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Major Article

Increase of blood culture contamination during COVID-19 pandemic. A retrospective descriptive study

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Key Words:
COVID-19
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Intensive Care Unit,
Personal Protective Equipment (PPE).

Background: Secondary bacterial infection during the care of coronavirus disease 2019 (COVID-19) patients poses risks to the patients, but there are concerns of an increase in blood culture contamination.
Methods: A retrospective comparative study was conducted from April 1 to December 31, 2020, when the patients with COVID-19 were taken care of (pandemic period, PP), and it was compared with the same period in 2019 (pre-pandemic period, pre-PP).
Results: A total of 346 patients with COVID-19 were hospitalized during the study period in 2020. A total of 1,040 and 918 blood cultures were taken during PPP and PP respectively. 38 and 56 contaminations occurred during pre-PP and PP respectively (3.7% [95% CI 2.6%-5.0%], vs 6.1% [95% CI 4.6%-7.8%], $P = .015$). For the ICU, 10 and 32 contaminations occurred during the same periods (5.0% [95% CI 2.4%-9.0%], vs 12.5% [95% CI 8.7%-17.1%], $P = .0097$). True bacteremia in the ICU per patient-day also increased during the PP.
Conclusions: We found a significant increase in blood culture contamination during the COVID-19 pandemic in the ICU setting, while true bacteremia also increased. A safe and effective way to obtain blood cultures from patients with COVID-19 should be sought.
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Bacterial co-infections, including bloodstream infections, among patients presenting with coronavirus disease 2019 (COVID-19) are reported to be rare,[1-3] and empirical antibiotic treatment upon diagnosis and hospitalization is usually not warranted. On the contrary, however, secondary bacterial infections during hospitalization among patients with COVID-19 are common, especially in patients admitted to the intensive care unit.[4,5] Patients with severe COVID-19 often require mechanical ventilation and multiple catheter insertions including those for extracorporeal membrane oxygenation (ECMO). The length of hospital stay in severe COVID-19 patients tends to be longer than for other acute infectious diseases such as influenza, making the risk of nosocomial infections much higher.[6] Yu et al reported a relatively high contamination rate of 8.4% in blood cultures taken from patients with COVID-19 in Stockholm, Sweden, but the characteristics of the practice of blood culture testing differ among different clinical settings.[3]

Therefore, we conducted a retrospective cohort study to investigate the incidence of blood culture contamination during the period COVID-19 patients were taken care of at our center.

METHODS

This is a retrospective comparative study to investigate the blood culture contamination rate after COVID-19 pandemic at Hyogo Prefectural Kakogawa Medical Center, Hyogo, Japan. Kakogawa Medical Center is a prefectural tertiary medical center and was designated as a medical facility to hospitalize COVID-19 patients since the beginning of the epidemic in 2020. It does not take care of children and only adult patients were included in our analysis. A period from April 1, 2019 to December 31, 2019, was set as the pre-pandemic period (pre-PP) when the center did not admit any single COVID-19 patient. Another period from April 1, 2020, to December 31, 2020, was set as the pandemic period (PP) when the center hospitalized COVID-19 patients while taking care of patients with other diseases too. Certain hospital beds, including intensive care unit (ICU) beds, were used for the care of patients with COVID-19 but the number of assignments changed in accordance with the size of the epidemic. Healthcare personnel was required to wear full personal protective equipment

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Table 1
The characteristics of blood cultures both in the ICU and non-ICU settings

	ICU			Non-ICU			Total		
	Pre-PP (%)	PP (%)	*P* value	Pre-PP (%)	PP (%)	*P* value	Pre-PP (%)	PP (%)	*P* value
The number of admitted patients	503	186		6,624	3,996		7,127	4,182	
Total patient-days	5,894	1,983		74,528	42,765		80,422	44,748	
Blood cultures	201	257		839	661		1,040	918	
Blood cultures per patient-day	0.03	0.13	<.001	0.01	0.02	<.001	0.01	0.02	<.001
True bacteremia	21 (10.4)	20 (7.8)	.41	158 (18.8)	85 (12.9)	.003	179 (17.2)	105 (11.4)	.0004
True bacteremia per patient-day	0.004	0.01	.0009	0.002	0.002	.68	0.002	0.002	.71
Contaminations	10 (5.0)	32 (12.5)	.0097	28 (3.3)	24 (3.6)	.65	38 (3.7)	56 (6.1)	.015
Contaminations per patient-day	0.002	0.016	<.001	0.0004	0.0006	.19	0.0005	0.0012	<.001

ICU, intensive care unit; *ppre-PP*, pre-pandemic period; *PP*, pandemic period.

(PPE), including double gloving, gown, face shields, and cap, during the care of patients with COVID-19. Blood cultures were taken at the discretion of the treating physicians upon events such as fever.

We counted all blood cultures taken from the patients hospitalized at the center during the study period regardless of the patient characteristics and the reasons for blood culture testing, and aimed at comparing the contamination rate between pre-PP and PP. Blood samples were collected by nonphlebotomists, mainly nurses and sometimes physicians, both during pre-PP and PP.

When the blood cultures were taken, this usually involved 2 separate venepunctures divided into 4 blood culture bottles at a time (2 sets), we counted these 2 sets of blood cultures as "one" procedure of blood culture acquisition. No alteration was made in terms of microbiology procedures or medical apparatuses, such as blood culture bottles or incubators during the study period. Blood culture results were judged to be contamination when culture yielded normal skin flora including but not limited to coagulase-negative staphylococci (CNoS) except for *Staphylococcus lugdnensis, Bacillus* spp., *Lactobacillus* spp., or *Corynebacterium* spp., from a single set among multiple sets of blood cultures. The final determination of whether the culture results were contamination or not was made by the Infection Control Team (ICT), which monitors all positive blood cultures daily to make sure antibiotics are being used appropriately. Cultures were considered to represent "true" infection when they yielded the same organisms from multiple sets, or a single set with an organism likely to be a true pathogen, such as *Staphylococcus aureus*, *Enterococcus* spp., Gram-negative organisms, or fungi. The final judgment to determine whether a positive blood culture result represented a true infection or not was also made by the ICT. The contamination rate and the true bacteremia rate was calculated both for pre-PP and PP, for ICU, where severe COVID-19 patients were taken care of, and for non-ICU where mild and moderate COVID-19 patients were treated.

The R software program, version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis. Clopper-Pearson 95% confidence intervals were calculated for each proportion. The Chi-square test was performed for comparison of 2 periods, pre-PP and PP.

RESULTS

A total of 7,127 and 4,182 patients were admitted during pre-PP and PP respectively, resulting in 80,422 and 44,748 patient-days respectively. A total of 346 patients with COVID-19 were hospitalized during PP at the Center.

For ICU, 503 and 186 patients were admitted during the same period respectively resulting in 5,894 and 1,983 person-days hospitalizations in ICU respectively.

A total of 1,040 and 918 blood cultures were taken during pre-PP and PP respectively, which means 0.01 and 0.02 blood cultures per patient-day respectively ($P < .001$). In the ICU, a total of 201 and 257 blood cultures were taken for the same periods, which means 0.03 and 0.13 blood cultures per patient-day respectively ($P < .001$) (Table 1).

For true bacteremia, blood cultures detected 179 bacteremias during the pre-PP and 105 for the PP in the medical center (17.2% [95% confidence interval 15.0%-19.6%], vs 11.4% [95% CI 9.5%-13.7%], $P = .0004$), but there was no difference in terms of true bacteremia per patient-day (0.002 vs 0.002. $P = .71$).

For the ICU, bacteremia occurred 21 and 20 times for the same periods (10.4% [95% CI 6.6%-15.5%], vs 7.8% [95% CI 4.8%-11.8%], $P = .41$), but there was a significant increase in true bacteremia per patient-day (0.004 vs 0.01. $P = .0009$). For the wards other than ICU, there was significant decrease in true bacteremia during PP comparing to pre-PP (18.8% [95% CI 16.2%-21.6%] vs 12.9% [95% CI 10.4%-15.7%], $P = .0030$), but there was no difference in terms of bacteremia per patient-day (0.002 vs 0.002. $P = .68$).

Thirty-eight and 56 contaminations occurred during pre-PP and PP respectively (3.7% [95% CI 2.6%-5.0%] vs 6.1% [95% CI 4.6%-7.8%], $P = .015$), and it remained significant for the contamination per patient-day (0.00005 vs 0.0012. $P < .0001$). For the ICU, 10 and 32 contaminations occurred during the same periods (5.0% [95% CI 2.4%-9.0%] vs 12.5% [95% CI 8.7%-17.1%], $P = .0097$), with a significant difference in contamination per patient-day (0.002 vs 0.016. $P < .0001$). There was no significant difference in the contamination rate between the 2 periods for the wards except for the ICU (3.3% [95% CI 2.2%-4.8%] vs 3.6% [95% CI 2.3%-5.4%], $P = .65$, and 0.0004 vs 0.0006 cases per patient-day, $P = .19$). The contamination rates among those with positive blood cultures during pre-PP for ICU and non-ICU patients were 32.3% and 15.1% respectively. The same for PP were 64.0% and 22.0% respectively. The details on the microorganisms detected during the study period was shown on the Supplementary file.

DISCUSSION

We found a significant increase of contaminations during the pandemic period, compared with the pre-pandemic period in an ICU setting where severely ill COVID-19 patients were taken care of. For non-ICU wards where only mild and moderate COVID-19 were taken care of, the contamination rate did not increase significantly. The number of blood cultures per patient-day significantly increased both at the ICU and non-ICU settings, probably reflecting the increase in febrile patients. In addition, true bacteremias per patient-day also increased during the PP compared with the pre-PP in ICU, reflecting the increase of secondary bacterial infections.

The increase of blood culture contamination could occur due to several reasons. First, the number of blood cultures per patient-day increased significantly, and it may subsequently increase the chance of contamination. The high burden of workload for the care of the patients with COVID-19, such as adjustment of oxygenation,

suctioning from the endotracheal tube, and prone positioning of the patients, might have made the procedure of blood cultures more tiring than ones taken at conventional settings. Wearing personal protective equipment (PPE) certainly could have made all procedures more difficult than those without. It is reasonable to suspect that the care of COVID-19 patients, particularly those that are severely unwell, are likely to yield more blood culture contamination.

What impact could blood culture contamination bring to the care of patients with COVID-19? Blood culture contamination could yield unnecessary use of broad-spectrum antibiotics, especially in the ICU setting, and this could result in an increase in drug-related complications and potentially worse outcomes for the patients. An increase in antibiotic resistance might make treatment of secondary bacterial infections more difficult. Workload may also increase for laboratory technicians and infection control team staff.

In our study, however, the number of true bacteremia per patient-day also increased in ICU during the pandemic period, making blood culture more important in this particular setting. The use of dexamethasone necessary to treat severe COVID-19 might make the risk of secondary bacterial infections much higher.[7] Therefore, we cannot skip the procedure to safely diagnose bacteremia during the care of COVID-19 patients, while we need to seek a way to avoid unnecessary contamination. The development of safer and easier-to-use PPE could aid such achievement.[8]

Bayo et al investigated the rate of bacteremia as well as blood culture contamination at a tertiary care hospital in Spain, and the overall contamination rate was higher than our results (12.3%).[9] Since Spain suffered from a much larger surge of infected patients compared with those in Japan, this might have reflected the difference in contamination. Yu et al also conducted a retrospective study to investigate the blood culture contamination rate in 6 tertiary care hospitals in Sweden, with a slightly higher contamination rate of 8.4%.[3] They also found a lower rate of true bacteremia compared with the control group, which is different from our findings. We are not able to delineate the reason for the difference but this may be due to a difference in patient volume and severity. Esquer Garrigos et al investigated the blood culture contamination rate at a tertiary-care center in the United States, and found the increase in blood culture contamination during COVID-19 pandemic.[10] Contamination rate during the pandemic was lower than our findings (3.5%), but was similar to our findings at non-ICU settings (3.6%). We were not able to find the detail of the hospital structure and the severity of the patient of the study in the article, and it may simply be explained by the difference in the patient/setting characteristics. Theire findings may be explained by the change of the persons who draw bloods, from dedicated phlebotomists to nonphlebotomist nurses. Our center, on the contrary, did not have change in the persons who draw bloods between pre-PP and PP, and which makes our findings unique from others.

Our study has inherent limitations. First, it is a retrospective comparative study comparing the pre-PP and PP, the possibility of the existence of confounding factors cannot be excluded. For example, many staff, particularly nurses had to move from and to COVID-19 care with varying staff-patient ratios constantly, depending on the increase and decrease of the patients with COVID-19, as well as suspected febrile cases. We were not able to adjust the staffing factor into our analysis. Second, since this is a study of a single-center setting, one may not be able to extrapolate our findings to other settings.

In conclusion, we found a significant increase in blood culture contamination in the ICU setting during the COVID-19 pandemic. Further studies will be needed to develop ways to avoid such an occurrence.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.ajic.2021.08.025.

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