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LETTER

Increased risk of central line-associated bloodstream infection in COVID-19 patients associated with dexamethasone but not with interleukin antagonists

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Dear Editor,

As a result of routine surveillance in our intensive care unit (ICU), we have noticed an increase over time in the incidence of central line-associated bloodstream infection (CLABSI) in patients with coronavirus disease 2019 (COVID-19). As dexamethasone and interleukin antagonists were later introduced as routine treatment of COVID-19, we performed a retrospective cohort study to explore whether these might be possible risk factors. All patients COVID-19 or non-COVID-19, admitted between January 1st, 2019 and January 1st, 2022 who were treated in our ICU and had at least one central venous line ≥ 48 h, were included. CLABSI was defined according to Centers for Disease Control and Prevention (CDC) guidelines as clinical signs of a central line infection with positive blood culture and positive culture of the catheter tip with more than 15 colony-forming units (CFUs) with the same microorganism in the absence of an alternative diagnosis [1]. Dexamethasone dose was 6 mg daily for 10 days or less if discharged earlier. Patients on long-term steroid treatment were not excluded. Interleukin antagonists (tocilizumab 400 mg or sarilumab 400 mg or anakinra 300 mg) were given within 24 h of admission. Central lines were always inserted using full sterile technique. The need for ethical approval or informed consent was waived.

672 patients were included in this study; 226 had COVID-19. The non-COVID-19 patients had higher Acute Physiology and Chronic Health Evaluation (APACHE) IV scores as compared to COVID-19 patients; hospital mortality was similar (27% vs 30%) (Table 1). The incidence of CLABSI was 1.99/1000 line days in non-COVID-19 patients compared to 6.25/1000 line days in COVID-19 patients. In COVID-19 patients, the incidence of CLABSI was 7.65/1000 line days in patients treated with dexamethasone versus 2.07/1000 without dexamethasone treatment; the latter being comparable to non-COVID-19 patients. At patient level, 4% of COVID-19 patients not treated with dexamethasone developed CLABSI compared to 2% in non-COVID-19 patients. This is most likely attributable to a longer period of ICU stay and central line use in COVID-19 patients. The risk of CLABSI was 13% in the dexamethasone-treated COVID-19 patients. We finally compared COVID-19 patients who only received dexamethasone to patients who received dexamethasone plus an interleukin antagonist with a CLABSI incidence of 7.47/1000 and 7.75/1000 line days and cumulative CLABSI incidence of 13% versus 12% per patient, respectively. Multivariate analysis confirmed dexamethasone treatment and COVID-19 as independent risk factors for CLABSI (Supplementary Table 2).

It is generally accepted that the incidence of nosocomial infections is higher in patients with COVID-19 [2, 3]. Adding interleukin antagonists which have become the mainstay of the treatment of COVID-19

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Table 1 Patient characteristics and results on central line-associated bloodstream infection (CLABSI) in 672 ICU patients with and without COVID-19

	A Non-COVID-19	B COVID-19	p value A vs B	C COVID-19 No dexamethasone	D COVID-19 With dexamethasone	p value C vs D	E COVID-19 Dexamethasone only	F COVID-19 Dexamethasone with interleukin antagonist	p value E vs F
Number of patients	446	226		51	175		60	115	
Male (%)	298 (66.8%)	157 (69.5%)	0.541[1]	36 (71%)	121 (69%)	1.000[1]	50 (83%)	71 (62%)	0.003[1]
Mean age (SD)	63 (13.6)	60.1 (11.1)	0.003[2]	61.9 (10.1)	59.6 (11.3)	0.196[2]	60.9 (10.4)	58.9 (11.77)	0.267[2]
Mean APACHE IV score (SD)	85.8 (28.8)	63.5 (17.9)	< 0.001[2]	63.5 (17.5)	63.6 (18.1)	0.994[2]	62.9 (16)	63.9 (19.3)	0.759[2]
Standardized mortality ratio (4)	0.7	1.02		1.03	1.02		1.13	0.96	
Median ICU length-of stay (days, IQR)	4.5 (3–9)	12 (6–24)	< 0.001[3]	16 (6–26)	11 (6–22)	0.435[3]	11 (6–25)	11 (6–22)	0.974[3]
Median hospital length-of-stay (days, IQR)	16 (9–29)	21 (11–35)	0.001[3]	23 (11–38)	21 (12–33)	0.524[3]	18.5 (11–32)	22 (13–34)	0.465[3]
ICU mortality	88 (20%)	62 (27%)	0.031[1]	14 (28%)	48 (27%)	1.000[1]	21 (35%)	27 (24%)	0.112[1]
Hospital mortality	122 (27%)	68 (30%)	0.415[1]	14 (28%)	54 (31%)	0.729[1]	24 (40%)	30 (27%)	0.085[1]
Number of central lines	701	480		101	379		148	231	
Femoral/ Jugular/ Subclavian/ PICC/Other	79/581/5/33/3	83/389/2/6/0	< 0.001[5]	19/81/0/1/0	64/308/2/5/0	0.853[5]	33/114/1/0/0	31/194/1/5/0	0.045[5]
Central line days	4009	3841		964	2877		1071	1806	
Median number of lines/ patient (IQR)	1 (1–2)	1 (1–3)	< 0.001[3]	2 (1–2)	1 (1–3)	0.832[3]	2 (1–3)	1 (1–2)	0.139[3]
Median number of line days per patient (IQR)	5 (3–9)	11.5 (6–24)	< 0.001[3]	14 (6–30)	11 (6–22)	0.177[3]	11 (4–25)	10 (6–20)	0.876[3]
Median insertion time/line (days, IQR)	4 (3–7)	7 (4–10)	< 0.001[3]	9 (5–13)	7 (4–10)	< 0.001[3]	6 (4–9)	7 (4–10)	0.468[3]
Number of CLABSI (% of patients with CLABSI)	8 (2%)	24 (11%)	< 0.001[1]	2 (4%)	22 (13%)	0.118[1]	8 (13%)	14 (12%)	0.814[1]
CLABSI/100 lines (95% CI)	1.14 (0.35–1.93)	5 (3.05–6.95)	< 0.0001[1]	1.98 (0–4.70)	5.8 (3.45–8.16)	0.195[1]	5.41 (1.76–9.05)	6.06 (2.98–9.14)	1.000[1]

Table 1 (continued)

	A Non-COVID-19	B COVID-19	p value A vs B	C COVID-19 No dexamethasone	D COVID-19 With dexamethasone	p value C vs D	E COVID-19 Dexamethasone only	F COVID-19 Dexamethasone with interleukin antagonist	p value E vs F
CLABSI/1000 line days (95% CI)	1.99 (0.61–3.38)	6.25 (3.76–8.74)	0.0039[1]	2.07 (0–4.95)	7.65 (4.46–10.83)	0.06[1]	7.47 (2.31–12.63)	7.75 (3.71–11.80)	1.000[1]
CNS / enterococci / both	5/3/0	15/6/3	0.513[5]	2/0/0	13/6/3	0.52[5]	7/1/0	6/5/3	0.109[5]
Femoral/Jugular/Subclavian/PICC/Other	0/8/0/0/0	2/22/0/0/0	0.399[5]	0/2/0/0/0/	2/20/0/0/0	0.656[5]	1/7/0/0/0	1/13/0/0/0	0.674[5]
Median days until CLABSI (IQR)	7.5 (7–9)	8.5 (6–11)	0.564[3]	13.5 (10–17)	7.5 (6–11)	0.116[3]	9 (7–13)	7 (5–10)	0.165[3]

Patients with COVID-19 were further analyzed with regard to treatment with dexamethasone or not and with regard to treatment with interleukin antagonists (tocilizumab, sarilumab, or anakinra). The table illustrates that CLABSI incidence increases when dexamethasone is added with or without interleukin antagonists. Results are presented as mean (standard deviation) or median (interquartile range) as appropriate

APACHE IV, acute physiology and chronic health evaluation IV; CI, confidence interval; CLABSI, central line-associated bloodstream infection; CNS, coagulase negative staphylococci; COVID-19, coronavirus disease 2019; ICU, intensive care unit; IQR, interquartile range; PICC, peripherally inserted central catheter; SD, standard deviation

[1] Fisher's exact test

[2] Student's *t* test

[3] Mann–Whitney *U* test

[4] Standardized mortality ratio = observed mortality/expected mortality according to the APACHE IV model. APACHE IV scores and SMR are not valid for patients admitted from other hospitals or discharged to other hospitals, these patients were excluded for this calculation

[5] Chi-square test

have further raised these concerns [4, 5]. In this study, we found that COVID-19 patients not treated with dexamethasone had a similar incidence of CLABSI compared to non-COVID-19 patients. We found that the risk of CLABSI was significantly increased among COVID-19 patients treated with dexamethasone with or without interleukin antagonists. Our results should be interpreted with caution as this is a small retrospective study, and we were unable to adjust for all potential confounders, like antibiotic use or ventilator-associated pneumonia among others. Nevertheless, we would like to suggest an exploration of the relationship between immunosuppressive drugs and risk of CLABSI in COVID-19 patients in future studies. Possibly, a post hoc analysis could be performed of the randomized controlled trials done with dexamethasone and interleukin antagonists for treatment of COVID-19 patients at ICU.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1007/s00134-022-06750-w.

Abbreviations

APACHE: Acute physiology and chronic health evaluation; CFUs: Colony forming units; CLABSI: Central line-associated bloodstream infection; CNS: Coagulase negative staphylococci; COVID-19: Corona Virus Disease (caused by SARS-CoV-2 virus); SD: Standard deviation; ICU: Intensive care unit; IQR: Interquartile range; PICC: Peripherally inserted central catheter; 95% CI: 95% Confidence interval.

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Author contributions

IAM conceived the study, performed the statistical analyses, and wrote the first draft. SR, NB, and IAM did the routine CLABSI surveillance. TO and CN assisted in the analysis and writing of the manuscript. All authors read and approved the final version of the manuscript.

Declarations

Conflicts of interest

None.

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