistical analysis

Qualitative variables are expressed as a frequency distribution. Quantitative variables are expressed as the mean and standard deviation (SD) and as the median and interquartile range (IQR) if their distribution was skewed. Normally distributed continuous variables were compared using the *t*-test; non-normally distributed continuous variables were compared using the Mann–Whitney test. The chi-squared or Fisher exact test was used to compare categorical variables. Statistical significance was set at $P \leq 0.05$.

We compared the incidence rate of catheter-related bacteraemia per 1000 admissions between the two periods using Epidat version 3.1.

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp, Armonk, NY, USA) and Epidat 3.1.

Results

Hospital admissions during the study periods (1st March to 31st May 2019 and 2020) were, respectively, 12,111 and 10,479 patients. Similarly, the number of blood cultures processed by the microbiology department was, respectively, 9520 (786.06/1000 admissions) and 8802 (839.96/1000 admissions) ($P < 0.001$), and the number of episodes of significant bloodstream infections was 358 (29.55/1000 admissions) and 379 (36.16/1000 admissions) in each three-month period in 2019 and 2020, respectively ($P = 0.007$). The rate of contaminated blood cultures was 2.8% and 3.8% ($P < 0.001$), before and during the pandemic.

The number of withdrawn catheters processed for culture in our laboratory was 302 (24.93/1,000 admissions) in 2019 and 617 (58.87/1000 admissions) in 2020 ($P < 0.001$), and the number of positive catheter tips was 59 (4.87/1,000 admissions) and 161 (15.36/1,000 admissions) ($P = 0.066$), respectively, in 2019 and 2020 study periods.

The number of patients with one or more CR-BSIs increased significantly in 2020 (Figure 1) (23 and 58 (1.89 vs 5.53/1000 admissions); $P < 0.001$). The number of CR-BSI episodes in the study periods 2019 and 2020 was, respectively, 24 and 65 (1.98 vs 6.20/1000 admissions) ($P < 0.001$). The proportion of CR-BSIs from all significant episodes of bloodstream infections was 6.7% in 2019 and 17.1% in 2020 ($P < 0.001$).

The underlying conditions and characteristics of both populations are compared in Table 1. A high proportion of the cases of CR-BSI in 2020 occurred in COVID-19 patients (77.58%), and the vast majority of episodes occurred during their ICU stay (91.37%). The median ICU stay in patients with CR-BSIs was much longer in 2020 than in 2019 (35.0 (17.0–59.7)) vs 17.0 (0.0–52.0); $P = 0.042$).

In 2019, 10 patients developed nosocomial infection (five of them had two or more infections): six urinary tract infections, eight respiratory infections, one surgical wound infection and one cytomegalovirus disease. Of these 10 patients, nine (90%) were in the ICU. In 2020, 47 patients developed nosocomial

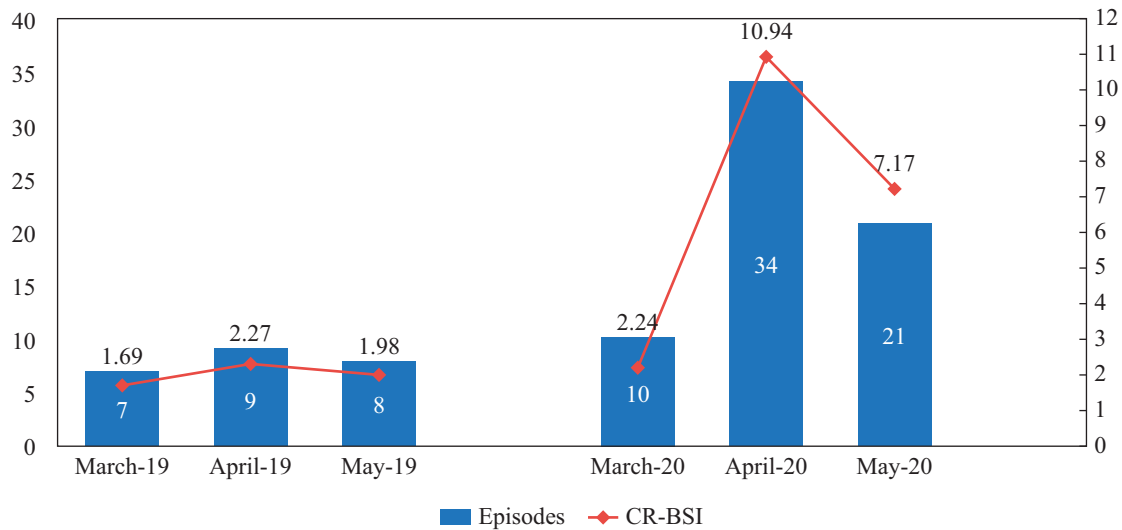


Figure 1. Incidence rate of catheter-related bloodstream infections (CR-BSIs)/1000 admissions during the study periods.

infection (22 had two or more infections): 15 urinary tract infection, 23 respiratory infections, one surgical wound infection, 13 cytomegalovirus disease, one *Clostridioides difficile* infection and six bloodstream infections. Forty-six patients (97.8%) were in the ICU.

The characteristics of the catheters in both populations are summarized in Table II. A large proportion of catheters in the 2020 patients were non-tunneled central lines (64.6%), and, of these, 78.6% were inserted into the jugular vein partially due to the prone position.

Median time from insertion to demonstration of CR-BSIs was 27.5 days (range, 11.75 to 126.00 days) in the 2019 cases and 16.0 days (range, 11.00–23.50 days) in 2020 ($P=0.032$).

The comparative aetiologies of the CR-BSI episodes in 2019 and 2020 are shown in Figure 2. We were unable to detect significant differences in the proportion of causative microorganisms of CR-BSIs between the 2019 cases and the 2020 cases.

The attributable mortality of CR-BSIs, in 2019 and 2020 was 28.6% and 40.0%, respectively ($P=0.465$).

Table I

Comparison of patients with catheter-related bloodstream infections (CR-BSIs) in 2019 and 2020

Patients	Total N = 81	2019 N = 23	2020 N = 58	P
Median age in years, adults (IQR)	65.0 (57.50–70.50)	69.00 (58.00–73.00)	64.50 (56.00–68.25)	0.168
Median age in years, children (IQR)	0.0 (0.0–27.50)	0.0 (0.0–99.00)	0.5 (0.0–27.50)	0.629
ICU (%)	68 (83.95)	15 (65.21)	53 (91.37)	0.007
Sex (%)				0.010
Male	60 (74.07)	12 (52.17)	48 (82.75)	
Female	21 (25.92)	11 (47.82)	10 (17.24)	
Underlying conditions (%)				
COVID-19	45 (55.55)	0 (0.0)	45 (77.58)	<0.001
Myocardial infarction	2 (2.46)	0 (0.0)	2 (3.44)	1.000
Congestive heart failure	1 (1.23)	0 (0.0)	1 (1.72)	1.000
Central nervous system disease	3 (3.70)	2 (8.69)	1 (1.72)	0.193
Chronic obstructive pulmonary disease	12 (14.81)	1 (4.34)	11 (18.96)	0.164
Renal dysfunction	7 (8.64)	2 (8.69)	5 (8.62)	1.000
Diabetes mellitus	18 (22.22)	5 (21.73)	13 (22.41)	1.000
Peptic ulcer disease	10 (12.34)	6 (26.08)	4 (6.89)	0.027
Peripheral vascular disease	2 (2.46)	1 (4.34)	1 (1.72)	0.490
Tumour	16 (19.75)	11 (47.82)	5 (8.62)	0.001
Median length of hospital stay in days (IQR)	47.00 (29.00–83.50)	35.00 (19.00–83.00)	53.00 (34.75–91.75)	0.059
Median length of ICU stay in days (IQR)	36.50 (21.25–65.75)	17.00 (0.00–52.00)	35.00 (17.00–59.70)	0.042
Other infections (%)	57 (70.37)	10 (43.47)	47 (81.03)	0.002
Mortality (%)	32 (39.50)	7 (30.43)	25 (43.10)	0.325
Mortality attributable to CR-BSI (N = 32) (%)	12 (37.5)	2 (28.57)	10 (40.00)	0.465

ICU, intensive care medicine; IQR, interquartile range.

Table II
Characteristics of the catheters

Catheters	Total N = 89	2019 N = 24	2020 N = 65	P
Type of catheter, adults, N (%)				
Non-tunneled central venous	49 (55.05)	7 (29.16)	42 (64.61)	0.004
Tunneled central venous	12 (13.48)	8 (33.33)	4 (6.15)	0.204
Peripheral venous catheter	3 (3.37)	0 (0.0)	3 (4.61)	1.000
Peripherally inserted central catheter	15 (16.85)	1 (4.16)	14 (21.53)	0.277
Arterial	10 (11.23)	8 (33.33)	2 (3.07)	1.000
Location of non-tunneled central venous, N=49 (%)				
Jugular	35 (71.42)	2 (28.57)	33 (78.57)	0.015
Subclavian	8 (16.32)	4 (57.14)	4 (9.52)	0.009
Femoral	6 (12.24)	1 (14.28)	5 (11.90)	1.00
Catheter days, median (IQR)	17.00 (11.00–28.50)	27.50 (11.75–126.00)	16.00 (11.00–23.50)	0.032
Catheter days, total	5222	3637	1585	NA

IQR, interquartile range.

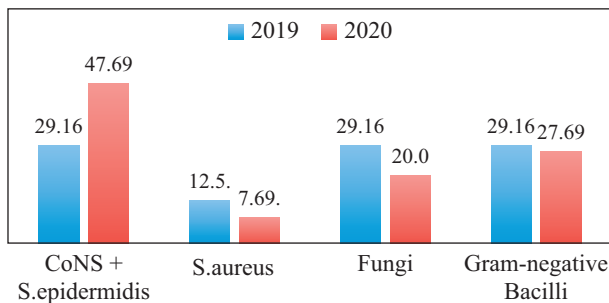


Figure 2. Aetiology of episodes of catheter-related bloodstream infection (CR-BSI). Percentages of micro-organisms causing CR-BSI in 2019 and 2020.

Discussion

Our results demonstrate the substantial quantitative and qualitative impact of the COVID-19 pandemic in CR-BSI. The incidence of CR-BSI increased at least three-fold during the first 3 months of the COVID-19 pandemic in our institution.

The damage caused by the COVID-19 pandemic in different aspects of healthcare and infection control has been devastating, although not yet sufficiently analysed [16–20]. At the beginning of the pandemic, it was already anticipated that patients with severe COVID-19 would develop superinfections, most commonly pneumonia due to nosocomial bacteria and invasive aspergillosis [21,22]. This was confirmed, and, nosocomial secondary infections have been estimated to have occurred in between 7% and 14.3% of hospitalized COVID-19 patients (95% confidence interval, 9.6–18.9%) [23,24]; these infections are more frequent in ICU patients [25,26].

Most common secondary infections in this population are nosocomial pneumonia, mainly associated with mechanical ventilation [27], and bloodstream infections. The most frequent micro-organisms, as expected, were *Staphylococcus aureus*, *Enterococcus* spp., *Escherichia coli*, and *Pseudomonas aeruginosa* [24]. The infections frequently involved multi-drug-resistant micro-organisms [25–29]. Surprisingly, and despite overuse of antibiotics during the pandemic, preliminary data suggest that the incidence of *C. difficile* infection decreased in COVID-19 cases [30–33].

Fungal superinfections are also a considerable problem [33,34] and include invasive candidiasis and candidaemia [35], coronavirus-associated pulmonary aspergillosis [36–39], and even *Saccharomyces fungaemia* [40].

Interestingly, data on episodes of bacteraemia were contradictory in the initial reports of the pandemic period and usually do not specify the policy of blood cultures drawing in different institutions [41,42]. However, it seems clear that prolonged hospital stay, in ICUs, has led most authors to report an increase in episodes of bacteraemia [43].

Our series includes 81 patients with proven CR-BSIs and compared a similar time period in 2019 and 2020; we found that the frequency of CR-BSIs increased three-fold during the COVID-19 period. Very recently, Le Rose *et al.* [30] reported an increase in the incidence of vascular catheter-related infections during the pandemic. The authors analysed a series of bloodstream infections, with no clear portal of entry, that they related with central-line-associated bloodstream infection (CLABSI). Of the 36 patients who developed CLABSI, six (17%) were in a pre-COVID-19 cohort, while 30 (83%) were in the COVID-19 cohort. The average monthly CLABSI rate increased from 0.40 to 1.7 during COVID-19 ($P < 0.01$). Data from an Italian institution showed that 30% of all BSI episodes during the COVID-19 pandemic originated in endovascular catheters [44]. In our study, this proportion is lower because we included only microbiologically confirmed episodes (CR-BSIs).

In our study 93.7% of the patients with CR-BSI during the pandemic period were in the ICU, in addition these patients received high doses of steroids and most of them were in the prone position, all risk factors for developing more nosocomial infections as described in other studies [43,44]. The use of the prone position to improve ventilation is used in many ICUs, and poses difficulties for both insertion and care of endovascular catheters and has been related to higher risk of CVC infectious complications [45,46].

Patients who developed CLABSI in the pre-COVID-19 cohort had a median length of stay of 19 days compared with patients in the COVID-19 cohort, who had a median length of stay of 27 days ($P = 0.12$) [30]. However, in our study, despite a longer ICU stay, episodes of CR-BSI occurred earlier after catheter insertion than in 2019. If we combine these findings with an increased rate of contaminated blood cultures and a higher

proportion of CR-BSI caused by coagulase-negative staphylococci, we can conclude that catheter insertion and care worsened.

Other risk factors reported in the literature include the use of corticosteroids and tocilizumab, although we have little insight into the role that other risk factors may have in these patients [44].

In our study, the micro-organisms causing CR-BSI were mainly Gram-positive. Other authors, analysing the aetiologies of CLABSI in a COVID-19 cohort, reported that 53.3% were caused by Gram-positive bacteria, followed by 26.7% fungal and 20% Gram-negative bacteria [30].

The main limitation of our study is that it was performed in a single hospital and further studies with multi-centre data would be welcome. While our study reflects findings from a single hospital, we believe that it appropriately quantifies a problem that may well have affected many centres throughout the world.

We hope that our findings will contribute to urge health professionals to immediately reinforce nosocomial infection control measures. These figures should and can be lowered [5,47].

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Author contributions

E.B. and M.J.P.G. participated in the conception and design of the study, carried out the analysis, interpreted the data and drafted the manuscript. C.S., P.M.R., M.V., M.O. and PM collected the samples and data and participated in drafting the manuscript. All of the authors read and approved the final version of the manuscript.

Conflict of interest statement

The authors declare no conflicts of interest.

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