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

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**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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sometimes physicians, both during pre-PP and PP. Samples were collected by nonphlebotomists, mainly nurses and aimed at comparing the contamination rate between pre-PP and PP. Blood characteristics and the reasons for blood culture testing, and aimed to represent the true pathogen, such as Staphylococcus aureus, Enterococcus 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., or Corynebacterium spp., 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 were 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. 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.

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%). 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%. 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. 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. Their 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.

References

1. Wang L, Amin AK, Khanna P, et al. An observational cohort study of bacterial coinfection and implications for empirical antibiotic therapy in patients presenting with COVID-19 to hospitals in North West London. J Antimicrob Chemother. 2021;76:796–803.
2. Sepulveda J, Westblade LF, Whitter S, et al. Bacteremia and blood culture utilization during COVID-19 surge in New York City. J Clin Microbiol. 2020;58:e00875–20.
3. Yu D, Ininbergs K, Hedman K, Giske CG, Stralin K, Ozeneci V. Low prevalence of bloodstream infection and high blood culture contamination rates in patients with COVID-19. PLOS ONE. 2020;15:e0242533.
4. Fu Y, Yang Q, Xu M, et al. Secondary Bacterial Infections in Critical Ill Patients of COVID-19. Open Forum Infect Dis. 2020. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7313762/. Accessed April 20, 2021.
5. Cusumano JA, Dupper AC, Malik Y, et al. Staphylococcus aureus bacteremia in patients infected with COVID-19: a case series. Open Forum Infect Dis. 2020;7:ofaa518.
6. Brehm TT, van der Meischen M, Hennings A, et al. Comparison of clinical characteristics and disease outcome of COVID-19 and seasonal influenza. Sci Rep. 2021;202:5803.
7. Nasir N, Rehman F, Omair SF. Risk factors for bacterial infections in patients with moderate to severe COVID-19: a case-control study. J Med Virol. 2021;93:4564–4569.
8. Honda H, Iwata K. Personal protective equipment and improving compliance among healthcare workers in high-risk settings. Curr Opin Infect Dis. 2016;29:400–406. Available at: https://covid19.elsevier.com/ja/publications/personal-proective-equipment-and-improving-compliance-among-health. Accessed April 20, 2021.
9. Marmeneo BS, Palacín Ruiz MP, Moreno HM, Villuendas UMC. Bacteremia during COVID-19 pandemic in a tertiary hospital in Spain. Enferm Infecc Microbiol Clin. 2021;21:90037–9.
10. Esquer GZ, Wingler MJ, Svoronos PA, et al. Increased rates of blood culture contamination during the coronavirus disease 2019 pandemic. Infect Control Hosp Epidemiol. 2021;1–3.