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## Original Article

# Nursing home-associated bloodstream infection: A scoping review

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**Abstract**

Objective: To update a 2005 review of nursing home–associated bloodstream infection (NHABSI) regarding sources, organisms, antibiotic resistance, and outcome.

Methods: A scoping review of studies of NHABSI identified by searching Google Scholar and Medline with OVID for the period January 1, 2004, to June 30, 2021, was conducted.

Results: Overall, 6 studies of NHABSI were identified. Only 1 study was conducted with residents in North American facilities whereas in the 2005 review all studies were conducted in North America. *Escherichia coli* was the most common blood isolate, the urinary tract was the most common source of NHABSI; and the case-fatality rates ranged from 21% to 28%. These findings were comparable to those in the 2005 review. However, the proportion of NHABSI episodes due to antibiotic-resistant organisms increased substantially compared to the 2005 review. The most common antibiotic-resistant organisms were extended-spectrum β-lactamase–producing *E. coli* and *Klebsiella* spp. The 2 studies that evaluated the relationship between appropriate empiric antibiotic therapy and outcome came to different conclusions.

Conclusions: The only major difference between the 2 reviews in the epidemiology of NHABSI was the marked increase in antibiotic resistance among blood isolates. Despite the increased antibiotic resistance, the case fatality rates in the current review were comparable to those reported in the 2005 review. However, the impact of appropriate empiric antibiotic therapy on outcome of NHABSI remains unclear.

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In 2005, a literature review spanning January 1, 1980, to August 31, 2003, identified 5 studies of nursing home–associated bloodstream infection (NHABSI).[1] Among them, 4 studies included residents from nursing homes in the United States[2–5] and 1 study involved residents of a single Canadian nursing home.[6] The study population comprised residents of a nursing home for military veterans in 3 studies,[3,4,6] residents of a single hospital-based nursing home,[2] and residents from multiple nursing homes admitted to the geriatrics unit of a public hospital.[5] The findings of this 2005 review can be summarized as follows: the incidence of bloodstream infection (BSI) was low (0.3 per 1,000 resident care days), the urinary tract was the most common source of BSI, and *Escherichia coli* was the most common organism causing BSI. Antibiotic resistance was uncommon overall among bloodstream insolates in these 5 studies; the most common antibiotic-resistant organism was methicillin-resistant *S. aureus* (MRSA).

The available research includes no update of the 2005 review of NHABSI.[1] Therefore, a scoping review was conducted (1) to identify studies of NHABSI published since 2005, (2) to compare the information on sources, organisms, antibiotic resistance, and outcomes of NHABSI to those reported in the 2005 review[1] and (3) to identify knowledge gaps that may need clarification.

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## Methods

For this scoping review, studies of NHABSI were identified by searching Google Scholar and Medline with OVID from January 1, 2004, to June 30, 2021. The following search terms were used in various combinations: nursing home, long-term care, skilled nursing facility, bacteremia, bloodstream infection, sepsis, and septicemia. Criteria for inclusion of studies in this review were (1) publication in English and (2) a focus exclusively on NHABSI (including letters to the editor with sufficient sample size) or (3) comparison of NHABSI with other categories of BSI (community-associated or hospital-associated BSI). References of studies included in this review were also evaluated to identify additional reports. Exclusions included (1) conference abstracts and (2) studies of BSI in geriatric hospitals or (3) studies of BSI in the elderly that included NHABSI but data for nursing home residents were not specifically reported.

## Results

The literature review identified 1 study[7] of NHABSI published in 2004 that covered the period 1995–1998 and was not included in the 2005 review[1] because that review included studies published between 1980 and 2003. The findings of this study[7] were consistent with studies in the 2005 review[1] and will not be discussed further. The literature review identified 6 studies published since 2005 that met the inclusion criteria[8–13]: 2 studies evaluated exclusively NHABSI[8,9] and 4 studies compared NHABSI to community- or hospital-associated BSI.[10–13]

### Studies that evaluated exclusively NHABSI

Table 1 summarizes the characteristics and findings of the 2 studies in which only NHABSI was evaluated. The study by Almog et al[8] was a letter to the editor and was included in this review because it evaluated a large number of cases of NHABSI (N = 177) and provided information on antibiotic resistance. This retrospective study of NHABSI included residents of 48 nursing homes in Israel who were admitted to 1 hospital from 2010 to 2014. A substantial percentage of residents had invasive devices (eg, urinary catheter, 35%; feeding tube, 11%). Microbiology information was limited, but 62% of the episodes were related to urinary tract infection. The important finding of this study was the high rate of resistance of gram-negative blood isolates. Among gram-negative blood isolates, 47% of *Enterobacteriaceae* produced extended-spectrum β-lactamase (ESBL), 55% were resistant to a fluoroquinolone, and 42% were resistant to gentamicin. The second study was a retrospective analysis with 107 episodes of BSI among nursing home residents admitted to 1 hospital in the United States between 2015 and 2018.[9] This study compared the outcomes of nursing home residents with BSIs due to multidrug-resistant organisms (MDROs) with the outcomes of nursing home residents with non-MDRO BSIs. Multidrug resistance was defined as resistance to at least 1 agent in 3 or more distinct antibiotic classes.[14] For gram-positive isolates, 57% met MDRO criteria; for gram-negative isolates, 35% were MDRO. The overall hospital mortality rate was 39%; the mortality rate among those with MDRO BSI was 49% compared to 30% among those with non-MDRO BSI. In a multivariate analysis, inappropriate empiric antibiotic therapy was not a significant predictor of mortality. However, the validity of the multivariate analysis is questionable due to the small study population and lack of information about invasive devices and sources of BSI.

### Studies that compared NHABSI to community- or hospital-associated BSI

Overall, 4 studies were identified that compared NHABSI with community- or hospital-associated BSI (Table 2).[10–13] The study population of the 4 studies differed: 2 studies included all episodes of BSI (community-, hospital-, and nursing home–associated)[10,12]; 1 study focused on those aged ≥ 65 years with community-BSI, hospital-BSI, and NHABSI[11]; and 1 study focused on those aged ≥65 years with community-onset BSI and NHABSI from a urinary tract source.[13] Only 1 study had a large sample size of NHABSI (N = 252 episodes);[11] in the other 3 studies, the number of episodes ranged from 57 to 77. None of the studies provided information on the use of devices or the presence of pressure ulcers in the study population. In terms of bacteriology, *E. coli* was the most common organism isolated in blood cultures in 3 studies that evaluated all episodes of BSI (27%–38%).[10–12] In 2 of these studies,[10,12] the urinary tract was the most common source of BSI. Also, 3 studies provided information about antibiotic resistance among bloodstream isolates.[10,11,13] In these studies, the occurrence rates of ESBL-producing *E. coli* and *Klebsiella* spp blood isolates were 14%,[10] 21%,[11] and 31%.[13] In 2 studies, MRSA BSI occurred in 44%[10] and 82%[11] of all *S.* aureus isolates, and MRSA BSI was not observed in the other studies.[12,13] The hospital mortality rates were similar in 2 studies, 24% and 26%,[10,12] whereasthe hospital mortality rate was low (8%) in the study by Gomez-Baldo et al,[13] which included only BSI related to urinary tract infection. In their retrospective study, Huang et al[11] stated that missing information regarding sources and outcome of BSI in many medical records precluded an assessment of these parameters.

### Comparison of the findings with the 2005 review

In the 2005 review,[1] all the studies were done in North America and were retrospective in design. In contrast, of the 6 studies published since 2005, only 1 was conducted in North America,[9] and 2 had a prospective design.[10,13]

### Sources

In the 3 studies that provided information on the source of NHABSI,[8,10,12] the urinary tract was the most common source, which is consistent with the findings of the 2005 review.[1]

### Bacteriology

Excluding the study by Gomez-Baldo et al,[13] which focused only on NHABSI from a urinary focus, in 4 of the remaining 5 studies, *E. coli* was the most common organism isolated in blood cultures.[8,10–12] *E.* coli was also the most common organism isolated in the 2005 review.[1] In the fifth study,[9] the most common blood isolate was *S. aureus*, but no information was provided regarding the antibiotic susceptibility of these isolates. Also, no information was provided regarding the presence of invasive devices or sources of BSI in this study,[9] nor did the authors provide an explanation for the predominance of *S. aureus* as a cause of NHABSI. In the 2005 review, the occurrence of *S. aureus* as a cause of NHABSI was low overall, 7%–13% of all episodes.[1]

### Antibiotic resistance

Minimal antibiotic resistance of blood isolates was reported in the 2005 review, and the most common antibiotic-resistant organism was MRSA.[1] In the present review, high rates of antibiotic resistance were documented in 5 of the 6 studies.[8–11,13] The main drug-resistant organisms were extended-spectrum β-lactamase–producing *E.coli* and *Klebsiella* spp in 4 studies.[8,10,11,13] The study by Aliyu et al[9] from the United States focused more generally on antibiotic-resistant organisms, with limited data on the type of resistance observed. However, they noted a high overall rate of multidrug-resistant organisms causing NHABSI for both gram-positive and gram-negative blood isolates.

### Mortality

In the present study, the mortality rate of NHABSI from all sources ranged from 21% to 28% in 3 studies.[8,10,12] In the 2005 review,[1] the mortality rates ranged from 18% to 22% in 4 of 5 studies.[3–6] Thus, despite the high rate of antibiotic resistance in 2 of the latest studies,[8,10] the mortality rate in the present review was comparable to that of the 2005 review. As in the 2005 review,[1] a urinary tract source of NHABSI had a low case-fatality rate.[8,13]

In the 2005 review,[1] 1 study[5] identified the following factors as independent predictors of mortality in residents with NHABSI: a pulmonary focus of BSI, systolic blood pressure <90 mm Hg on admission, and white cell count >20,000 cells/mm$^3$. In the present review, 2 studies investigated risk factors for mortality related to NHABSI. In a multivariate analysis, skin or soft-tissue infection, presence of a feeding tube, and inappropriate empiric antibiotic treatment were independent predictors of hospital mortality.[8] In contrast, Aliyu et al[9] did not find that inappropriate empiric antibiotic therapy was an independent predictor of mortality.

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**Table 1.** Studies That Focused Exclusively on Nursing Home-Associated Bloodstream Infection, 2004–June, 2021

| Characteristic | Almog et al[8,a] | Aliyu et al[9,b] |
|---|---|---|
| Country | Israel | United States |
| Study period | 2010–2014 | Jan 2015–Dec 2018 |
| Setting | 1 hospital | 1 hospital |
| Study population | NH residents from 48 NHs admitted to hospital | NH residents admitted to hospital |
| Design | Retrospective | Retrospective |
| No. of cases | 177 | 107 |
| Age, mean y | 82 | 68 |
| Sex | 55% male | 52% female |
| Polymicrobial BSI | NS | NS |
| **Devices** | | |
| Foley | 35% | NS |
| IV catheter | NS | |
| Feeding tube | 11% | |
| Pressure ulcer | NS | NS |
| **Organism** | | |
| *E. coli* | 41% | 14% |
| *Providencia* | | . . . |
| *Proteus* | | 13% |
| *K. pneumoniae* | | 6% |
| *Ps. aeruginosa* | | NS |
| *Enterobacter* sp | | NS |
| MSSA/MRSA | MRSA 3% | 24% total SAB |
| *S. pneumoniae* | | NS |
| *Enterococcus* | | 7% |
| CNS | | 8% |
| Other | | NS |
| **Sources** | | NS |
| Urinary tract | 62% | |
| SSTI | 7% | |
| Respiratory | 21% | |
| GI | NS | |
| Unknown | NS | |
| Other | NS | |
| Antibiotic resistance | 47% of Enterobacteriaceae produced ESBL;<br>quinolone R 55%;<br>gentamicin R 42% | GP BSI 57% MDRO<br>GN BSI 35% MDRO |
| Hospital mortality | 21% | 39% |
| | | MDRO BSI 49% |
| | | Non-MDRO BSI 30% |

Note. VA, Veterans' Affairs; NS, not stated; BSI, bloodstream infection; IV, intravascular; MSSA/MRSA, methicillin-sensitive *S. aureus*/methicillin-resistant *S. aureus*; CNS, coagulase-negative staphylococci; total SAB, total *S. aureus* bacteremia (including MSSA and MRSA); SSTI, skin or soft-tissue infection; GI, gastrointestinal; VRE, vancomycin-resistant enterococci; Ceftax R, ceftazidime resistant; ESBL, extended spectrum β-lactamase; GP BSI, gram-positive bloodstream infection; MDRO, multidrug-resistant organism; GN BSI, gram-negative bloodstream infection.
[a]Letter to the editor.
[b]Only studied bacteremia from the urinary tract.

However, this latter finding must be interpreted cautiously because this study did not take into consideration the source of BSI.[9] In the study by Yang et al[12] using logistic regression analysis, residence in a nursing home was associated with significantly lower hospital mortality. However, the latter finding must also be interpreted cautiously because only 57 cases of NHABSI were included in this study, and 40% were due to a urinary tract focus, which is associated with lower mortality than BSI.

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**Table 2.** Studies That Compared NHABSI to Community-Acquired or Hospital-Acquired BSI[a]

| Characteristic | Chazen et al[10] | Huang et al[11] | Yang et al[12] | Gomez-Baldo et al[13] |
|---|---|---|---|---|
| Country | Israel | Republic of China (Taiwan) | Republic of China (Taiwan) | Spain |
| Study period | 2001–2002 | May 2005–Jun 2008 | Jan 2005–Dec 2007 | Feb 2016–Dec 2016 |
| | 2005–2006 | | | |
| Setting | Adm to 1 hospital | Adm to 1 hospital | Adm to 1 community hospital | Adm to 5 hospitals |
| Study population | CA, HA, NHA BSI | Patients aged ≥65 y with CA, HA, NHA BSI | CA, HA, NHA BSI[a] | Elderly (≥65 y) with UTI BSI of CO or NH onset |
| Design | Prospective | Retrospective | Retrospective | Prospective |
| No. of cases | 2001–2002 and 2005–2006<br>Tot 755 and Tot 791<br>NH 34 and NH 43 | 190 residents with 252 episodes of BSI | Total cases = 222; 57 (26%) NHABSI | Total BSI = 181<br>CO BSI = 116<br>NHA BSI = 65 |
| Age, mean y | 76 and 81 | 81 | NS | 83 |
| Sex, male % | 53% and 37% | 43% | NS | 54% |
| Polymicrobial BSI | NS | NS | Excluded | 14% |
| **Devices** | NS | NS | NS | NS |
| Foley | | | | |
| IV catheter | | | | |
| Feeding tube | | | | |
| Pressure ulcer | NS | NS | NS | NS |
| **Organism, no. (%)** | 2001–2002 and 2005–2006 | | | |
| *E. coli* | 16 (47) and 13 (30) | 78 (27)[c] | 16 (28) | 44 (68) |
| *Providencia* | 0 and 0 | | | |
| *Proteus* | 3 (9) and 13 (30) | 12 (4) | 5 (9) | |
| *K. pneumoniae* | 3 (9) and 5 (12) | 19 (7) | 5 (9) | 0 |
| *Ps. aeruginosa* | 3 (9) and 3 (7) | 7/(2) | | 6 (9) |
| *Enterobacter* sp | 0 and 0 | | | 5 (8) |
| MSSA/MRSA | 5 (15) and 4 (9) | 6 (2)/28 (12) | MSSA 5 (9) | 3 (5) |
| *S. pneumoniae* | 1 (3) and 1 (2) | | | |
| *Enterococcus* | 1 (3) and 2 (5) | 13 (4) | | 3 (5) |
| CNS | 0 and 0 | 33 (12) | | |
| Other | 6 (5) and 4 (5) | 157 (40) | | |
| **Sources** | | NS | | |
| Urinary tract | 56% and 58% | | 23 (40) | 65 (100) |
| SSTI | 9% and 9% | | | |
| Respiratory | 9% and 9% | | 20 (35) | |
| GI | 3% and 5% | | | |
| Unknown | 3% and 14% | | | |
| Other | 20% and 4% | | | |
| Antibiotic resistance | *E. coli* 28/29 ESBL-<br>*Kleb* spp 50% ESBL+<br>*S. aureus* 5/9 MRSA | *E. coli* 18/78 ESBL+<br>*K pn* 4/19 ESBL+<br>NH residence associated with significant increase risk of MRSA and ESBL-producing Enterobacteriaceae BSI | No information about resistance for NHABSI isolates | ESBL-producing Enterobacteriaceae<br>15 (31%) |
| Mortality rate | 2001–2002[b] and 2005–2006[b]<br>NH 24% and 28%<br>CA 15% and 12%<br>HA 21% and 25% | NS | Overall hospital mortality, 104/222 (47%);<br>NHABSI 26%<br>CA BSI 34%<br>HA BSI 59% | 8%[b] |

Note. MDR, multidrug resistant, defined as resistance to all antibiotics in 3 or more antibiotic classes; Adm, admissions; CA, community associated; HA, hospital, associated; NHABSI, nursing home–associated bloodstream infection; Tot, total; NH, nursing home; MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; CNS, coagulase-negative staphylococci; SSTI, skin or soft-tissue infection; GI, gastrointestinal; Antib, antibiotic; *Kleb* spp, *Klebsiella* spp; NS, not stated; Pt, patients; *K pn*, *Klebsiella pneumoniae*; ESBL, extended-spectrum β-lactamase; HCO, healthcare onset; UTI, urinary tract infection; CO, community-onset.

[a]In this table, except for mortality, only data on nursing home -associated bloodstream infection is provided.

[b]Hospital mortality rate.

[c]Denominator is total number of isolates (N = 292).

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## Discussion

Between the 2005 review[1] and the present review of NHABSI, studies differed in design, sample size, and country of origin. Importantly, there are differences in the nursing home population between countries related to cultural factors and variation in how medical care is delivered. Nevertheless, some comparisons of the findings between the 2 reviews are notable. First, in both reviews, the urinary tract was the most common source of NHABSI and had the lowest mortality rate compared to all other sources of BSI. Second, antibiotic resistance, which was infrequently present in the studies in the 2005 review,[1] increased dramatically in the studies in the present review. This increase was mainly due to increasing resistance among *E. coli* and *Klebsiella pneumoniae* blood isolates due to the production of extended-spectrum β-lactamases. The trend in increasing antibiotic-resistant organisms causing NHABSI, especially among gram-negative bacteria, is consistent with the findings in nursing home studies demonstrating increasing rates of colonization with antibiotic-resistant organisms.[15–17] This trend is important for antibiotic stewardship activities in hospitals because all the studies of NHABSI have been conducted among hospitalized residents, as shown in both the 2005 review[1] and the present review. Third, the impact of appropriate empiric antibiotic therapy on outcome of NHABSI remains unclear. This factor was not explored in studies in the previous review,[1] and the 2 studies that evaluated appropriateness of empiric treatment in the present review had conflicting findings. Both studies had methodological limitations.[8,12]

In the 2005 review, 4 studies reported a low incidence of BSI (0.04–0.3 per 1,000 resident care days),[2–4,6] but it is difficult to apply these findings to community nursing homes because 3 of the 4 studies were conducted in Veterans' Administration facilities.[3,4,6] In addition, the study period of these 4 studies[2–4,6] was the 1980s, and the findings regarding incidence of NHABSI may not be relevant now. Thus, the true incidence of BSI in residents of community nursing homes remains unknown, and this is not likely to change. Only a small number of community nursing homes have the capability to perform blood cultures, and this procedure is not routinely recommended.[18]

The apparent low incidence of NHABSI and infrequent use of blood cultures in nursing homes overall creates the impression that BSI in nursing home residents is not a priority area for research in this population. However, further study of NHABSI may provide important insights into several areas for which data are limited. For example, the findings of this review found that mortality related to NHABSI has not changed in the past 3 decades or more. However, there are few modifiable risk factors for mortality in residents with NHABSI. A potential modifiable factor is the decision-making process regarding empiric antibiotic treatment. Based on the findings of the present review, it remains uncertain whether appropriate empiric treatment of NHABSI can improve outcome given the increasing importance of antibiotic-resistant organisms causing NHABSI in a population that is aged with significant chronic disease. Secondly, studying residents with NHABSI could be useful for evaluating the syndrome of sepsis in this population, for which information is very limited.[19]

To provide valid information, future studies of NHABSI need to be carefully designed. These suggestions regarding study design may benefit such efforts. First, studies should be prospective to avoid problems regarding identification of the source and outcome of NHABSI. Second, the level of debility of residents, such as utilizing measures of comorbidity and functional status, needs to be accounted for when assessing outcome. Third, as stated in a recent review,[20] acute severity of illness of residents with BSI needs to be defined because it may affect outcome independent of other factors such as duration of illness prior to hospital admission, source of infection, and appropriateness of empiric antibiotic treatment. For example, in a retrospective study of 169 episodes of NHABSI, 50% of all hospital deaths occurred within 3 days of hospital admission.[5] The impact of acute severity of illness and other factors on early mortality of NHABSI need to be explored more carefully to determine how they may influence outcome regardless of the appropriateness of empiric antibiotic treatment. Fourth, sources of NHABSI need to be carefully determined and accounted for because there is clearly a difference in outcome of NHABSI related to a urinary tract focus compared to a pulmonary focus. The increasing use of intravascular devices (eg, percutaneous intravenous central catheters and dialysis catheters) in nursing home residents must also be evaluated carefully as a source of BSI.[21] Fifth, the sample size must be large; studies with small sample size, as demonstrated in the present review, provide limited useful information about NHABSI. This factor is particularly important when evaluating the impact of antibiotic-resistant organisms on NHABSI outcomes. Sixth, only after controlling for the aforementioned factors and other potential confounding facility-level factors (eg, nursing home staffing levels, urban versus rural location, proprietary versus nonproprietary nursing homes, etc) can one perform a valid analysis of the impact of empiric antibiotic therapy on NHABSI outcomes.

In conclusion, the uncertainty regarding the impact of appropriate antibiotic therapy on outcome of BSI in nursing home residents and the limited information on sepsis in nursing home residents provides motivation to continue to the study NHABSI. However, whether interest and funding opportunities exist to conduct further studies of NHABSI remains to be determined, and those factors will have an impact on the prevention and management of this serious infection.

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