Seasonal variation of hospital-acquired bloodstream infections: A national cohort study

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Abstract

Background: Hospital-acquired bloodstream infections (HABSI) cause increased morbidity, mortality, and hospital costs that are partially preventable. HABSI seasonality has been described for gram-negative bacteria but has not been stratified per infection origin.

Objective: To assess seasonality among all types of HABSIs and their associations with climate.

Methods: Hospitals performing surveillance for at least 1 full calendar year between 2000 and 2014 were included. Mixed-effects negative binomial regression analysis calculated the peak-to-low monthly ratio as an adjusted HABSI incidence rate ratio (IRR) with 95% confidence intervals (CIs). Another regression model examined associations between HABSI rates and climate variables. These analyses were stratified by microorganism and infectious origin.

Results: The study population included 104 hospitals comprising 44,111 HABSIs. Regression analysis identified an incidence rate ratio (IRR) peak in August for gram-negative HABSIs (IRR, 1.59; 95% CI, 1.49–1.71), CLABISIs (IRR, 1.49; 95% CI, 1.30–1.70), and urinary tract HABSI (IRR, 1.52; 95% CI, 1.34–1.74). The gram-negative incidence increased by 13.1% (95% CI, 9.9%–16.4%) for every 5°C increase in temperature. Seasonality was most present among E. coli, K. pneumoniae, E. cloacae, and the nonfermenters. Gram-positive and pulmonary HABSIs did not demonstrate seasonal variation.

Conclusions: Seasonality with summer spikes occurred among gram-negative bacteria, CLABISIs, and urinary tract HABSIs. Higher ambient temperature was associated with gram-negative HABSI rates. The preventable causative factors for seasonality, such as the nurse-to-patient ratio, indoor room temperature or device-utilization, need to be examined to assess areas for improving patient safety.

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Participants

Participation in the surveillance program entails case-based recording of all HABSIIs for a minimum of 1 trimester per year. Participation was voluntary but became mandatory from 2014 onward. Eligible hospitals were all hospitals with >150 beds. To analyze seasonal variation, hospitals included in this cohort study performed surveillance for HABSIIs (numerator) with patient day (denominator) data for a full year, that is, 4 trimesters within a calendar year, during at least 1 year.

Case definitions and variables

A laboratory-confirmed BSI requires at least 2 separate samples if the causal microorganism is a skin commensal and at least 1 sample if the causal microorganism is a recognized pathogen (Appendix 1 online). HABSIIs were those not present or incubating at the time of admission to the acute-care setting (≥48 hours). An episode in the same patient caused by the same microorganism was considered a novel occurrence if 14 days elapsed between the 2 episodes. HABSII origins were classified as central-line associated; unknown origin; secondary to pulmonary, urinary, skin and soft-tissue, abdominal infection; or surgical sites. HABSI diagnosis could be classified as confirmed instead of probable when the same microorganism was cultured from the probable infectious focus. Catheter-related BSI diagnosis required a concomitant positive central venous catheter (CVC) tip and blood culture with identification of the same microorganism (Appendix 2 online). Central-line–associated BSI consisted of a BSI without microbiological confirmation but with a CVC in place within 48 hours, unrelated to an infection from another site, and considered by the clinician to originate from the CVC.

Collected data included infection onset date, infectious origin, causal microorganism(s), and university-affiliated hospital status. Denominator data included number of hospitalwide patient days and admissions per trimester. HABSI incidence was reported as a rate per 10,000 patient days.

Statistical methods

Mixed-effects negative binomial distribution regression model calculated the adjusted incidence rate ratio (IRR) with 95% confidence interval (CI) for both monthly HABSI rates. This method allowed the identification of a peak-to-low ratio between 2 months, which describes the amplitude of the seasonal pattern by comparing the month with the lowest incidence rate to the month with the highest incidence rate. Further stratification analyzed incidence rate ratios for gram-positive, gram-negative, and fungal infections. The least common Enterobacter spp (E. proteus, E. serrata, E. morgannella, and E. citrobacter spp) were grouped together for regression analysis. The analysis was performed hospital-wide and includes the intensive care unit. Fixed effects included year, acute versus chronic care hospitals, university hospital status, and infection risk exposure expressed as monthly patient days. Varying hospital participation and heterogeneity were accounted for by applying individual hospital units as random effects. Although denominator patient-day data were reported per trimester, it was averaged between the 3 months to allow for monthly patient-day exposure and incidence rate analysis.

Statistical significance depends on both the strength of the association and the amount of data and thus does not measure the strength of seasonal occurrence. Instead, measures that compare estimates of rates should be used. To graph and describe the seasonal changes, composite monthly HABSI rates were estimated based on the regression analysis results. In this way, both the relative (incidence rate ratio) and absolute changes (mean incidence rate per patient days) could be presented. Because the regression analysis may identify a single statistically significant peak incidence within 1 month, a peak-to-low ratio comparing the seasonal peak-to-low incidence rate ratio (ie, winter to summer period) was calculated to determine whether significant variation occurred between seasons. In this manner, we were able to distinguish between a monthly outlier versus a relevant, continued, absolute incidence rate change within an entire season.

To assess the influence of climate on the infection incidence, monthly average temperature (°C), humidity (%), and precipitation (mm) from 2000 through 2014 were collected from an online data system. A separate mixed-effects negative binomial regression model applied climate variables to identify associations with HABSI. A second model examined temperature and humidity per season with weather-by-season interaction terms (Appendix 3 online). Thus, we were able to distinguish between a warm versus a cold season. Seasons were defined as winter (December–February), spring (March–May), summer (June–August), and autumn (September–November).

All statistical analyses were performed using Stata version 14 software (StataCorp, College Station, TX). The mixed-effects negative binomial regression analysis was performed with the menbreg function. Interquartile ranges (IQR) were reported as the 25th–75th percentile. Statistical significance was set at P ≤ .05; however, considering the number of analytical computations and the large data set, a P ≤ .01 should be considered more relevant to indicate statistical significance.

Results

In total, 49,021 cultured microorganisms from 44,111 HABSIIs were reported by 104 hospital sites (Table 1). Selection of hospitals performing surveillance for an entire calendar year led to the exclusion of 20,034 HABSIIs (31.2%). Only 63 HABSIIs (0.1%) were excluded due to missing patient-day data.

The hospitalwide median HABSI incidence rate was 7.0 per 10,000 patient days (IQR, 4.93–9.47), with a CLABSI rate of 1.14 per 10,000 patient days (IQR, 0.64–2.14). Monthly average ambient temperature ranged from a minimum of −0.7 to a maximum of 23°C with higher temperature during June–August. Relative humidity showed a range between 62% and to 92%, with higher percentages during December–February.

The most common pathogens consisted of coagulase-negative staphylococci (CNS), Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Enterococcus faecalis, and Klebsiella pneumoniae. The most frequent HABSI foci were of central-line, urinary tract, pulmonary, or intra-abdominal origin (Appendix 4 online). Polymicrobial infection occurred among 4,317 (9.8%) of 44,111 HABSIIs. A definite diagnosis of the infectious origin (ie, culture of the same microorganism from blood and primary infectious site) was reported among 13,636 (27.8%) of 49,021 HABSI microorganisms. Approximately one-third of HABSI cases were classified as being of unknown origin (34.1%). Appendix 5 (online) displays the distribution of microorganisms per HABSI origin. CLABSI consisted primarily of CNS, followed by gram-
negative bacteria, S. aureus and Candida spp. Nearly all urinary-tract HABSIIs were caused by gram-negative pathogens.

Mixed-effects regression analysis identified significant seasonal (IRR, 1.22; 95% confidence interval [CI], 1.18–1.26 CI; P < .001) and monthly peak-to-low relative rate changes (IRR, 1.42; 95% CI, 1.34–1.50; P < .001) for total HABSIIs. When stratified, this seasonality was present for most microorganisms and HABSIIs per infectious origin but at varying levels of magnitude. Table 2 lists the HABSIIs peak-to-low seasonal (summer-to-winter) and monthly IRRs, stratified by microorganism and infectious origin. Gram-negative HABSIIs demonstrated a larger seasonal peak-to-low ratio during the summer (IRR, 1.37; 95% CI, 1.32–1.43; P < .001) compared to gram-positive pathogens (IRR, 1.07; 95% CI, 1.03–1.12; P = .002).

Based on monthly peak-to-low IRRs, HABSII estimates were plotted to quantify absolute incidence rate seasonality (Fig. 1). Figure 1a displays the monthly incidence of all pathogens with significant monthly peak-to-low IRRs. Figure 1b illustrates monthly variation among pathogens with lower incidence rates. They display a seasonal pattern, with a trough incidence rate during February that peaks 5–6 months later in July or August. Some HABSII rates only displayed significant IRR during 1 peak month and not the entire summer, which statistically appears as a discrepancy between the seasonal and monthly peak-to-low IRR, as in the cases of S. aureus, CNS, and P. aeruginosa.

When examining Figure 1a, pathogens that displayed the clearest seasonality with a spike during July–August were CNS, E. coli, K. pneumoniae, E. cloacae, and a group of less common Enterobacteraceae. Despite their relatively lower peak-to-low seasonal and monthly IRRs, CNS and E. coli demonstrated important absolute rate changes (Fig. 1a). Although S. aureus demonstrated significant peak-to-low IRR increases during the summer, seasonality was less clear when examining absolute rate changes. P. aeruginosa, Acinetobacter spp, K. oxytoca, and Stenotrophomonas spp (bacteria with lower incidence rates) also demonstrated summer seasonality (Fig. 1b). S. pneumoniae displayed the opposite trend, with peaks during the winter.

HABSIIs from different infectious origins also exhibited seasonal variation showing summer spikes (Table 2). The clearest examples were central-line– and urinary tract–associated HABSIIs (Fig. 2). Subgroup analysis of catheter-related blood-stream infections (ie, with concomitant positive catheter tip or catheter blood culture) confirmed this seasonal variation. The seasonal peak-to-low IRR was statistically significant among intra-abdominal, skin and soft-tissue, and surgical site infections; however, the effect size was smaller as evidenced by the smaller absolute rate changes. HABSIIs of pulmonary origin exhibited no seasonal variation. Subgroup analysis of gram-negative pulmonary HABSI showed subtle increases during the summer months (Appendix 6 online).

Table 3 describes the associations between ambient climate variables and HABSI incidence rates per microorganism or per infectious focus. Gram-negative bacteria displayed significant associations between climate and IRR both year-long and within all seasons. Those that demonstrated the highest correlation with temperature were Stenotrophomonas, Acinetobacter, and Klebsiella spp. Although P. aeruginosa displayed seasonality with summer peaks, a period that is paired with lower relative humidity, there was no positive association with ambient temperature but rather with humidity. Stenotrophomonas spp and Bacteroides spp also displayed positive associations with higher relative humidity (Table 3). Streptococcus pneumoniae incidence was negatively associated with temperature. The only type of HABSI that demonstrated clear associations with climate was CLABSI, with increased incidence at higher temperatures. Urinary tract HABSI also showed an association with temperature but with a very small effect size. Precipitation was not associated with any HABSI microorganism nor type of infection.

### Discussion

This national surveillance program identified seasonal variation in HABSI incidence rates. Summer incidence spikes occurred among Enterobacteriales (E. coli, K. pneumoniae, and E. cloacae), nonfermenters (P. aeruginosa, Acinetobacter, and Stenotrophomonas spp), CLABSIIs, and urinary tract HABSIIs. Higher monthly ambient temperature was associated with increased gram-negative HABSI and CLABSI incidences. There was no association between HABSI and precipitation because precipitation has a confounding effect that influences temperature and humidity.

Previous reports have also identified summer increases in gram-negative infections and associations with ambient temperature. One tertiary-care center also identified CLABSI seasonal variation but was limited by the single-center design, short-term surveillance of 24 months, and lack of microorganism data. There was no clear hospital-acquired S. aureus seasonality, which is in line with a previous literature review. The strengths of this study include nationwide long-term surveillance over multiple hospitals, detailed microorganism and infectious origin identification, and mixed-effects regression analysis with correction for confounding factors such as hospital heterogeneity, patient days, years, and seasons. This is the first

### Table 1. Hospitalwide Hospital-Acquired Bloodstream Infection (HABSI) Incidence by Season*

| Variable           | Winter | Spring | Summer | Autumn | Total   |
|--------------------|--------|--------|--------|--------|---------|
| HABSI              | 10,689 | 10,474 | 11,675 | 11,273 | 44,111  |
| Patient days       | 13,130,543 | 12,755,878 | 12,091,905 | 12,546,358 | 50,524,684 |
| Patient admissions | 5,275,204 | 5,164,098 | 4,887,702 | 5,053,537 | 20,380,541 |
| Mean HABSI rate    | 8.14   | 8.21   | 9.65   | 8.98   | 8.73    |
| Temperature, median °C (IQR) | 4 (3–6) | 11 (8–14) | 18 (17–19) | 11 (9–15) | 11 (6–16) |
| Relative humidity, median % (IQR) | 87 (83–89) | 73 (70–76) | 74 (71–77) | 84 (80–88) | 79 (74–90) |

Note. IQR, interquartile range.

*Seasonal data on hospitalwide mean HABSI rates per 10,000 patient days.
national study to analyze both seasonality of microorganism and infections per origin. Seasonality is a phenomenon that manifests due to interconnected changes in patient, pathogen, hospital, and environmental variables. For example, the number of available hospital beds decreases during the summer, which leads to lower patient admissions and possibly a selection bias of hospitalized patients with relatively higher comorbidities, which increases the risk of HABSI.

This study had several limitations. Insufficient information was available for confounding factors such as in-hospital temperature and humidity, patient comorbidities, nurse-to-patient ratio, and invasive device use (eg, central lines, endotracheal intubation, and urinary catheterization).

Notably, CLABSIIs and urinary-tract HABSIIs, infections associated with invasive device use, demonstrated seasonal variation. Although most CLABSIIs are caused by gram-positive skin commensals, there was an association between higher ambient temperature and CLABSI rates. Catheter dressing disruption due to increasing skin perspiration or a changing nurse-to-patient ratio could not identify clear seasonal nurse-staffing patterns. These reports did not collect nurse staffing data during July–August, during the influenza season. Another study in an acute-care hospital and summer) and between months (monthly peak-to-low ratio).

### Table 2. Peak-to-Low Hospital-Acquired Bloodstream Infection (HABSI) Seasonal and Monthly Incidence Rate Ratios (IRRs) per Microorganism and Origin of Infection*  

| Variable                  | Seasonal Peak-to-Low Ratio | Monthly Peak-to-Low Ratio |
|---------------------------|----------------------------|---------------------------|
|                           | IRRa| 95% CI  | P Value | IRRb| 95% CI  | P Value |
| Total HABSI               | 1.22| 1.18–1.26| <.001  | 1.42| 1.34–1.50| <.001  |
| **Microorganism**         |     |      |        |     |      |        |
| Gram-positive bacteria    | 1.07| 1.03–1.12| .002  | 1.26| 1.17–1.36| <.001  |
| CNS                       | 1.10| 1.03–1.18| .006  | 1.37| 1.22–1.54| <.001  |
| S. aureus                 | 1.09| 1.01–1.18| .03   | 1.36| 1.19–1.55| <.001  |
| S. pneumoniae             | 0.47| 0.38–0.60| <.001 | 0.29| 0.19–0.46| <.001  |
| Enterococcus spp          | 1.10| 1.01–1.21| .03   | NS  |      |        |
| Viridans streptococci     | 1.25| 1.03–1.52| .03   | NS  |      |        |
| Gram-negative bacteria    | 1.37| 1.32–1.43| <.001 | 1.59| 1.49–1.71| <.001  |
| Stenotrophomonas spp      | 2.22| 1.57–3.14| <.001 | 3.02| 1.67–5.45| <.001  |
| E. cloacae                | 2.06| 1.79–2.38| <.001 | 2.70| 2.11–3.46| <.001  |
| Acinetobacter spp         | 1.77| 1.47–2.14| <.001 | 2.74| 1.97–3.81| <.001  |
| K. pneumoniae             | 1.69| 1.50–1.89| <.001 | 2.00| 1.64–2.45| <.001  |
| K. oxytoca                | 1.39| 1.17–1.65| <.001 | 1.71| 1.26–2.32| <.001  |
| P. aeruginosa             | 1.29| 1.15–1.43| <.001 | 1.77| 1.47–2.14| <.001  |
| Other Enterobacterales    | 1.29| 1.16–1.44| <.001 | 1.61| 1.33–1.95| <.001  |
| E. coli                   | 1.24| 1.17–1.32| <.001 | 1.41| 1.27–1.56| <.001  |
| K. aerogenes              | 1.15| 0.97–1.35| .10   | 1.66| 1.24–2.23| <.001  |
| Bacteroides spp           |     |      |        | NS  |      |        |
| Candida spp               | 1.12| 1.01–1.26| .04   | 1.36| 1.13–1.66| .002   |
| **Infectious origin**     |     |      |        |     |      |        |
| Central-line-associated   | 1.26| 1.17–1.36| <.001 | 1.48| 1.30–1.67| <.001  |
| Catheter-related          | 1.31| 1.21–1.41| <.001 | 1.49| 1.30–1.70| <.001  |
| Urinary tract             | 1.30| 1.21–1.40| <.001 | 1.52| 1.34–1.74| <.001  |
| Pulmonary                 |     |      |        | NS  |      |        |
| Intra-abdominal           | 1.30| 1.16–1.46| <.001 | 1.46| 1.20–1.78| <.001  |
| Deep surgical site        | 1.32| 1.10–1.59| .003  | 1.79| 1.29–2.48| <.001  |
| Skin and soft tissue      | 1.41| 1.19–1.68| <.001 | 2.09| 1.54–2.85| <.001  |

Note. NS, non-significance; CNS, coagulase-negative staphylococci; HABSI, hospital-acquired bloodstream infections. Group of other Enterobacterales includes Proteus, Serratia, Morganella and Citrobacter spp.

*Estimates of the mixed-effects negative binomial regression model adjusted for year, acute vs chronic care hospitals, university-affiliated status, and infection risk exposure expressed as monthly patient days. Peak-to-low monthly incidence rates vary per HABSI, but the trough levels are usually in February with a peak during July–August, with the exception of S. pneumoniae. Figures 1 and 2 display these monthly peak and trough incidence rates.

bIRRs are expressed as a peak-to-low ratio between the lowest and highest incidence rate between seasons (seasonal peak-to-low ratio between winter and summer) and between months (monthly peak-to-low ratio).
when a lower level may have been expected due to personnel vacation. In a similar vein, varying skill mix as inexperienced nurses and physician residents begin during the summer period could also have influenced the HABSI risk. Unfortunately, available data were insufficient to perform a subgroup analysis on urinary tract HABSIs associated with catheterization.

Nonetheless, the regression model identified associations between temperature, humidity, and gram-negative HABSI incidence.
after adjustment for different seasons. This model partially corrects for possible seasonal nurse-to-patient ratio variations. The association with temperature and gram-negative HABSI remained significant within the summer season, indicating a difference in gram-negative incidence between warmer and colder summers. Gram-negative incidence was also associated with higher relative humidity, which is actually lower during the summer period. Although the landmass of Belgium is relatively small (30,700 km²), the climate variables in the country’s center may not represent all geographic regions of the country. Climate factors were limited to ambient measurements, and although not all hospitals in Belgium are climate controlled, this method acts as a proxy for in-hospital climate. Heating, ventilation, and air-conditioning systems may maintain a relatively constant indoor temperature. However, not all hospitals use hospitalwide air-conditioning systems, and changes in ambient temperature and humidity may affect water reservoirs or moisture in the hospital environment. Another explanation is that the changes in ambient temperature influence human activities and subsequently the risk of infection. Higher incidence of severe trauma during the summer may introduce certain pathogens into the hospital environment.

Gram-negative bacteria grow more readily in aquatic milieus and show optimal growth at warmer temperatures of 32–36°C. Increases in gram-negative bacterial loads have been observed during the warm months in pond water and city water reservoirs. Multidrug-resistant gram-negative bacteria have been described as waterborne pathogens causing healthcare-associated infections, commonly linked to contaminated sinks as a reservoir. Biological studies have demonstrated that closer distance to the equator (i.e., higher ambient temperature) is associated with higher proportions of anaerobic gram-negative bacteria and lower gram-positive bacteria in the human gut microbiome. However, in this study, we did not focus on aerobic bacteria such as Enterobacteriales. It has been suggested that the influx of patients or personnel into the hospital could carry microorganisms over onto the inanimate hospital environment. Associated with higher proportions of anaerobic gram-negative bacteria and other Enterobacteriales includes Enterobacter, Serratia, E. morganii, and E. coli. The mixed-effects negative binomial regression model adjusts for year, university-affiliated status and infection risk exposure expressed as monthly patient days. IRRs are expressed as a % change with 95% confidence intervals per increase in monthly average of ambient temperature by 5°C or 10% relative humidity. Only microorganisms with significant associations with climate variables year-round are reported.

Note. CI, confidence interval; IRR, incidence rate ratio; CNS, coagulase-negative staphylococci.

Table 3. Associations Between Hospital-Acquired Bloodstream Infection (HABSI) Microorganisms and Climate, Year-Long and by Season

| HABSI                  | All seasonsb | Winterc | Springc | Summerc | Autumnc |
|------------------------|--------------|---------|---------|---------|---------|
| **Temperature**        |              |         |         |         |         |
| Gram-positive bacteria | 3.7 (0.3–7.2)* | −0.5 (−8.3 to 7.5) | 4.1 (−3.0 to 6.7) | 13.6 (5.4–21.8)*** | 5.1 (0.8–9.5)* |
| S. pneumoniae          | −36.6 (−51.2 to 21.5)*** | −24.6 (−55.1 to 8.1) | −34.3 (−62.9 to −23.9)*** | −25.9 (−68.9 to 21.3) | −30.0 (−51.3 to −7.8)*** |
| S. aureus              | 9.3 (3.9–14.7)*** | −1.2 (−13.5 to 11.4) | 10.0 (2.2–17.9)* | 26.2 (13.5–39.2)*** | 9.5 (2.8–16.3)*** |
| **Gram-negative bacteria** | 13.1 (9.9–16.4)*** | 9.7 (2.1–17.4)* | 10.1 (5.4–14.8)*** | 22.3 (15.1–29.7)*** | 15.3 (11.2–19.4)*** |
| Stenotrophomonas spp   | 60.7 (29.7–93.6)*** | 37.7 (−34.4 to 121.0) | 45.9 (−2.4 to 98.9) | 40.4 (−16.6 to 104.3) | 72.4 (35.0–112.5)*** |
| K. aerogenes            | 23.4 (10.0–37.2)*** | 34.8 (2.3–69.4)* | 20.1 (0.2–40.8)* | 22.3 (−8.1 to 54.6) | 23.3 (6.9–40.3)*** |
| Acinetobacter spp      | 20.0 (4.7–35.8)* | 2.5 (−33.2 to 40.8) | 12.4 (−11.3 to 37.1) | 18.6 (−12.8 to 51.9) | 27.2 (8.8–46.2)*** |
| K. pneumoniae          | 16.6 (7.3–26.0)*** | 15.5 (−6.8 to 38.9) | 9.8 (−4.2 to 24.2) | 24.4 (4.9–44.8)* | 19.9 (8.8–31.2)*** |
| Other Enterobacteralesc | 16.2 (7.8–24.7)*** | 4.6 (−15.2 to 24.7) | 16.1 (4.0–28.5)*** | 24.0 (5.1–43.5)* | 18.1 (7.6–28.8)*** |
| E. cloacae             | 15.4 (4.1–27.0)*** | −10.7 (−37.9 to 18.1) | 4.6 (−12.4 to 22.3) | 36.1 (12.6–60.7)** | 24.6 (10.7–38.8)*** |
| K. oxytoca             | 13.6 (0.01–27.6)* | −0.5 (−31.3–32.3) | 20.6 (0.1–41.9)* | 18.7 (−10.7 to 49.9) | 14.0 (−3.0 to 31.5) |
| E. coli               | 8.9 (4.3–13.6)*** | 13.9 (2.9–25.2)* | 6.3 (−0.4 to 13.1) | 19.5 (8.8–30.4)*** | 9.1 (3.2–15.0)*** |
| Central line           | 12.2 (6.0–18.5)*** | −13.9 (−28.2 to 0.9) | 9.0 (0.1–17.9)* | 18.7 (4.7–33.2)* | 19.1 (11.4–27.0)*** |
| Urinary tract          | 6.4 (0.4–12.5)* | 3.1 (−11.0 to 17.6) | 5.3 (−3.1 to 13.9) | 17.4 (3.8–31.3)* | 6.3 (−1.2 to 14.0) |
| **Humidity**           |              |         |         |         |         |
| Gram-positive bacteria | 6.8 (3.0–10.7)*** | 8.8 (4.7–12.9)*** | 8.8 (4.3–13.3)*** | 5.0 (0.8–9.2)* | 8.1 (4.3–12.0)*** |
| Stenotrophomonas spp   | 35.1 (1.5–69.8)* | 36.3 (−0.2 to 74.0) | 32.9 (−7.8 to 75.3) | 38.4 (3.7–74.3)* | 26.9 (−7.4 to 62.3) |
| Bacteroides spp        | 22.3 (4.2–40.7)* | 19.8 (1.1–38.9)* | 21.6 (0.9–42.6)* | 23.0 (2.5–43.9)* | 19.2 (1.4–37.3)* |
| P. aeruginosa          | 11.9 (1.6–22.3)* | 14.4 (3.3–25.1)* | 14.8 (2.6–26.9)* | 9.4 (−1.9 to 20.8) | 12.8 (2.5–23.2)* |

Note. CI, confidence interval; IRR, incidence rate ratio; CNS, coagulase-negative staphylococci.

**The mixed-effects negative binomial regression model adjusts for year, university-affiliated status and infection risk exposure expressed as monthly patient days. IRRs are expressed as a % change with 95% confidence intervals per increase in monthly average of ambient temperature by 5°C or 10% relative humidity. Only microorganisms with significant associations with climate variables year-round are reported.

bRegression analysis model included season, temperature, humidity and precipitation as fixed effects.

bRegression analysis model was performed with climate-by-season interaction terms as fixed effects.

cGroup of other Enterobacterales includes E. proteus, E. serrata, E. morganii, and E. citrobacter.

* P < 0.05; ** P ≤ 0.1; and ***P ≤ 0.01.

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as nurse-to-patient ratio, indoor climate, and device-utilization practices influence HABSI seasonality. In general, quality improvement and infection prevention interventions should be continuously applied. Depending on the underlying cause of seasonality, targeted preventive measures could be implemented during the summer, when HABSI risk is highest.

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References

1. Blot SI, Depuydt P, Annemans L, et al. Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. Clin Infect Dis 2005;41:1391–1398.
2. Umscheid CA, Mitchell MD, Doshi JA, Agarwal R, Williams K, Brennan PJ. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. Infect Control Hosp Epidemiol 2011;32:101–114.
3. Blot K, Haemmami N, Blot S, Vogelaers D, Lambert M-L. Increasing burden of Escherichia coli, Klebsiella pneumoniae, and Enterococcus faecium in hospital-acquired bloodstream infections (2000–2014): a national dynamic cohort study. Infect Control Hosp Epidemiol 2019;40:705–709.
4. Richet H. Seasonality in gram-negative and healthcare-associated infections. Clin Microbiol Infect 2012;18:934–940.
5. Leekha S, Diekema DJ, Perencevich EN. Seasonality of staphylococcal infections. Clin Microbiol Infect 2012;18:927–933.
6. He J, Stagg VS, Bergquist-Berger S, Dunton N. Unit-level time trends and seasonality in the rate of hospital-acquired pressure ulcers in US acute-care hospitals. Res Nurs Health 2015;36:171–180.
7. Suda KJ, Hicks LA, Roberts RM, Hunkler RJ, Taylor TH. Trends and seasonal variation in outpatient antibiotic prescription rates in the United States, 2006 to 2010. Antimicrob Agents Chemother 2014;58:2763–2766.
8. Sun L, Klein EY, Laxminarayan R. Seasonality and temporal correlation between community antibiotic use and resistance in the United States. Clin Infect Dis 2012;55:687–694.
9. Tascher D, Stein M, Sinoes EAF, Shohat T, Bromberg M, Somekh E. Invasive bacterial infections in relation to influenza outbreaks, 2006–2010. Clin Infect Dis 2011;53:1199–1207.
10. Denning DW, Chakrabarti A. Pulmonary and sinus fungal diseases in immunocompromised patients. Lancet Infect Dis 2017;17:e357–e366.
11. Fisman D, Patrozou E, Carmeli Y, et al. Geographical variability in the likelihood of bloodstream infections due to gram-negative bacteria: correlation with proximity to the equator and health care expenditure. PLoS ONE 2014;9: e114548–18.
12. Christiansen CF, Pedersen HT, Rotnham KJ. Methods to assess seasonal effects in epidemiological studies of healthcare-associated infections—exemplified by application to the occurrence of meningococcal disease. Clin Microbiol Infect 2012;18:963–969.
13. Monthly climatological parameter in Ukkel. MeteoBelgique website. https://www.meteobelgie.be/klimatologie/grafische-gegevens/ukkel-vanaf-1833.html. Accessed February 25, 2018.
14. Eber MR, Shardell M, Schweizer ML, Laxminarayan R, Perencevich EN. Seasonal and temperature-associated increases in gram-negative bacterial bloodstream infections among hospitalized patients. PLoS ONE 2011;6:e25298.
15. Perencevich EN, McGregor JC, Shardell M, et al. Summer peaks in the incidences of gram-negative bacterial infection among hospitalized patients. Infect Control Hosp Epidemiol 2008;29:1124–1131.
16. 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;47:1011–1013.
17. Timsit J-F, Boudalma L, Ruckly S, et al. Dressing disruption is a major risk factor for catheter-related infections. Crit Care Med 2012;40:1707–1714.
18. Aiken LH, Sloane DM, Brucey NL, et al. Nurse staffing and education and hospital mortality in nine European countries: a retrospective observational study. Lancet 2014;383:1824–1830.
19. Kane RL, Shamliyan TA, Mueller C, Duval S, Wilt TJ. The association of registered nurse staffing levels and patient outcomes: systematic review and meta-analysis. Med Care 2007;45:1195–1204.
20. Needleman J, Buerhaus P, Mattke S, Stewart M, Zelevinsky K. Nurse-staffing levels and the quality of care in hospitals. N Engl J Med 2002;346:1715–1722.
21. He J, Stagg VS, Bergquist-Berger S, Dunton N. Nurse staffing and patient outcomes: a longitudinal study on trend and seasonality. BMC Nurs 2016;15:60–10.
22. Staggs VS, Olds DM, Cramer E, Shorr RI. Nursing skill mix, nurse staffing level, and physical restraint use in US hospitals: a longitudinal study. J Gen Intern Med 2017;32:35–41.
23. Griffiths P, Maruotti A, Recio Saezco A, et al. Nurse staffing, nursing assistants and hospital mortality: retrospective longitudinal cohort study. BMJ Qual Saf 2019;28:609–617.
24. FOD Volksgezondheid VV de VEL. Minimaal Ziekenhuis Gegevens: Personeelsgegevens. Belgium Ministry of Health website. https://www.health.belgium.be/nl/mzg-personeelsgegevens. Accessed October 12, 2019.
25. McDonald C, Banerjee S, Jarvis W, NNIS. Seasonal variation of Acinetobacter infections: 1987–1996. Clin Infect Dis 1999. doi: 10.1086/313441.
26. Hostáčková A, Ciznár I, Steklovová M. Temperature and pH affect the production of bacterial biofilm. Folia Microbiol (Praga) 2010;55:75–78.
27.Průš BM, Verma K, Samanta P, et al. Environmental and genetic factors that contribute to Escherichia coli K-12 biofilm formation. Arch Microbiol 2010;192:715–728.
28. Donlan RM. Biofilms and device-associated infections. Emerg Infect Dis 2001;7:277–281.
29. Toscano CM, Bell M, Zukerman C, et al. Gram-negative bloodstream infections in hematopoietic stem cell transplant patients: the roles of needleless device use, bathing practices, and catheter care. Am J Infect Control 2009;37:327–334.
30. Al-Harbi AH. Faecal coliforms in pond water, sediments and hybrid tilapia Oreochromis niloticus × Oreochromis aureus in Saudi Arabia. Aquaculture Res 2003; 34:517–524.
31. Kanamori H, Weber DJ, Rutala WA. Healthcare outbreaks associated with a water reservoir and infection prevention strategies. Clin Infect Dis 2016;62:1423–1435.
32. Suzuki TA, Worobey M. Geographical variation of human gut microbial composition. Biol Lett 2014;10:20131037.
33. Maki DG, Alvarado CJ, Hassemer CA, Zilz MA. Relation of the inanimate water reservoir and infection prevention strategies. Infect Control Hosp Epidemiol 2001;22:232–235.
34. Maki DG, Alvarado CJ, Hassemer CA, Zilz MA. Relation of the inanimate water reservoir and infection prevention strategies. Infect Control Hosp Epidemiol 2003; 34:517–524.
35. Maki DG, Alvarado CJ, Hassemer CA, Zilz MA. Relation of the inanimate water reservoir and infection prevention strategies. Infect Control Hosp Epidemiol 2009;30:517–524.
36. Maki DG, Alvarado CJ, Hassemer CA, Zilz MA. Relation of the inanimate water reservoir and infection prevention strategies. Infect Control Hosp Epidemiol 2012;33:917–921.
37. Maki DG, Alvarado CJ, Hassemer CA, Zilz MA. Relation of the inanimate water reservoir and infection prevention strategies. Infect Control Hosp Epidemiol 2014;35:232–236.
38. Maki DG, Alvarado CJ, Hassemer CA, Zilz MA. Relation of the inanimate water reservoir and infection prevention strategies. Infect Control Hosp Epidemiol 2015;36:232–236.