



The Seasonality of Peripheral Venous Catheter-Related Bloodstream Infections

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ABSTRACT

Introduction: Although the seasonality of infectious diseases has been widely reported, the seasonality of peripheral venous catheter-related bloodstream infection (PV-CRBSI) has not been investigated. This study investigated the seasonality of PV-CRBSI and its relationship with meteorological conditions.

Methods: A retrospective cohort study of PV-CRBSI at Tokyo Medical University Hospital

(Tokyo, Japan), from 2009 to 2019, provided the data for descriptive and time series analyses used to evaluate the number of PV-CRBSI cases per 1000 admissions that occurred each month for each causative organism. By performing univariate and multivariate analyses, the researchers investigated the seasonality of cases and the relationships between meteorological conditions, other external factors, and PV-CRBSIs.

Results: This study included a total of 184 PV-CRBSI cases. The mean numbers of PV-CRBSI cases per 1000 admissions caused by all organisms, *Bacillus cereus*, Gram-positive cocci, and Gram-negative rods were 0.67, 0.15, 0.37, and 0.16 per month, respectively, during the study period. The time series analysis showed that the incidences of PV-CRBSI cases associated with *B. cereus* and Gram-negative rods were significantly different in the winter/spring from those in the summer/autumn ($P < 0.05$). The incidence of PV-CRBSI cases caused by *B. cereus* peaked during summer. The incidence of PV-CRBSI cases caused by *B. cereus* was significantly positively associated with average monthly temperature, whereas the incidence of PV-CRBSIs caused by Gram-negative rods was significantly negatively associated with average daylight hours.

Conclusion: The incidence of PV-CRBSIs caused by *B. cereus* showed seasonality, peaking during the summer, and a significant correlation was found between PV-CRBSIs caused by

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B. cereus and average monthly temperature.

Keywords: *Bacillus cereus*; PV-CRBSI; Relative humidity; Seasonality; Summer; Temperature

Key Summary Points

The seasonality of peripheral venous catheter-related bloodstream infection (PV-CRBSI) has not been investigated.

A retrospective cohort study of PV-CRBSI at Tokyo Medical University Hospital was conducted.

The time series analysis showed that PV-CRBSI associated with *B. cereus* and Gram-negative rods had a significant difference in the number of cases between winter/spring and summer/autumn.

The number of PV-CRBSI cases caused by *B. cereus* was significantly positively associated with average temperature, whereas the number of PV-CRBSI caused by Gram-negative rods was significantly negatively associated with average daylight.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.13607579>.

INTRODUCTION

Peripheral venous catheters (PVCs) are frequently used in inpatient healthcare settings. Previous studies have reported that the incidence of peripheral venous catheter-related bloodstream infections (PV-CRBSIs) per catheter is lower than the per catheter incidence of

central venous catheter-related bloodstream infections (CV-CRBSIs), which have been the subject of more research. However, according to a previous report, 330 million peripheral venous catheters are sold in the USA annually [1], and the incidence of PV-CRBSIs may be higher than previously assumed.

The PV-CRBSI incidence rate was reported to be 0.5/1000 catheter days in the USA [2, 3], 0.04% of 616,405 PVCs in Australia [2, 4, 5], and 2.91/1000 PVC-catheter days in India [6]. Another systematic review indicated that, on average, 22% (range 7–60%) of 7860 evaluated nosocomial CRBSIs were due to PVCs [2]. Although the mortality rate of PV-CRBSIs reportedly ranges from 11.5% to 12.9% [6, 7], little attention has been paid to the risk of PV-CRBSI, compared to that of CV-CRBSI over the last decade, with limited studies focused on the clinical features of and the measures necessary to prevent PV-CRBSIs [2].

Various risk factors have been reported for PV-CRBSI, including catheter dwelling time, catheter colonization, and the location of catheter insertion [2, 8]. Catheter dwelling time is an independent risk factor for catheter colonization. However, whether meteorological factors may also be a risk factor for PV-CRBSI remains unclear.

The seasonality of infectious diseases, including tuberculosis and influenza, has been widely reported [9, 10]. The mechanisms that underlie seasonality have been associated with various factors, such as hormonal cycles [11], vitamin D deficiency due to lack of sunlight [12], climate conditions that affect the survivability of organisms [13], and interactive relationships with other infections [9]. Most research has attributed healthcare-associated infections (HAIs) with external factors rather than with seasonality. Interestingly, a study from Switzerland suggested the seasonality of central line-associated bloodstream infections (CLABSIs), with the highest incidence occurring during the third quarter, and identified a significant correlation between precipitation and infections [14]. In addition to studies of CV-CRBSIs and CLABSIs, other studies have identified seasonality (with a peak in the summer) in urinary tract infections, which have been

associated with high temperatures [15, 16]. Another study reported an association between increased humidity and increased methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) colonization [17]. However, the seasonality of PV-CRBSI incidence has not been reported.

Clarifying the seasonality of PV-CRBSI and the relationships between PV-CRBSI and meteorological factors can be useful for intensive interventions. This study investigated the seasonality of PV-CRBSIs and the relationships between seasonality and the organisms that cause these infections.

METHODS

Study Design

The researchers conducted a retrospective observational cohort study of PV-CRBSIs to examine the seasonality of PV-CRBSI and the relationships between the incidence of PV-CRBSIs and meteorological conditions. The study was conducted at Tokyo Medical University Hospital (tertiary hospital, Tokyo, Japan) from 1 January 2009 to 31 December 2019. The Ethical Committee of Tokyo Medical University approved this study and waived the need for consent (approval number T2020-0078). This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Diagnosis of Peripheral Venous Catheter Bloodstream Infection

PV-CRBSI was diagnosed on the basis of the clinical guidelines established by the Infectious Diseases Society of America (IDSA) [18], including cases where the catheter tip and blood culture were positive for the same organism. In addition to the IDSA criteria, for cases with a positive blood culture in which the catheter tip culture was not obtained, local signs of infection at the catheter insertion site were also used to define the diagnosis in this study. Local signs of infection at the catheter

insertion site included phlebitis, thrombophlebitis, cellulitis, and subcutaneous abscesses.

Meteorological Factors

Japan is located in the northern hemisphere and experiences four seasons: spring, summer, autumn, and winter. The researchers obtained meteorological data from 1 January 2009 to 31 December 2019 from the Japan Meteorological Agency of Tokyo, where the hospital is located [19], to use as independent variables. Monthly climate data included average temperature (degrees Celsius), average relative humidity (percent), precipitation (millimeters), average wind speed (meters per second), and total daylight hours (hours) for Tokyo, Japan (Supplemental Table S1). The researchers obtained and used the number of total PV-CRBSI cases, and the numbers of PV-CRBSIs cases associated with *Bacillus cereus*, Gram-positive cocci (GPC), and Gram-negative rods (GNR), as dependent variables.

Other External Factors

In addition to meteorological factors, other external factors, including both microbiological and environmental factors, were included in the analysis. The researchers used the average number of blood culture bottles, the average hand hygiene index, the average number of admission days, and the average population of the hospital staff per month during the study period as independent variables (see Supplemental Table S2). Average hand hygiene index (the number of times that hand hygiene was performed per patient day) was calculated on basis of the total amount of alcohol-based hand rubs and the total number of inpatient days.

Data Analysis

Statistical Analysis

The researchers performed statistical analysis using SPSS software, version 26 (IBM, Chicago, IL), using a two-sided significance level of 5% for all statistical tests.

Descriptive Analysis

To evaluate the data features, the researchers performed descriptive statistical analyses for the monthly number of PV-CRBSI cases per 1000 admissions (incidence) associated with four variables (all causative organisms, *B. cereus*, GPC, and GNR) to determine the proportion, mean, median, and standard deviation (SD).

Time Series Analysis

To analyze the seasonality of PV-CRBSIs associated with each causative organism, the researchers performed a descriptive analysis of the incidence of PV-CRBSI cases due to *B. cereus*, GPC, and GNR, using simple run-sequence plots. According to the Japan Meteorological Agency, the definitions of spring, summer, autumn, and winter were March to May, June to August, September to November, and December to February, respectively.

Univariate and Multivariate Analyses

To investigate associations between each meteorological condition, other external factors, and the incidence of PV-CRBSIs associated with each causative organism, the researchers calculated Pearson's product-moment correlation coefficients. They compared continuous variables, such as the incidence of PV-CRBSIs associated with each causative organism, using the non-parametric Mann–Whitney *U* test.

Multivariate analyses were conducted using multiple regression models, performed with the forward–backward stepwise selection method, to investigate the correlations between independent variables and dependent variables. Independent variables included monthly meteorological factors and other external factors, such as average temperature, relative humidity, precipitation, wind speed, the number of daylight hours, and the average number of blood culture bottles, the average hand hygiene index, the average number of admission days, and the average population of the hospital staff. Dependent variables included the monthly incidence per 1000 admissions of total PV-CRBSI cases and of PV-CRBSI cases due to *B. cereus*, GPC, and GNR.

RESULTS

This study included a total of 184 PV-CRBSI cases. The average number of causative organisms for each PV-CRBSI case was 1.16. The number of PV-CRBSI cases due to single, double, and triple causative organisms were 159, 21, and 4, respectively. The number of PV-CRBSI cases associated with *B. cereus* was 41. Causative GNR organisms included *Enterobacter* sp. (10 cases), *Klebsiella pneumoniae* (12 cases), *Klebsiella oxytoca* (3 cases), *Escherichia coli* (6 cases), *Serratia marcescens* (5 cases), *Pseudomonas aeruginosa* (3 cases), *Citrobacter koseri* (1 case), other Enterobacteriaceae (1 case), and non-fermenting GNR (10 cases), except *P. aeruginosa* (3 cases). The causative GPC organisms included coagulase-negative *Staphylococcus* (51 cases), methicillin-sensitive *Staphylococcus aureus* (40 cases), MRSA (8 cases), and *Enterococcus* sp. (6 cases) (Supplemental Table S3). The mean, median, and SD values for the incidence of total PV-CRBSI cases per month during the study period were 0.67, 0.63, and 0.19, respectively. The mean, median, and SD values for the incidence of PV-CRBSI cases due to *B. cereus* were 0.15, 0.13, and 0.10, respectively. The mean, median, and SD values for the incidence of PV-CRBSI cases associated with any GPC were 0.37, 0.35, and 0.11, respectively, and these values were 0.16, 0.17, and 0.05 for cases associated with any GNR.

Figure 1 presents the number of PV-CRBSI cases per 1000 admissions associated with *B. cereus* that occurred in each month, summed over all 11 years of the study period. The peak number of PV-CRBSI cases due to *B. cereus* occurred during the late summer month of August and the early autumn month of September. The lowest number of cases occurred during January, February, and April. These results suggested the seasonality of PV-CRBSI due to *B. cereus*, which appeared to peak in the late summer and early autumn and occurred the least frequently during the winter.

Figure 2 presents the total number of PV-CRBSI cases per 1000 admissions due to any GPC for each month, summed over the 11 years of the study period. The highest incidence of

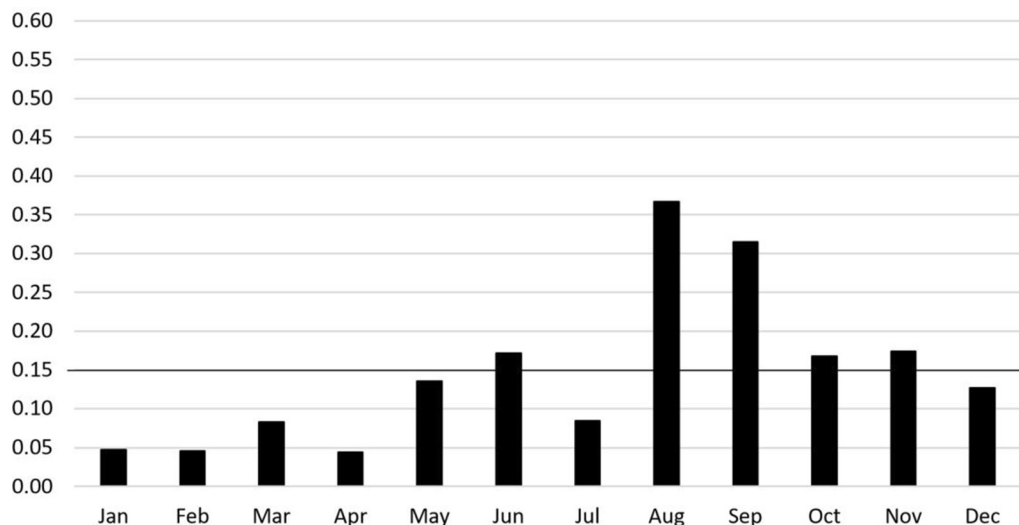


Fig. 1 Total PV-CRBSI cases per 1000 admissions due to *B. cereus* by month, 2009–2019. Horizontal axis, month; vertical axis, the number of PV-CRBSI cases; black line, the average number (0.15) of PV-CRBSI cases per 1000

admissions due to *B. cereus* during the study period. PV-CRBSI peripheral venous catheter-related bloodstream infection

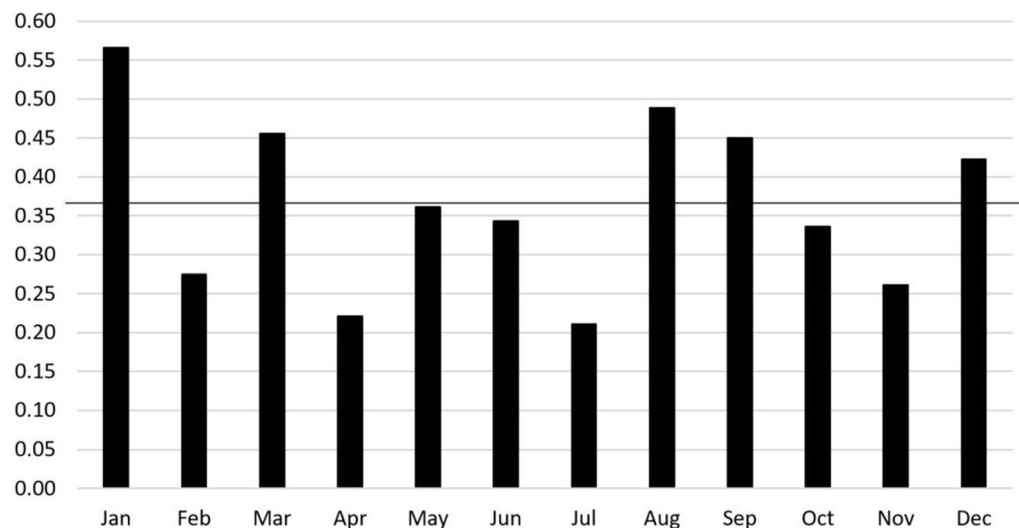


Fig. 2 Total PV-CRBSI cases per 1000 admissions due to GPC by month, 2009–2019. Horizontal axis, month; vertical axis, the number of cases of PV-CRBSI; black line, the average number (0.37) of PV-CRBSI cases per 1000

admissions due to GPC during the study period. PV-CRBSI peripheral venous catheter-related bloodstream infection, GPC Gram-positive cocci

PV-CRBSI cases due to any GPC occurred in January and August, followed by March, September, and December. The lowest incidence occurred in April and July. These results indicated regular fluctuations and no obvious

seasonality for the incidence of PV-CRBSI cases due to any GPC. Figure 3 provides the total number of PV-CRBSI cases per 1000 admissions due to any GNR for each month, summed over the 11 years of the study period. The highest

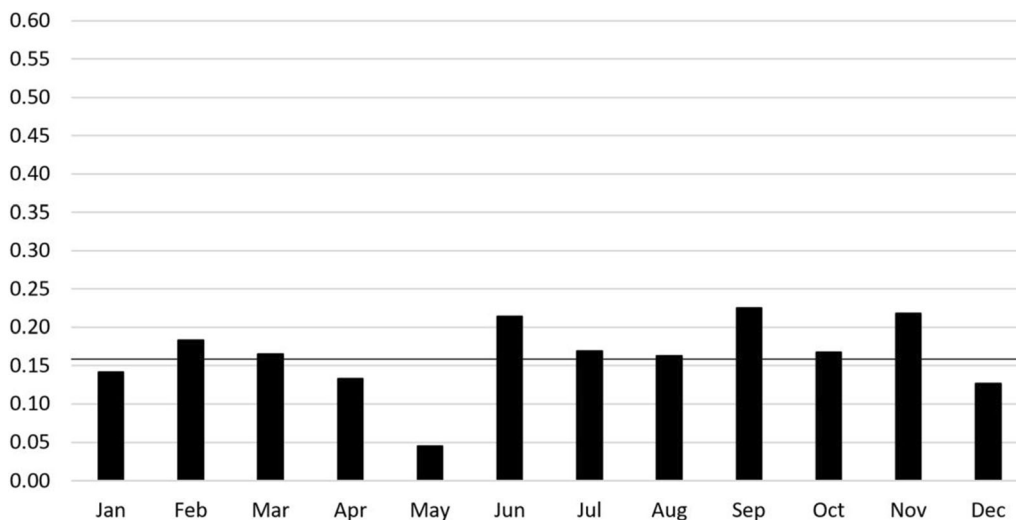


Fig. 3 Total PV-CRBSI cases per 1000 admissions due to GNR by month, 2009–2019. Horizontal axis, month; vertical axis, the number of cases of PV-CRBSI; black line, the average number (0.16) of PV-CRBSI cases per 1000

admissions due to GNR during the study period. PV-CRBSI peripheral venous catheter-related bloodstream infection, GNR Gram-negative rods

rates for PV-CRBSI cases due to any GNR occurred in June, September, and November, whereas the lowest rates occurred in May, followed by January, April, and December. As with PV-CRBSIs due to GPC, the incidence of PV-CRBSIs due to any GNR tended to fluctuate and presented no obvious seasonality.

Employing univariate analyses, the researchers found that the numbers of PV-CRBSI cases per 1000 admissions due to *B. cereus* and due to GNR were significantly different between winter/spring and summer/autumn ($p = 0.021$ and $p = 0.023$, respectively; see Table 1). In contrast, they observed no significant differences for the number of total PV-CRBSIs per 1000 admissions and the number of PV-CRBSIs per 1000 admissions due to GPC between winter/spring and summer/autumn ($p = 0.179$, and $p = 0.600$, respectively; see Table 1).

Table 2 provides Pearson's product-moment correlation coefficients between each causative organism (all causative organisms, *B. cereus*, GPC, and GNR) associated with PV-CRBSIs, each meteorological condition, and other external factors. Significant positive correlations were identified between the incidence of PV-CRBSIs due to *B. cereus* and both average temperature and relative humidity. A

significant negative correlation coefficient was calculated between the incidence of PV-CRBSIs caused by any GNR and the number of daylight hours. No other correlations among any of the other factors were significant.

Multivariate analysis of the incidence of PV-CRBSIs due to *B. cereus* and GNR, meteorological factors, and other external factors (Table 3) suggested that the incidence of PV-CRBSI cases due to *B. cereus* was significantly positively associated with the average temperature in the best-fit model, which predicted that the incidence of PV-CRBSI cases due to *B. cereus* would increase by 0.009 cases per 1000 admissions for each increase in degree Celsius when excluding the effects of relative humidity. The incidence of PV-CRBSI cases due to any GNR was significantly and negatively associated with the number of daylight hours. The best-fit model predicted that the incidence rate would decrease by 0.001 cases per 1000 admissions with each additional hour of daylight. The relationships among the other factors assessed by the multivariate adjustments were not significant.

Table 1 Average number of monthly PV-CRBSI cases per 10,000 admissions for winter/spring and summer/autumn

	Winter/spring	Summer/autumn	<i>p</i> value ^a
All	0.59	0.74	0.179
<i>Bacillus cereus</i>	0.08	0.21	0.021*
GPC	0.39	0.35	0.600
GNR	0.13	0.19	0.023*

Spring, summer, autumn, and winter are defined as March to May, June to August, September to November, and December to February, respectively

All all causative organisms, including *Bacillus cereus*, *Corynebacterium* sp., GPC Gram-positive cocci, GNR Gram-negative rods

*The difference between winter/spring and summer/autumn was significant

^a Mann–Whitney *U* test was used

DISCUSSION

This study revealed a seasonal trend in the incidence of PV-CRBSIs, especially for those cases associated with *B. cereus*. The incidence of PV-CRBSI cases associated with *B. cereus* peaked in the summer, with a significant difference in the incidence of cases between summer/autumn and winter/spring. The incidence of PV-CRBSIs due to *B. cereus* rose significantly with increasing average monthly temperatures. Although the incidences of PV-CRBSI cases associated with GNR were significantly different between summer/autumn and winter/spring, the peaks and troughs in the number of cases were not obvious in the time series analysis. The incidence of PV-CRBSI cases due to any GNR significantly decreased with an increasing number of daylight hours. However, the incidence of PV-CRBSI cases associated with GPC displayed no obvious seasonality or significant variations between seasons.

Many previous studies have examined the seasonality of infectious diseases: tuberculosis peaks mainly in spring and summer [10, 12]; seasonal influenza peaks mainly in winter [9, 13, 20]; respiratory syncytial virus peaks in winter; rhinovirus peaks in spring or summer/fall [20–22]; and legionellosis increases during hot and humid seasons [23]. However, few studies have explored the seasonality of HAIs, although one previous study indicated a seasonal trend in bloodstream infections

associated with *B. cereus* in hospitals in Japan [24]. Some research has been conducted on CV-CRBSIs and CLABSIs, which are bloodstream infections of the central line, using device-related surveillance or examinations of clinical infections. One study reported seasonal differences in the incidence of CLABSIs, with the highest number of cases reported from July to September in Switzerland [14]. Other studies have reported the seasonality of urinary tract infections, which peak in the summer and are associated with higher temperatures [15, 16]. Umbilical contaminations and bloodstream infections due to *B. cereus* during the summer season have been reported in the UK [25] and Japan [26], but no reports have examined the existence of seasonal trends for PV-CRBSIs. This study is the first to explore seasonal trends in the number of PV-CRBSI cases caused by *B. cereus*.

A previous study performed in Switzerland [14] did not detect a significant association between temperature and the incidence of CLABSIs, based on an analysis of all causative organisms, without a subgroup analysis for *B. cereus*. Our study revealed a significant association between temperature and the incidence of PV-CRBSIs due to *B. cereus*, which appears to increase in warmer temperatures. For example, milk production requires the maintenance of low temperatures during all steps because elevated temperatures may create conditions that support the growth of *B. cereus* [27]. A similar

Table 2 Correlation coefficients between PV-CRBSI cases per 10,000 admissions associated with each causative organism and meteorological conditions

Causative organism	Meteorological factors				Other external factors				
	Temperature (mean)	Relative humidity	Precipitation	Wind speed	Daylight hours	Average number of blood culture bottles	Average hand hygiene index	Average length of admission (days)	Average population of hospital staff
All	0.351	0.293	0.412	- 0.280	- 0.180	0.018	- 0.311	- 0.083	- 0.130
<i>Bacillus cereus</i>	0.665*	0.650*	0.570	- 0.251	- 0.378	0.298	- 0.043	- 0.435	0.320
GPC	- 0.160	- 0.287	- 0.059	- 0.184	0.348	- 0.140	- 0.462	- 0.202	- 0.432
GNR	0.154	0.355	0.316	- 0.517	- 0.792*	- 0.029	- 0.078	- 0.251	- 0.208

Average hand hygiene index: the monthly number of times that hand hygiene was performed per patient day

All all causative organisms, including *Bacillus cereus*, *Corynebacterium* sp., GPC Gram-positive cocci, GNR Gram-negative rods

* $p < 0.05$

relationship between temperature and improved growth conditions may also exist in the healthcare setting. The previous study [14] did not identify relative humidity as a significant factor for the incidence of CLABSIs. However, another study indicated that increased humidity was related to MRSA and VRE colonization [17]. According to the univariate analysis in this study, relative humidity was significantly associated with PV-CRBSIs due to *B. cereus*; however, a correlation was also identified between temperature and relative humidity, indicating that these variables may be confounding factors. In Japan, the summer season tends to be associated with high precipitation, resulting in high humidity, whereas the winter season tends to have low precipitation and low humidity. Therefore, during the multivariate analysis, this study removed relative humidity and retained temperature to generate the best-fit model. If the seasonal trend for PV-CRBSI incidence identified in this study is specific to Japan and not observed in other countries, the combination of high temperature and high humidity may play a role in this seasonal trend.

Although the incidence of PV-CRBSI cases due to GNR showed a significant difference between summer/autumn and winter/spring, the seasonal peaks were not obvious, based on the time series analysis performed in this study. Some other studies have reported a seasonal trend in GNR-associated infections. For example, *K. pneumoniae* bloodstream infections were found to be associated with high temperatures, with increases in temperature predicting increases in infection rates [27]. Another study reported that average temperatures were predictive of the increasing incidence of *E. coli* bloodstream infections [28]. This study identified no relationship between temperature and the incidence of PV-CRBSIs per 10,000 admissions due to GNR. However, this research did find a relationship between the number of daylight hours and GNR PV-CRBSI infections. Whether sunlight can influence the incidence of HAIs remains unclear; however, sunlight might prevent the growth of GNR related to PV-CRBSIs. The mechanism underlying the

Table 3 Multiple linear regression between PV-CRBSI cases per 10,000 admissions [due to *Bacillus cereus* and Gram-negative rods (GNR)] and meteorological conditions

Causative organism	Included variables for the best-fit model	<i>p</i> value	Linear regression model	Excluded variables to obtain the best-fit model
<i>Bacillus cereus</i>	Average temperature	0.018*	$0.001 + 0.009 \times (\text{average temperature})$	Relative humidity, precipitation, wind speed, daylight hours, the average hand hygiene index, the average number of admission days, the average population of hospital staff, the average number of blood culture bottles
GNR	Daylight hours	0.002*	$0.408 - 0.001 \times (\text{daylight hours})$	Average temperature, relative humidity, precipitation, wind speed, the average hand hygiene index, the average number of admission days, the average population of hospital staff, the average number of blood culture bottles

GNR Gram-negative rods

*Statistically significant

relationship between GNR-associated infections and daylight hours requires further study.

In this study, the proportion of PV-CRBSIs caused by *B. cereus* tended to be higher. Although the reason remains unclear, meteorological conditions such as high temperatures and high humidity in Japan can result in a high incidence of PV-CRBSIs due to *B. cereus*. Although *B. cereus* is generally transmitted by contaminated linens or towels, the hospital in this study cleans their linens and towels approximately once per week. Reasons other than meteorological factors that may contribute to the high incidence of PV-CRBSIs due to *B. cereus*, such as personal infection control precautions, should be examined in future studies.

This study has several limitations. First, this study was conducted at a single center, using a small sample. Multicenter studies examining larger samples would be required to gain more reliable results and to verify the relationships between infection incidence and meteorological factors.

Second, a metric of PV-CRBSI rates per 1000 catheter days would be better than the number of PV-CRBSIs per 1000 admissions. Collecting data for 1000 catheter days of peripheral venous

line would require access to the records of all peripheral line cases and the number of indwelling days, including non-infectious cases. The number of cases with indwelling peripheral catheters was very large, making it difficult to calculate on the basis of 1000 catheter days. However, the next study should use a metric of 1000 catheter days for more accurate results.

Third, although warmer temperatures can stimulate the growth of other pathogenic organisms and increase the incidence of HAIs, this study found no relationships between temperature and PV-CRBSIs associated with other causative organisms. Other factors, in addition to meteorological conditions, may contribute to the increase or decrease in PV-CRBSI rates.

Fourth, in addition to meteorological factors, microbiological and environmental factors were included as other external factors. However, some factors that may contribute to the seasonality of PV-CRBSIs could not be analyzed in this study, such as staff turnover rates or the relationship with other HAIs. The average hand hygiene index, the average number of admission days, and the average population of all hospital staff reflect the increased likelihood of contamination due to manipulation; however,

in this study, these factors were not found to have significant effects. For example, staff turnover rates may increase during the summer or Christmas holidays, although the holiday-related staff turnover rates are presumed to be lower in Japan than in Western countries because Japanese healthcare workers do not have such long holidays. Furthermore, although other HAIs may also display seasonality trends, evidence supporting relationships between temperature and infection remains limited. Further studies are required to analyze the effects of these factors on the seasonality of PV-CRBSIs. Finally, some cases of PV-CRBSI had two or three causative organisms, which may have affected the analysis.

CONCLUSIONS

The seasonality revealed in this study will contribute to the selection of antibiotics as empiric therapy. It also suggests that further education for healthcare workers and infection-prevention practices such as the use of disinfectants and the regular replacement of linens. Moreover, if the relationship between external meteorological conditions and the growth of microorganisms is responsible for the seasonality, in-hospital external conditions, such as room temperature or relative humidity, can be modified as an infection-prevention strategy.

This study provides new insights into the relationships between healthcare-associated infections, causative organisms, and temperature. PV-CRBSIs caused by *B. cereus* showed seasonality, peaking during the summer. This study found a significant correlation between PV-CRBSIs caused by *B. cereus* and average temperature. Further research examining the relationships between meteorological factors and healthcare-associated infections remains necessary to verify these findings.

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Compliance with Ethics Guidelines. This study was approved by the Ethical Committee of Tokyo Medical University (approval number T2020-0078). The need for consent was formally waived by the Ethical Committee of TMU. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Data Availability. The dataset supporting the conclusions of this article is included in the article.

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REFERENCES

- Hadaway L. Short peripheral intravenous catheters and infections. *J Infus Nurs*. 2012;35:230–40.
- Mermel LA. Short-term peripheral venous catheter-related bloodstream infections: a systematic review. *Clin Infect Dis*. 2017;65:1757–62.
- Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. *Mayo Clin Proc*. 2006;81:1159–71.
- Collignon PJ, Munro R, Sorrell TC. Systemic sepsis and intravenous devices. A prospective survey. *Med J Aust*. 1984;141:345–8.
- Collignon PJ, Dreimanis DE, Beckingham WD, Roberts JL, Gardner A. Intravascular catheter bloodstream infections: an effective and sustained hospital-wide prevention program over 8 years. *Med J Aust*. 2007;187:551–4.
- Rosenthal VD, Gupta D, Rajhans P, et al. Six-year multicenter study on short-term peripheral venous catheters-related bloodstream infection rates in 204 intensive care units of 57 hospitals in 19 cities of India: International Nosocomial Infection Control Consortium (INICC) findings. *Am J Infect Control*. 2020;48:1001–8.
- Sato A, Nakamura I, Fujita H, et al. Peripheral venous catheter-related bloodstream infection is associated with severe complications and potential death: a retrospective observational study. *BMC Infect Dis*. 2017;17:434.
- O’Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis*. 2011;52:e162–93.
- Lipsitch M, Viboud C. Influenza seasonality: lifting the fog. *Proc Natl Acad Sci USA*. 2009;106:3645–6.
- Wingfield T, Schumacher SG, Sandhu G, et al. The seasonality of tuberculosis, sunlight, vitamin D, and household crowding. *J Infect Dis*. 2014;210:774–83.
- Dowell SF. Seasonal variation in host susceptibility and cycles of certain infectious diseases. *Emerg Infect Dis*. 2001;7:369–74.
- Ralph AP, Ralph AR, Lucas RM, Norval M. Vitamin D and solar ultraviolet radiation in the risk and treatment of tuberculosis. *Lancet Infect Dis*. 2013;13:77–88.
- Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. *Proc Natl Acad Sci USA*. 2009;106:3243–8.
- Schreiber PW, Dunic M, Wolfensberger A, et al. Seasonal differences in central line-associated bloodstream infection incidence rates in a Central European setting: results from prospective surveillance. *Am J Infect Control*. 2019;47:1011–3.
- Rosignol L, Pelat C, Lambert B, Flahault A, Charrier-Kastler E, Hanslik T. A method to assess seasonality of urinary tract infections based on medication sales and Google trends. *PLoS One*. 2013;8:e76020.
- Falagas ME, Peppas G, Matthaïou DK, Karageorgopoulos DE, Karalis N, Theocharis G. Effect of meteorological variables on the incidence of lower urinary tract infections. *Eur J Clin Microbiol Infect Dis*. 2009;28:709–12.
- Blanco N, Perencevich E, Li SS, et al. Effect of meteorological factors and geographic location on methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci colonization in the US. *PLoS One*. 2017;12:e0178254.
- Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;49:1–45.
- Japan Meteorological Agency. Search past weather data. 2021. http://www.data.jma.go.jp/obd/stats/etrn/index.php?prec_no=44&block_no=47662&year=2009&month=&day=&view=p5. Accessed 1 Feb 2021.
- Lekana-Douki SE, Nkoghe D, Drosten C, Ngoungou EB, Drexler JF, Leroy EM. Viral etiology and seasonality of influenza-like illness in Gabon, March 2010 to June 2011. *BMC Infect Dis*. 2014;14:373.
- Li X, Li J, Meng L, et al. Viral etiologies and epidemiology of patients with acute respiratory infections based on sentinel hospitals in Gansu Province, Northwest China, 2011–2015. *J Med Virol*. 2018;90:828–35.
- Radin JM, Hawksworth AW, Kammerer PE, et al. Epidemiology of pathogen-specific respiratory

- infections among three US populations. PLoS One. 2014;9:e114871.
23. Simmering JE, Polgreen LA, Hornick DB, Sewell DK, Polgreen PM. Weather-dependent risk for legionnaires' disease, United States. Emerg Infect Dis. 2017;23:1843–51.
 24. Kato K, Matsumura Y, Yamamoto M, et al. Seasonal trend and clinical presentation of *Bacillus cereus* bloodstream infection: association with summer and indwelling catheter. Eur J Clin Microbiol Infect Dis. 2014;33:1371–9.
 25. Hosein IK, Hoffman PN, Ellam S, et al. Summertime *Bacillus cereus* colonization of hospital newborns traced to contaminated, laundered linen. J Hosp Infect. 2013;85:149–54.
 26. Dohmae S, Okubo T, Higuchi W, et al. *Bacillus cereus* nosocomial infection from reused towels in Japan. J Hosp Infect. 2008;69:361–7.
 27. Anderson DJ, Richet H, Chen LF, et al. Seasonal variation in *Klebsiella pneumoniae* bloodstream infection on 4 continents. J Infect Dis. 2008;197:752–6.
 28. Al-Hasan MN, Lahr BD, Eckel-Passow JE, Baddour LM. Seasonal variation in *Escherichia coli* bloodstream infection: a population-based study. Clin Microbiol Infect. 2009;15:947–50.