Edwardsiella tarda Bacteremia, Okayama, Japan, 2005–2016

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Edwardsiella tarda is primarily associated with gastrointestinal disease, but an increasing number of cases involving extraintestinal disease, especially E. tarda bacteremia, have been reported. Using clinical information of E. tarda bacteremia patients identified during January 2005–December 2016 in Japan, we characterized the clinical epidemiology of E. tarda bacteremia. A total of 182,668 sets of blood cultures were obtained during the study period; 40 (0.02%) sets from 26 patients were positive for E. tarda. The most common clinical manifestations were hepatobiliary infection, including cholangitis, liver abscess, and cholecystitis. Overall 30-day mortality for E. tarda bacteremia was 12%, and overall 90-day mortality was 27%. The incidence of E. tarda infection did not vary by season. We more frequently observed hepatobiliary infection in patients with E. tarda bacteremia than in patients with nonbacteremic E. tarda infections. E. tarda bacteremia is a rare entity that is not associated with high rates of death.
**Edwardsiella tarda**, a gram-negative, facultative anaerobe that is a member of the family *Enterobacteriaceae*, typically is isolated from water environments and animals that inhabit water. It is primarily associated with gastrointestinal disease, but the number of reports of extraintestinal disease, such as septicaemia, meningitis, cholecystitis, and osteomyelitis, has increased (7). However, little is known about the clinical epidemiology of *E. tarda* bacteremia. Therefore, we aimed to document the clinical epidemiology of *E. tarda* bacteremia, including common sources of infection, antimicrobial susceptibility, and seasonal distribution.

**Materials and Methods**

We retrospectively reviewed electronic medical records and clinical microbiology records in Kurashiki Central Hospital (Okayama, Japan), a 1,166-bed, tertiary-care hospital that provides care to ≈300,000 persons annually. Clinical specimens submitted to the microbiology laboratory included blood, sputum, urine, bile, ascites, feces, placenta, tissue, and pus. Information about identified bacteria and antimicrobial susceptibility were kept as microbiology laboratory records for each specimen. We considered bacteremia to exist when >1 set of blood cultures was positive. We identified all cultures growing *E. tarda* from clinical specimens submitted during January 2005–December 2016.

We processed blood culture samples using the BacT/Alert system (Sysmex bioMérieux Co. Ltd., https://www.biomerieux.com) and conducted microbial culture using KBM Chocolate HB Agar (Kohjin Bio Co. Ltd., http://www.kohjin-bio.jp/english), KBM Sheep Blood Agar (Kohjin Bio Co. Ltd.), and BTB agar (Kyokuto Pharmaceutical Co. Ltd., https://ssl.kyokutoseiyaku.co.jp/english/index.html). We used different bacterial identification and antimicrobial susceptibility testing methods in our hospital throughout the study period. We used ID test EB-20 Nissui (Nissui Pharmaceutical Co. Ltd., https://www.nissui-pharm.co.jp/english) for bacterial identification and Kirby–Bauer disk (Eiken Chemical Co. Ltd., http://www.eiken.co.jp) for antimicrobial susceptibility testing from January 2005 through June 2007. EB-20 is a system to identify glucose-fermenting gram-negative rods by 20 patterns of biochemical properties, using hydrogen sulfide, indole, lysine, ONPG (2-nitrophenyl-β-D-galactopyranoside), adonit, inositol, rhamnose, mannit, esculin, Voges–Proskauer, arginine, urea, inositol, sorbitol, arabinoose, phenylpyruvic acid, citric acid, ornithine, malonic acid, raffinose, and sugar. Thereafter, automatic systems were introduced at our hospital: DPS192 (Eiken Chemical Co. Ltd, http://www.eiken.co.jp) during July 2007–February 2013 and MicroScan WalkAway (Beckman Coulter, Inc, https://www.beckmancoulter.com/en) during March 2013–March 2014. Since April 2014, we have used MALDI Biotyper (Bruker Daltonics GmbH, https://www.bruker.com), using the manufacturer-provided database, for bacterial identification. We judged the drug susceptibility of a microorganism based on clinical breakpoints set by the Clinical and Laboratory Standards Institute; in particular, we used the document M100-S22 (2) during June 1, 2013–December 31, 2016.

We collected all clinical information of patients with positive *E. tarda* bacteremia results from electronic medical records, including age, sex, underlying diseases, source of infection, antimicrobial drug administered, treatment period, and outcome. We defined chronic kidney disease as a serum creatinine level of ≥2.0 mg/dL (reference range 0.65–1.07 mg/dL) and chronic liver disease as liver cirrhosis or chronic hepatitis B or C infection. We defined nosocomial bloodstream infection, healthcare-associated bloodstream infection, community-acquired bloodstream infection, and febrile neutropenia according to the previous study and guideline (3,4). We defined 30-day mortality as patient death within 30 days after the onset of *E. tarda* bacteremia and 90-day mortality as patient death within 90 days after onset. We also collected information of patients with *E. tarda* nonbacteremic infections.

We described the clinical characteristics and 30-day mortality of patients with *E. tarda* bacteremia, along with the source of infection and antimicrobial susceptibility. We then compared the characteristics of patients with *E. tarda* bacteremia by 30-day mortality. We also compared the characteristics of patients with bacteremic and nonbacteremic *E. tarda* infections. We also conducted an exploratory multivariable logistic regression analysis to investigate the risk for *E. tarda* bacteremia incidence among all *E. tarda* infections.

Because a previous literature review suggested seasonal variation in the occurrence of *E. tarda* bacteremia (5), we thus examined whether such variation or trend existed in the cases in our study by using Cochran-Armitage test. We tested dichotomous variables with Fisher exact test and continuous variables by Wilcoxon signed-rank test. Statistical analysis was performed using Stata version 15.1 (StataCorp, http://www.stata.com). We considered p<0.05 to be statistically significant.

The Ethics Committee of Kurashiki Central Hospital approved this study (no. 2,527). Only persons with appropriate authorization had access to participants’ records, and patient confidentiality was maintained. Given the nature of a retrospective chart review, written consent from the patients was waived.

**Results**

We obtained 182,668 sets of blood cultures during the study period, of which 19,234 sets were positive for some organisms and 40 sets from 26 patients were *E. tarda*–positive.
E. tarda bacteremia was diagnosed in 26 patients (13 men and 13 women); their median age was 75 years (range 45–101 years) (Table 1).

**Clinical Characteristics**

Some patients had ≥1 underlying disease: solid tumors (12 patients), cardiovascular diseases (4 patients), diabetes mellitus (3 patients), gallstone disease (3 patients), chronic liver disease (2 patients), cerebrovascular disease (2 patients), and hematologic malignancy (1 patient) (Table 1). Four patients had no underlying disease. Sites of solid tumors included pancreas (3 patients), gallbladder/bile duct (3 patients), colon (2 patients), and esophagus, gastric, liver, and thyroid (1 patient each). Of the 12 patients with solid tumors, 4 were receiving chemotherapy for their cancer when E. tarda bacteremia occurred.

Clinical diagnoses by the site of infection were cholangitis (9 patients); liver abscess (6 patients); enterocolitis (4 patients); cholecystitis (3 patients); and spontaneous bacterial peritonitis, mycotic aneurysm, necrotizing fasciitis, empyema, osteomyelitis, and secondary peritonitis (1 patient each) (Table 2). Seventeen patients had community-acquired bloodstream infections. The source of infection was not identified in 5 patients, including 1 with febrile neutropenia; 3 patients had nosocomial bloodstream infections, and 6 had healthcare-associated bloodstream infections.

Patients with E. tarda bacteremia were older and more likely to have solid tumors than were patients with E. tarda nonbacteremic infections (Table 3). In addition, we observed hepatobiliary infection, such as cholangitis and liver abscess, more frequently in patients with bacteremia.

Because the cohort included 26 E. tarda bacteremia patients, we conducted a multivariable logistic regression analysis adjusted with 2 explanatory variables. We hypothesized that underlying liver disease and old age could be associated with the incidence of E. tarda bacteremia and selected these 2 variables as the covariates. Our analysis

Table 1. Characteristics of patients with Edwardsiella tarda bacteremia, Kurashiki Central Hospital, Okayama, Japan, 2005–2016*

| Characteristic                          | Total, N = 26 | Survivors, n = 23 | Patients who died within 30 d after bacteremia onset, n = 3 | p value |
|----------------------------------------|--------------|------------------|-------------------------------------------------------------|---------|
| Median age, y (IQR) [range]            | 75 (63–85) [45–101] | 75 (64–85) [45–101] | 63 (30–87) [60–87] | 0.55 |
| Sex, no. patients                      |              |                  |                                                             |         |
| M                                      | 13           | 11               | 2                                                           | 1.00    |
| F                                      | 13           | 12               | 1                                                           |         |
| Underlying disease, no. patients       |              |                  |                                                             |         |
| Solid tumor                            | 12           | 10               | 2                                                           | 0.58    |
| Cardiovascular disease                 | 4            | 4                | 0                                                           | 1.00    |
| Diabetes mellitus                      | 3            | 3                | 0                                                           | 1.00    |
| Gallstone                              | 3            | 3                | 0                                                           | 1.00    |
| Chronic liver disease                  | 2            | 1                | 1                                                           | 0.22    |
| Cerebrovascular disease                | 2            | 2                | 0                                                           | 1.00    |
| Hematologic malignancy                 | 1            | 1                | 0                                                           | 0.00    |
| Chronic kidney disease                 | 0            | 0                | 0                                                           | NE      |
| Ulcerative colitis                     | 0            | 0                | 0                                                           | NE      |
| Crohn disease                          | 0            | 0                | 0                                                           | NE      |
| None                                   | 4            | 2                | 2                                                           | 0.052   |
| Other                                  | 0            | 0                | 0                                                           | NE      |
| Behavioral/dietary risk factors, no. patients |              |                  |                                                             |         |
| Alcoholism                             | 4            | 2                | 2                                                           | 0.052   |
| Exposure to raw food                   | 3            | 3                | 0                                                           | 1.00    |
| Exposure to fresh or marine water, animal feces | 1           | 1                | 0                                                           | 1.00    |
| Clinical diagnosis, no. patients       |              |                  |                                                             |         |
| Cholangitis                            | 9            | 9                | 0                                                           | 0.53    |
| Liver abscess                          | 6            | 6                | 0                                                           | 1.00    |
| Enterocolitis                          | 4            | 4                | 0                                                           | 1.00    |
| Cholecystitis                          | 3            | 3                | 0                                                           | 1.00    |
| Spontaneous bacterial peritonitis      | 1            | 0                | 1                                                           | 0.115   |
| Mycotic aneurysm                       | 1            | 1                | 0                                                           | 1.00    |
| Necrotizing fasciitis                  | 1            | 0                | 1                                                           | 0.115   |
| Empyema                                | 1            | 0                | 1                                                           | 0.115   |
| Febrile neutropenia                    | 1            | 1                | 0                                                           | 1.00    |
| Osteomyelitis                          | 1            | 1                | 0                                                           | 1.00    |
| Secondary peritonitis                  | 1            | 1                | 0                                                           | 1.00    |
| Focus unknown                          | 5            | 4                | 1                                                           | 0.49    |
| Receipt of chemotherapy for cancer     | 4            | 4                | 0                                                           | 1.00    |
| Median duration of treatment for infection, d (IQR) [range] | 12 (7–27) [1–77] | 13 (8–30) [1–77] | 5 (2–11) [2–11] | 0.084 |

*IQR, interquartile range; NE, not evaluated.*
Table 2. Clinical characteristics of 26 patients with Edwardsiella tarda bacteremia, Kurashiki Central Hospital, Okayama, Japan, 2005–2016*  

| Patient no. | Age, y/sex | Clinical diagnosis | Underlying disease | Treatment | Treatment duration, d | Concurrent organisms (source) | Outcome |
|-------------|------------|-------------------|--------------------|-----------|-----------------------|--------------------------------|---------|
| 1           | 77/M       | Focus unknown     | Cerebrovascular disease | LVX       | 3                     | E. coli, B. fragilis (pus)     | Recovered |
| 2           | 79/M       | Liver abscess     | Cardiovascular disease | CFP/SUL → IPM/CIL → PIP → MEP; CLI → MEM | 38                   | Recovered |
| 3           | 70/F       | Cholangitis, cholecystitis | None                  | CRO       | 8                     | Recovered |
| 4           | 87/M       | Focus unknown     | Hepatocellular carcinoma | FEP      | 11                    | Died at 12 d                   |
| 5           | 62/M       | Myotic aneurysm, liver abscess, osteomyelitis | Diabetes mellitus | IPM/CIL → AMP, GEN → SAM → VCM, PNP → VCS → PZX | 30                   | Died at 39 d                   |
| 6           | 92/F       | Focus unknown     | Colon cancer         | CRO       | 30                    | Died at 32 d                   |
| 7           | 89/F       | Focus unknown     | Colon cancer         | CRO       | 16                    | Recovered |
| 8           | 85/F       | Liver abscess, enterocolitis | Thyroid cancer  | MEM       | 21                    | Recovered |
| 9           | 88/F       | Cholangitis       | Cholangiocarcinoma   | CRO       | 7                     | Died at 40 d                   |
| 10          | 75/F       | Cholecystitis     | None                 | IPM/CIL → PZX | 3                  | Recovered |
| 11          | 101/F      | Cholangitis       | Cardiovascular disease | CFP/SUL → MEM → MI N → AMP, MIN | 77                   | E. faecalis, E. faecium, C. freundii, Bacteroides sp. (pus) | Recovered |
| 12          | 61/M       | Enterocolitis     | Gallbladder cancer, invasion of liver | CFP/SUL → MEM → LVX | 10                   | Recovered |
| 13          | 58/M       | Liver abscess     | Gallbladder cancer, invasion of liver | CFP/SUL → MEM → MI N → AMP, MIN | 77                   | E. faecalis, E. faecium, C. freundii, Bacteroides sp. (pus) | Recovered |
| 14          | 84/F       | Cholangitis       | Cardiovascular disease, cerebrovascular disease | CRO       | 6                     | Recovered |
| 15          | 83/F       | Cholangitis       | Pancreatic cancer    | CFP/SUL → MEM → LVX | 1                   | Recovered |
| 16          | 66/M       | Liver abscess     | Pancreatic cancer    | CFZ → LEX | 46                   | Recovered |
| 17          | 85/M       | Enterocolitis     | Cardiovascular disease | CRO → LVX | 12                   | Recovered |
| 18          | 64/F       | Enterocolitis     | Chronic liver disease, diabetes mellitus | CMZ → AMP  | 13                   | Recovered |
| 19          | 74/F       | Secondary peritonitis | Diabetes mellitus     | CMZ → TZP | 27                   | E. coli, K. pneumoniae, S. anginosus, F. nucleatum (ascites) | Recovered |
| 20          | 63/M       | Necrotizing fascitis | None                 | MEM, CLI  | 2                     | Died at 2 d                   |
| 21          | 45/F       | Liver abscess, cholangitis | Pancreatic cancer | CFP/SUL → AMP  | 31                   | S. anginosus (blood) | Died at 45 d |
| 22          | 65/M       | Cholangitis, cholecystitis | Gastric cancer     | CFP/SUL → AMP  | 13                   | S. gallolyticus (blood) | Recovered |
| 23          | 81/M       | Cholangitis       | Gallstone, esophageal cancer | CFP/SUL → AMP  | 16                   | Recovered |
| 24          | 64/M       | Cholangitis       | Cholangiocarcinoma, gallstone | CFP/SUL → AMP  | 8                    | Recovered |
| 25          | 59/M       | Focus unknown, febrile neutropenia | Peripheral T-cell lymphoma | CZO     | 12                   | Recovered |
| 26          | 60/F       | Spontaneous bacterial peritonitis, empyema | Chronic liver disease | TZP → AMP | 5                    | Died at 6 d                   |

*AMP, ampicillin; B. fragilis, Bacteroides fragilis; CFP/SUL, ceftoperazon–sulbactam; C. freundii, Citrobacter freundii; CFZ, cefozolin; CLI, clindamycin; CMZ, cefmetazole; CRO, ceftriaxone; CZO, cefozopran; E. faecalis, Enterococcus faecalis; E. faecium, Enterococcus faecium; E. coli, Escherichia coli; FEP, cefepime; F. nucleatum, Fusobacterium nucleatum; GEN, gentamycin; IPM/CIL, imipenem–cilastatin; K. pneumoniae, Klebsiella pneumoniae; LEX, cephalixin; LVX, levofloxacin; MEM, meropenem; MIN, minocycline; PNP, panipenem; PIP, piperacillin; PZX, pafloxacin; SAM, ampicillin sulbactam; S. anginosus, Streptococcus anginosus; S. gallolyticus, Streptococcus gallolyticus; Tx, treatment; TZP, piperacillin tazobactam. Arrows indicate the order of antimicrobial drugs used. Blank cells indicate no other concurrent organisms.

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suggested that age ≥65 years was significantly associated with an increased risk for *E. tarda* bacteremia incidence (odds ratio 2.70; 95% CI 1.11–6.55; *p* = 0.028). However, underlying chronic liver disease was not the risk factor for *E. tarda* bacteremia (odds ratio 2.48; 95% CI 0.41–14.99; *p* = 0.32).

**Treatment and Outcomes**

All *E. tarda* strains isolated from blood cultures were susceptible to all tested antimicrobial drugs. *E. tarda* bacteremia patients were treated with a variety of antimicrobial drugs according to the treating physicians’ discretion (Table 3). The median duration of treatment was 12 days (range 1–77 days). Overall 30-day mortality for *E. tarda* bacteremia was 12% (3/26) and overall 90-day mortality 27% (7/26).

Patient 4 had end-stage hepatocellular carcinoma and liver failure. On day 2 after admission, *E. tarda* bacteremia developed; the source of infection was unidentified. He was treated with cefepime and promptly became afebrile. *E. tarda* bacteremia was considered controlled by cefepime; however, the patient died of hepatic failure on day 11.

In patient 20, necrotizing fasciitis was diagnosed, and *E. tarda* was detected from wound and blood cultures. Although meropenem and clindamycin were administered, he died on day 2.

| Table 3. Comparison of characteristics of patients with bacteremic and nonbacteremic Edwardsiella tarda infection, Kurashiki Central Hospital, Okayama, Japan, 2005–2016* |
|-----------------------------------------------|-----------------|-----------------|-----------------|
| Patient characteristic                      | Patients with bacteremic infection, n = 26 | Patients with nonbacteremic infection, n = 124 | p value |
| Median age, y (IQR) [range]                 | 75 (63–85) [45–101] | 56 (12–73) [0–89] | <0.001 |
| Sex, no. patients                            |                      |                  | 0.178 |
| M                                           | 13                 | 82               |       |
| F                                           | 13                 | 42               |       |
| Underlying disease, no. patients             |                      |                  |       |
| Solid tumor                                  | 12                 | 22               | 0.004 |
| Cardiovascular disease                       | 4                  | 22               | 1.00  |
| Diabetes mellitus                            | 3                  | 13               | 1.00  |
| Gallstone                                    | 3                  | 13               | 1.00  |
| Chronic liver disease                        | 2                  | 7                | 0.65  |
| Cerebrovascular disease                      | 2                  | 1                | 0.078 |
| Hematologic malignancy                       | 1                  | 1                | 0.32  |
| Chronic kidney disease                       | 0                  | 1                | 1.00  |
| Ulcerative colitis                           | 0                  | 14               | 0.13  |
| Crohn disease                                | 0                  | 1                | 1.00  |
| None                                         | 4                  | 52               | 0.013 |
| Other                                        | 0                  | 2                | 1.00  |
| Behavioral/dietary risk factors, no. patients|                      |                  |       |
| Alcoholism                                   | 4                  | 9                | 0.24  |
| Exposure to raw food                         | 3                  | 7                | 0.38  |
| Exposure to fresh or marine water, animal feces| 1                  | 0                | 0.173 |
| Clinical diagnosis, no. patients              |                      |                  |       |
| Cholangitis                                  | 9                  | 8                | <0.001|
| Liver abscess                                | 6                  | 1                | <0.001|
| Enterocolitis                                | 4                  | 74               | 0.076 |
| Cholecystitis                                | 3                  | 9                | 0.44  |
| Spontaneous bacterial peritonitis            | 1                  | 0                | 0.173 |
| Myotic aneurysm                              | 1                  | 1                | 0.32  |
| Necrotizing fascitis                         | 1                  | 0                | 0.173 |
| Empyema                                      | 1                  | 0                | 0.173 |
| Febrile neutropenia                          | 1                  | 0                | 0.173 |
| Osteomyelitis                                | 1                  | 0                | 0.173 |
| Secondary peritonitis                        | 1                  | 0                | 0.173 |
| Focus unknown                                | 5                  | 1                | 0.001 |
| Endometriosis                                | 0                  | 1                | 1.00  |
| Appendicitis                                 | 0                  | 4                | 1.00  |
| Congenital infection                         | 0                  | 1                | 1.00  |
| Cystitis                                     | 0                  | 1                | 1.00  |
| Intraabdominal abscess                       | 0                  | 1                | 1.00  |
| Perianal abscess                             | 0                  | 1                | 1.00  |
| Pneumonia                                    | 0                  | 2                | 1.00  |
| Pyometra                                     | 0                  | 1                | 1.00  |
| Secondary peritonitis                        | 0                  | 2                | 1.00  |
| Superficial surgical site infection          | 0                  | 1                | 1.00  |
| Receipt of chemotherapy for cancer, no. patients| 4                  | 7                | 0.099 |
| Median duration of treatment for infection, d (IQR) [range] | 12 (7–27) [1–77] | 5 (3–9) [0–36] | <0.001 |

*IQR, interquartile range.*
Patient 26, who had end-stage alcoholic liver cirrhosis, was admitted for massive pleural effusion and ascites. *E. tarda* was detected from pleural effusion but not from ascites. Empyema and spontaneous bacterial peritonitis caused by *E. tarda* were diagnosed. Although these fluids were drained and antimicrobial drugs were given, she died on day 5.

Patient 5 was admitted for evaluation of fever and back pain. Blood cultures drawn on admission day revealed *E. tarda*, and he was treated with imipenem–cilastatin. However, his fever persisted. Computed tomography scan of the chest and abdomen revealed mycotic thoracic aneurysm, liver abscess, and vertebral osteomyelitis. He was treated with multiple antimicrobial drugs but died of a ruptured mycotic aneurysm on day 39.

In patients 6, 9, and 21, *E. tarda* bacteremia developed and improved with antimicrobial therapy. However, these patients died of underlying diseases.

**Seasonal Variation in *E. tarda* Bacteremia**

The incidence of *E. tarda* infection did not vary by season (Figure). We found no trend of *E. tarda* bacteremia incidence among all *E. tarda* infections when we examined them by month (p = 0.46) or by season, defined as a set of 3 months (p = 0.53).

**Discussion**

*E. tarda* is associated with freshwater and marine life, including fish, reptiles, and amphibians (1). The organism resembles *Salmonella* biochemically and clinically (1). *Salmonella* usually ferments D-mannitol, urease, oxidase, and D-sorbitol, whereas *E. tarda* produces hydrogen sulfide and indole (6).

*E. tarda* is a rare human pathogen and is primarily associated with gastrointestinal diseases, including the asymptomatic carrier state (1). Approximately 80% of infections are intestinal. *E. tarda* causes a *Salmonella*-like gastrointestinal infection, usually self-limited enteritis, with intermittent watery diarrhea and low-grade fever (1,7).

The pathogenesis of *E. tarda* and its disease-causing mechanism remain unclear. Twelve classes of bacterial protein secretion systems are known; these systems transport virulence proteins into the cell and, in some cases, directly into the cytoplasm of a target cell (8). The bacterial type III and type VI secretion systems (T3SS and T6SS) are believed to play an essential role in *E. tarda* survival, replication, and virulence inside the host. In particular, T6SS is proposed to enable *E. tarda* to establish inside the host, cause severe systemic infection, and eventually kill the host.

We reviewed 26 cases of *E. tarda* bacteremia. Clinical diagnoses included 15 (58%) biliary tract infections (cholangitis, cholecystitis, and liver abscess). Eight of these patients had hepatobiliary diseases including cholangiocarcinoma, gallbladder cancer, pancreatic cancer, gallstone disease. Therefore, hepatobiliary diseases may be a predisposing factor of *E. tarda* biliary tract infections. However, our multivariable logistic regression found that only age ≥65 years was associated with the incidence of *E. tarda* bacteremia. We acknowledge that the sample size of our study and the number of *E. tarda* bacteremia incidence were still small, and thus the finding from our multivariable analysis might be only exploratory.

Previous studies reported high rates of death for *E. tarda* bacteremia, ranging from 22.7% to 44.6% (1,5,9). In contrast, the death rate for patients with *E. tarda* bacteremia in the cohort reported here was low at 12%. However, 2 of these 3 patients had end-stage liver disease; only 1 death among these patients was attributed to *E. tarda* bacteremia.

*E. tarda* is susceptible to most antimicrobial drugs, including tetracyclines, aminoglycosides, quinolones, antifolates, chloramphenicol, nitrofurantoin, fosfomycin, and most β-lactams (10), and is naturally resistant to benzylpenicillin, colistin, and polymyxin B (1,11). In our study, *E. tarda* was susceptible to most commonly used antimicrobial drugs. *E. tarda* susceptibilities to colistin and polymyxin B are unknown because susceptibility testing is not routinely performed for these drugs in our institution. Previous studies have shown that all strains of *E. tarda* were positive for β-lactamase production examined with nitrocefin β-lactamase disks, but an ampicillin-resistant *E. tarda* strain has not been reported (10,11). Whether *E. tarda* isolates detected in our institution produced β-lactamase is not clear because we did not perform the β-lactamase test, but 5 cases were successfully treated with ampicillin.
Hirai et al. suggested that *E. tarda* bacteremia is likely to develop during summer and autumn months in the Northern Hemisphere (8). The authors conducted a literature review of 77 *E. tarda* bacteremia cases reported from diverse areas and suggested seasonal variation in incidence for 22 cases. Our study of 26 *E. tarda* bacteremia cases suggests no such seasonal distribution. Several possible reasons might account for this discrepancy. First, *E. tarda* can colonize. In our study, hepatobiliary infection (such as cholangitis, cholecystitis, and liver abscess) was diagnosed in 58% (15/26) patients, and patients colonizing *E. tarda* developed *E. tarda* bacteremia. Second, diversity might exist in the patients’ dietary patterns. *E. tarda* frequently infects fish. Hirai et al. included patients from many parts of the world, so the intake of fish might have differed according to the season or geographic area across reports. In contrast, our study included only people in a single area of Japan who habitually ate raw seafood, such as sashimi, throughout the year; this tendency might have led to no seasonal variation of *E. tarda* bacteremia incidence. Third, our study had no missing clinical data for any patients, whereas Hirai et al. examined 22 of all 77 eligible patients, which might have rendered their analysis vulnerable to information bias.

Our study had some strengths. First, we elucidated that no seasonal variation existed in *E. tarda* bacteremia in this population. Second, we described the characteristics of each patient with *E. tarda* bacteremia and provided risk factors for *E. tarda* bacteremia incidence among all *E. tarda* infections.

Our study also had some limitations. First, the number of blood cultures submitted increased in recent years in our hospital. The number of blood cultures submitted in 2016 nearly doubled that for 2005. This increase might have resulted in the underestimation of *E. tarda* bacteremia in the earlier years of our study period. Second, ours was a retrospective and single-center study. However, our study had no missing data regarding clinical information. Furthermore, we successfully presented a particularly large case series of *E. tarda* bacteremia.

In conclusion, *E. tarda* bacteremia is a rare disease that is not associated with high rates of death. *E. tarda* bacteremia patients in our cohort in Japan had more severe underlying diseases, such as hepatobiliary disease and solid tumors, than did patients in previous studies. Hepatobiliary infections, such as cholangitis, cholecystitis, and liver abscesses, are the most common clinical manifestations in patients with *E. tarda* bacteremia. The major underlying diseases in this study were hepatobiliary diseases and malignancy. Furthermore, *E. tarda* strains we isolated were susceptible to most antimicrobial drugs, including β-lactams, aminoglycoside, tetracycline, fosfomycin, fluoroquinolone, and trimethoprim/sulfamethoxazole, and *E. tarda* bacteremia was successfully treated with ampicillin. Finally, we observed no seasonal distribution of *E. tarda* bacteremia. Risk factors for *E. tarda* bacteremia—related death remain to be investigated.

About the Author
Dr. Kamiyama is the medical director at Kurashiki Central Hospital. His primary research interests include cytomegalovirus infections in critically ill patients and transplant patients.

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