Risk factors of fecal colonization with extended-spectrum β-lactamase-producing Enterobacteriaceae in special nursing homes in Japan

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Abstract
Objective: Japanese welfare facilities for the elderly are called as special nursing home (SNH), providing conventional-type with group care or unit-type with individual care. We investigated the risk factors of fecal colonization with extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-E) of elderly who required care at SNH in Japan.

Methods: The feces discharged on diaper were obtained from the total of 100 residents with fecal incontinence in 9 SNHs located in Tokyo, Japan. The samples were cultured on ESBL selection agar, and ESBL-E were determined by the antimicrobial susceptibility test and genetic analysis. The status of the residents and the characteristics of facilities, especially about the incontinence care, were obtained by questionnaire methods. Statistical analysis was performed to determine the factors related to carriage of ESBL-E.

Results: Extended-spectrum β-lactamase-producing Enterobacteriaceae was isolated from 53 of 100 SNH residents. Risk factors of colonization among the individual residents were not found. The prevalence of ESBL-E carriage was significantly higher in the 6 conventional-type facilities than in the 3 unit-type facilities (P = .015). The cart for diaper exchange was used in 5 of 6 conventional-type facilities in 9 SNHs, and their residents tended to show high of ESBL-E colonization rate. The residents living in unit-type facilities which do not use gloves for changing diaper tended to show high ESBL-E colonization rate than other 2 facilities using gloves.

Conclusions: It is suggested that using the cart for changing diaper has relation to carry ESBL-E. In the facilities using cart, revision of their methods of excretion care will be needed.

Keywords
elderly, extended-spectrum β-lactamase-producing Enterobacteriaceae, facility types, fecal carriage, geriatrics, infection, Japanese special nursing home, nursing care, risk factor
1 | INTRODUCTION

Extended-spectrum β-lactamase-producing Enterobacteriaceae is an emerging infectious species raising global concerns.\textsuperscript{1-6} Many Enterobacteriaceae species are part of the endogenous bacterial flora of the intestinal tract in humans, which poses a challenge in efforts to prevent spread of ESBL-E as part of healthcare-related infection control.

It was reported that the isolation rate of cefotaxime-resistant Escherichia coli from clinical samples at Japanese medical institutions had increased from 1% in 2000 to 12.9% in 2014.\textsuperscript{17} Furthermore, the isolation rate of ESBL-E was higher in inpatients than in outpatients, although an increase over time was observed in both patient groups.\textsuperscript{9} Japan Nosocomial Infections Surveillance under the jurisdiction of the Ministry of Health, Labor, and Welfare (JANIS) was launched in 2000, but the surveillance system remains nonexistent at care facilities for the elderly.

Publicly run care facilities for the elderly are categorized into 3 types based on the medical dependency and admission purpose of residents: sanatorium medical facilities, long-term healthcare facilities for the elderly, and special nursing homes for the elderly (SNH, welfare facilities, sanatorium medical facilities, long-term healthcare facilities for the elderly).\textsuperscript{10} Of these, SNHs admit people who have difficulties living at home and become living places as an alternative to home. A study investigating the colonization risk of ESBL-E found that old age, need for nursing care, being bedridden, history of antimicrobial use, history of hospitalization, and diabetes were among the risk factors for colonization.\textsuperscript{11-15} Thus, residents of SNH are estimated to be particularly at high risk of ESBL-E colonization.

Japanese SNH has 2 different types based on its structure: conventional-type and unit-type facilities. Conventional-type facilities generally consist of multibed rooms with 2 to 4 residents in 1 room, and a team of several caregivers assists their activity of daily living, such as eating and taking a bath. Excretion care at conventional-type facilities is also often performed on a set time schedule, and to efficiently provide care for multiple residents, conventional-type facilities use diaper carts loaded with unused clean instruments as well as used soiled instruments. In contrast, at unit-type facilities, approximately 9 residents are housed in individual rooms in a single unit, to which 1 or 2 caregivers are assigned. The resident’s living environment is similar to home, and the care is performed in accordance with each resident’s character and life rhythm. In addition, a single caregiver provides one-on-one care to each resident and can change diapers at each excretion by the residents without using diaper carts. The aims of this study were to reveal the prevalence and types of ESBL-E in feces of elderly residents in Japanese SNHs and the risk factors of ESBL-E colonization, including personal factors, facility factors, and excretion care methods.

2 | MATERIALS AND METHODS

2.1 | Samples collection and ESBL-E screening culture

The samples of feces discharged on diaper were obtained from the total of 100 residents who were bedridden and using diaper for fecal incontinence in 9 SNHs located in Tokyo, Japan, between August and December in 2015. The feces discharged on diaper were sampled in the sterile tube and were cultured on ChromID ESBL agar (SYSMEX bioMerieux, France) for screening of ESBL-E within 6 hours after sampling. The colonies on the agar were isolated on Drigalski agar. All strains with different morphotypes were identified by MALDI-Biotyper, with methodology of the matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Germany). This study had the approval of the ethics committee of Faculty of Health Care and Nursing, Juntendo University with approval number 27-15. The written consents from the residents and/or substitute family for them and the president of SNH were obtained.

2.2 | Antimicrobial susceptibility test

For ESBL-E, E. coli, Klebsiella spp., and Proteus mirabilis isolated by screening culture, antimicrobial susceptibility tests for screening were performed using Dry-plate DP31 (Eiken Chemical, Japan) including 18 antimicrobials: piperacillin, ceftazolin, cefotiam, cefotaxime, ceftazidime, cefepime, flomoxef, cefpodoxime, sulbactam/amoxicillin, aztreonam, imipenem, meropenem, gentamicin, amikacin, sulfamethoxazole-trimethoprim, fosfomycin, minocycline, and levofloxacin. For confirming ESBL-E, Dry-plate DPD1 (Eiken Chemical, Japan) including cefotaxime, ceftazidime and cefpodoxime (with and without clavulunate for each of them), and ciprofloxacin was used following the instruction manual. ESBL-E was determined by the criteria of Clinical and Laboratory Standards Institute.\textsuperscript{16}

2.3 | Genetic analysis

For extracting DNA from ESBL-E, Cica Geneus DNA Extraction Reagent (Kanto Kagaku Co. Ltd., Japan) was used according to the manufacturer’s protocol. β-lactamase genes, such as CTX-M, TEM, SHV, OXA, IMP, KPC, and VIM, were investigated using PCR methods as previously described.\textsuperscript{17,18} The CTX-M genes were identified by sequencing and Basic Local Alignment Search Tool search. Complete sequence match with known CTX-M could be accepted as identification of CTX-M.

2.4 | Questionnaire methods

The status of the residents and the characteristics of SNHs were obtained by questionnaire methods. The questionnaire was composed of following contents: age, gender, required care level, urinary catheter placement, previous history of urinary tract infection, previous use of antimicrobials in the previous 3 months, and previous hospitalization within 1 year before sampling of stool. For SNHs, information of capacity, type of facility (conventional-type or unit-type), procedure of excretion care such as wearing personal protective equipment, frequency and timing of diaper change, using cart and role assignment for changing diaper, were obtained from the caregivers or the nurses in charge.
2.5 Statistical analysis

Characteristics of the residents and SNHs of the ESBL-E carriers were compared with those of the noncarriers. The statistical analysis was performed using IBM SPSS ver.19. For univariate analysis, Chi-square test or Fisher's exact test was used for categorical variables, and a P-value of < .05 was considered as significant. Multivariate analysis using logistic regression analysis with stepwise method was performed to evaluate the risk factors of ESBL-E carriage. Odds ratios (OR) and 95% confidence interval (CI) were calculated.

3 RESULTS

3.1 Detection of ESBL-E

A total of 57 ESBL-E strains were detected in the fecal samples of 100 residents (53.0%) living in 9 SNHs in the Tokyo metropolitan area. The following bacterial species were isolated from the residents; E. coli (n = 46), K. pneumoniae (n = 1), K. oxytoca (n = 2), and P. mirabilis (n = 8).

Extended-spectrum β-lactamase-producing Enterobacteriaceae exhibited resistance to a high percentage of fluoroquinolones, with 97% of ciprofloxacin and 88% of levofloxacin, 95% of fourth-generation cephalosporins, and 75% of monobactams. Meanwhile, all detected ESBL-E were susceptible to carbapenems.

Of the 57 strains identified as ESBL-E, 54 strains (94.7%) possessed CTX-M. Specifically, CTX-M (n = 44), CTX-M + OXA (n = 1), CTX-M + SHV (n = 1), and CTX-M + TEM (n = 8) were found by PCR, respectively. Among the 54 strains with CTX-M, 36, 9, and 8 strains belonged to the CTX-M-9, CTX-M-1, and CTX-M-2 groups, respectively, whereas the group was not identified in 3 CTX-M strains. One strain was assigned to both of CTX-M-9 group and CTX-M-1 group (Figure 1). One strain possessed TEM alone, and no β-lactamase gene could be found in 2 strains.

FIGURE 1 Percentage of CTX-M group typing of extended-spectrum β-lactamase-producing Enterobacteriaceae (n = 54) isolated from special nursing home residents.

3.2 Personal factors for colonization with ESBL-E

Table 1 shows the relationship between personal factors collected from questionnaires and detection of ESBL-E. ESBL-E were detected at a significantly higher rate among the residents of conventional-type facilities than among the residents of unit-type facilities in detail. 45 of 75 residents (60%) at conventional-type facilities and 8 of 25 residents (32%) at unit-type facilities carried ESBL-E (P = .015). In other factors, no significant differences were observed between the ESBL-E carriers and noncarriers.

3.3 Characteristic of facilities participated in this study

Table 2 describes the characteristics of the facilities included in this study. No differences in basic characteristics of study participants were observed between the residents of the 2 facility types, except for mean age and mean length of SNH stay.

The percentage of ESBL-E carriers was significantly higher among the residents of convention-type facilities, as mentioned above, but the percentage of the carriers varied from 25% to 100% among convention-type facilities, and from 22% to 66% among unit-type facilities.

The procedures of changing diapers also varied among the facilities. All 6 conventional-type facilities carried out scheduled rounds for changing diapers several times a day, and the 5 facilities (83.3%) used diaper carts, loading clear unused materials and trash boxes to discard used diapers as well. All the conventional facilities used disposable gloves when they changed diapers, but in contrast, all 3 unit-type facilities did not use diaper carts and tended not to use personal protective equipment for changing diapers, even though a facility which did not use any protective equipment seemed to show relatively higher percentage of ESBL-E carriers.

4 DISCUSSION

This study found that 53% of residents among Japanese SNH residents in need of nursing care carried ESBL-E, with CTX-M as the major ESBL type. The prevalence of ESBL-E carriers was significantly higher among residents living in convention-type facilities.

The prevalence of ESBL-E among SNH residents in this study was reasonable, compared with the previous studies investigating facility residents, ranging widely from 3.4% to 71.6%. However, compared with the 12.9% isolation rate of cefotaxime-resistant E. coli in clinical samples reported in the 2014 surveillance of medical institutions in Japan, the prevalence of ESBL-E carriers was higher...
among the participants of our study.\textsuperscript{7} Fecal incontinence and need of nursing care were recognized as related factors for colonization with ESBL-E, so the participants of this study reflected high-risk population of ESBL-E carriage.\textsuperscript{2,13}

The 2007 Guideline for Isolation Precautions issued by the US Centers for Disease Control and Prevention states that ESBL-E is the subject to implement contact precautions.\textsuperscript{20} Among the subjects investigated in this study, none of the carriers of ESBL-E exhibited infection symptoms; thus, these carriers usually do not have chance of bacterial testing at the time of hospitalization with causes unrelated to infection. However, medical institutions should anticipate the possibility of colonization with resistant bacteria in hospitalized residents of SNH, based on the high prevalence of ESBL-E carriers among the residents of long-term care facilities, for successful prevention of their nosocomial spread.\textsuperscript{21}

The major ESBL-coding gene in Japan is CTX-M,\textsuperscript{4,8,9,17,22-26} and in this study, CTX-M was found in 94.7\% of ESBL-E. The most prevalent CTX-M type found in each facility was different from each other. Furthermore, detection rates and CTX-M types of ESBL-E differed between facilities, raising concerns of the possibility of horizontal transmission in each facility. Future studies using molecular epidemiological analysis are needed to verify horizontal transmission within facilities.

Among the SNH residents investigated in this study, few had used antimicrobials within a year and no relationship between antimicrobial use and ESBL-E carriage was found. However, third-generation cephalosporins and fluoroquinolones accounted for the majority of the antimicrobials used in the present study (date not shown). It is known that prescription of fluoroquinolones for treatment of SNH applies selective pressure and may increase resistance to fluoroquinolones.\textsuperscript{6,19,21} The ESBL-E detected in this study showed resistance to several antimicrobials, including β-lactams and fluoroquinolones, suggesting that fluoroquinolone resistance is becoming the norm for ESBL-E. Unnecessary use of third-generation cephalosporins and fluoroquinolones should be avoided not to increase ESBL-E among residents in SNH.\textsuperscript{27,28}

Our results did not identify personal risk factors of SNH residents for colonization with ESBL-E. In addition to old age and need for nursing care, personal risk factors of colonization with ESBL-E include use of antimicrobials in the last 3 months, previous history of hospitalization in the last year, indwelling urinary catheter, previous history of urinary tract infection, and diabetes.\textsuperscript{2,11-15} Dementia is also a risk factor of carrying multidrug-resistant organisms.\textsuperscript{21,29} The small number of study participants with such complicated risk factors in this study was likely to underlie our findings.

We found that colonization with ESBL-E was significantly more frequent among the residents of conventional-type facilities (60\%) than those resided at the unit-type facilities (32\%). Diaper carts are used in the most of conventional-type facilities in this study and good for the efficiency of excretion care for groups, but are likely linked to the spread of ESBL-E. A study on colonization with ESBL-E in nursing homes in Sweden found that 11\% of nursing home residents living in individual rooms carried ESBL-E.\textsuperscript{30} Our results support

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**TABLE 1** Risk factors of ESBL-E colonization for residents living SNH

| Risk Factor                        | Positive (n = 53) | Negative (n = 47) | OR  | (95% CI) | P value |
|------------------------------------|-----------------|-----------------|-----|---------|---------|
| Gender (men), n (%)                |                 |                 |     |         |         |
| Age (<80-y)                        | 10 (19\%)       | 6 (13\%)        | 1.22| (0.79-1.88) | .41     |
| Indwelling urinary catheter        | 2 (4\%)          | 1 (2\%)         | 1.27| (0.56-2.89) | 1.00    |
| Previous history of UTI            | 7 (13\%)         | 6 (13\%)        | 1.02| (0.59-1.75) | .95     |
| Previous use of antimicrobials within 3 mo | 7 (13\%) | 11 (23\%) | 0.50 | (0.18-1.41) | .19     |
| Previous hospitalization within 1 y | 13 (25\%)       | 9 (19\%)        | 1.15| (0.77-1.76) | .52     |
| Length of SNH stay (<24 mo)        | 18 (34\%)        | 21 (45\%)       | 0.80| (0.54-1.20) | .27     |
| Comorbidity                        |                 |                 |     |         |         |
| Diabetes mellitus                  | 7 (13\%)         | 5 (11\%)        | 1.12| (0.67-1.87) | .69     |
| Cardiac diseases                   | 14 (26\%)        | 8 (17\%)        | 1.27| (0.87-1.87) | .26     |
| Cerebrovascular disease            | 14 (26\%)        | 14 (30\%)       | 0.92| (0.60-1.42) | .71     |
| Musculoskeletal disorder           | 16 (30\%)        | 14 (30\%)       | 1.01| (0.68-1.51) | .97     |
| Urogenital disease                 | 4 (8\%)          | 3 (6\%)         | 1.09| (0.56-2.12) | 1.00    |
| Pressure ulcer                     | 3 (6\%)          | 0 (0\%)         | 1.94| (1.60-2.35) | .25     |
| Gastrogavage                       | 6 (11\%)         | 3 (6\%)         | 1.29| (0.78-2.13) | .50     |
| Type of facility for living resident|                |                 |     |         |         |
| Conventional-type (6 facilities; n = 75) | 45 (60\%) | 30 (40\%) | 1.88| (1.03-3.42) | .015*   |

CI, confidence interval; ESBL-E, extended-spectrum β-lactamase-producing Enterobacteriaceae; OR, odds ratio; SNH, special nursing home.

\*P value < .05.
### Table 2  Characteristic of facilities participated in this study

| Facility ID | Type of facility | Conventional-type | Unit-type |
|-------------|-----------------|-------------------|-----------|
|             | A               | C                 | D         | E         | G         | H         | Total     | B         | F         | I         | Total     |
|             | Capacity of facility (beds) | 70 | 50 | 90 | 100 | 54 | 80 | 444 | 120 | 52 | 93 | 265 |
|             | Number of participants of this study (%) | 31 (44) | 2 (4.0) | 8 (8.9) | 13 (13) | 9 (17) | 12 (15) | 75 (17)* | 10 (8.3) | 9 (17) | 6 (6.5) | 25 (9.4)* |
|             | Number of participants of ESBL-E colonization (%) | 24 (77) | 2 (100) | 2 (25) | 8 (62) | 4 (44) | 5 (42) | 45 (60) | 6 (66) | 2 (22) | 0 (0.0) | 8 (32) |
|             | Mean age of participants (±SD) | 88.4 ± 6.8 | 83.0 ± 7.1 | 86.5 ± 7.9 | 90.5 ± 7.4 | 89.1 ± 4.5 | 85.6 ± 8.9 | 88.1 ± 7.2* | 85.5 ± 9.2 | 86.3 ± 11.8 | 88.5 ± 10.5 | 86.5 ± 10.1* |
|             | Mean of required care level of participants | 4.9 | 5 | 5 | 5 | 4.7 | 4.3 | 4.81 | 4.9 | 4.8 | 4.5 | 4.76 |
|             | Mean length of SNH stay (months, ±SD) | 31.9 ± 35.5 | 51.5 ± 29.0 | 26.0 ± 11.3 | 46.5 ± 34.8 | 56.0 ± 23.5 | 41.3 ± 38.4 | 38.7 ± 33.2* | 53.0 ± 47.1 | 69.3 ± 43.2 | 31.2 ± 30.5 | 53.6 ± 43.2* |
|             | Number of methods of changing diaper implemented (%) | 3 (100) | 1 (33) | 3 (100) | 3 (100) | 2 (67) | 3 (100) | median 3 (83) | 0 (0) | 1 (33) | 2 (67) | median 1 (33) |
|             | Timing on schedule | Y | Y | Y | Y | Y | Y | Y | 6 (100) | Y | Y | 1 (33) |
|             | Assignment to particular staff | Y | Y | Y | Y | Y | Y | 4 (67) | Y | Y | 2 (67) |
|             | Using of diaper cart | Y | Y | Y | Y | Y | Y | 5 (83) | 0 (0) |
|             | Number of infection prevention practices implemented (%) | 4 (100) | 2 (50) | 1 (25) | 2 (50) | 3 (75) | 3 (75) | median 3 (63) | 0 (0) | 1 (25) | 2 (50) | median 1 (25) |
|             | Wearing gloves | Y | Y | Y | Y | Y | Y | 6 (100) | Y | Y | 2 (67) |
|             | Wearing apron | Y | Y | Y | Y | 4 (67) | 0 (0) |
|             | Wearing mask | Y | Y | 2 (33) | Y | 1 (33) |
|             | Carrying hand antiseptic | Y | Y | Y | 3 (50) | 0 (0) |

In long-term care insurance in Japan, 8 daily living care categories are used to certificate the needs of care level for the elderly: "long-term care level" 1-5, "support level" 1 and 2, and "not certified." The elderly in bedridden status, with dementia, etc., are certified as "long-term care level" and require long-term care services, especially the elderly in "long-term care level 5" need care at all of the activity of daily living.

SD, standard deviation; SNH, special nursing home; Y, yes.

*P value < .05.
the efficacy of unit-type facilities to prevent ESBL-E colonization in Japan, as well.

Wearing personal protective equipment is recognized as a standard precaution to handle excreted materials. Actually, only staff at conventional-type facilities used diaper carts, carried hand sanitizers, and wore aprons during diaper exchange, whereas these practices were not used at unit-type facilities, even though conventional-type facilities showed higher percentage of ESBL-E carriers than unit-type facilities. The higher carriage rate in conventional-type facilities suggests that the use of personal protective equipment and hand sanitizers do not have sufficient effects to prevent transmission of ESBL-E in SNH. Considering these results, the structure of the multibed conventional-type facility and use of carts for changing diaper seem to have large influence on the transmission ESBL-E because of the excretion care for the residents is performed continuously. Further evaluation of the effectiveness of strict space isolation of each resident in conventional-type facilities is necessary for the future. As the essential basis, staff must have appropriate knowledge and skills of standard precaution that are paramount for infection control under limited number of staff and structures; referring nursing care methods, elimination of shared instruments, proper implementation of hand hygiene, and personal protective equipment because 1 unit-type facility without any precautions showed relatively higher carriage rate than other unit-type facilities.15,20,29,31

Some limitations exist in this study. First, this study focused on elderly people with fecal incontinence using diaper in SNHs. Therefore, the prevalence of ESBL-E found in this study cannot be extrapolated to all SNH residents without using diaper. Second, the number of subjects at each facility who participated in this study varied, and detailed genetic analysis of ESBL-E detected was not performed; thus, the evaluation of horizontal transmission at each facility and whether carrying ESBL-E occurred via humans or environmental factors could not be performed.

In conclusion, we detected ESBL-E in 53 of a total of 100 residents of SNH in Japan. We found no personal risk factors for colonization with ESBL-E. However, it is suggested that living in conventional-type facilities and scheduled diaper change using the cart for changing diaper has relation with carriage of ESBL-E. In multibed, conventional-type facilities using cart, revision of their methods of excretion care is necessary.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflict of interest connection with this article.

REFERENCES

1. Woerther PL, Burdet C, Chachaty E, Andremont A. Trends in human fecal carriage of extended-spectrum β-lactamases in the community: toward the globalization of CTX-M. Clin Microbiol Rev. 2013;26:744–58.
2. Luvsansharav UO, Hirai I, Niki M, et al. Fecal carriage of CTX-M β-lactamase-producing Enterobacteriaceae in nursing homes in the Kinki region of Japan. Infect Drug Resist. 2013;6:67–70.
3. Yano H, Uemura M, Endo S, et al. Molecular characteristics of extended-spectrum β-lactamases in clinical isolates from Escherichia coli at a Japanese tertiary hospital. PLoS ONE. 2013;8:e64359.
4. Kanayama A, Iyoda T, Matsuzaki K, et al. Rapidly spreading CTX-M-type beta-lactamase-producing Proteus mirabilis in Japan. Int J Antimicrob Agents. 2010;36:340–2.
5. Manning S, Lautenbach E, Tolomeo P, Han JH. Risk factors for infection with Escherichia coli in nursing home residents colonized with fluoroquinolone-resistant E. coli. Infect Control Hosp Epidemiol. 2015;36:575–7.
6. Kanayama A, Kobayashi I, Shibuya K. Distribution and antimicrobial susceptibility profile of extended-spectrum β-lactamase-producing Proteus mirabilis strains recently isolated in Japan. Int J Antimicrob Agents. 2015;45:113–8.
7. Japan Nosocomial Infections Surveillance. JANIS Open Report. Ministry of Health, Labour and Welfare website. http://www.nih-janis.jp/english/index.asp. Published 2013. Accessed Aug 23, 2016.
8. Suzuki S, Shibata N, Yamane K, Wachino J, Ito K, Arakawa Y. Change in the prevalence of extended-spectrum-beta-lactamase-producing Escherichia coli in Japan by clonal spread. J Antimicrob Chemother. 2009;63:72–9.
9. Chong Y, Shimoda S, Yakushiji H, et al. Community spread of extended-spectrum β-lactamase-producing Escherichia coli, Klebsiella pneumoniae and Proteus mirabilis: a long-term study in Japan. J Med Microbiol. 2013;62:1038–43.
10. Annual Health, Labour and Welfare Report 2015. Health and Welfare Services for the Elderly. Ministry of Health, Labour and Welfare website. http://www.mhlw.go.jp/english/wp/wp-hw9/dl/10e.pdf. Published 2015. Accessed Aug 6, 2016.
11. Rooney PJ, O’Leary MC, Loughrey AC, et al. Nursing homes as a reservoir of extended-spectrum beta-lactamase (ESBL)-producing ciprofloxacin-resistant Escherichia coli. J Antimicrob Chemother. 2009;64:635–41.
12. Rodríguez-Baño J, López-Cerero L, Navarro MD, Diaz de Alba P, Pascual A. Faecal carriage of extended-spectrum beta-lactamase-producing Escherichia coli: prevalence, risk factors and molecular epidemiology. J Antimicrob Chemother. 2008;62:1142–9.
13. Lautenbach E, Han J, Santana E, Tolomeo P, Blikr WB, Maslow J. Colonization with extended-spectrum β-lactamase-producing Escherichia coli and Klebsiella species in long-term care facility residents. Infect Control Hosp Epidemiol. 2012;33:302–4.
14. March A, Aschbacher R, Dhanji H, et al. Colonization of residents and staff of a long-term-care facility and adjacent acute-care hospital geriatric unit by multiresistant bacteria. Clin Microbiol Infect. 2010;16:934–44.
15. O’Fallon E, Pop-Vicas A, D’Agata E. The emerging threat of multidrug-resistant gram-negative organisms in long-term care facilities. J Gerontol A Biol Sci Med Sci. 2009;64:138–41.
16. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. CLSI; Wayne, PA: 2015. CLSI document M100-S25.

17. Shibata N, Kurokawa H, Doi Y, et al. PCR classification of CTX-M-type beta-lactamase genes identified in clinically isolated gram-negative bacilli in Japan. Antimicrob Agents Chemother. 2006;50:791–5.

18. Dallenne C, Da Costa A, Decré D, Favier C, Arlet G. Development of a set of multiplex PCR assays for the detection of genes encoding important beta-lactamases in Enterobacteriaceae. J Antimicrob Chemother. 2010;65:490–5.

19. Jallad MA, Naoufal R, Irani J, Azar E. Extended spectrum beta-lactamase carriage state among elderly nursing home residents in Beirut. ScientificWorldJournal. 2015;2015:987580.

20. Nordmann P, Naas T, Poirel L. Global spread of Carbapenemase-producing Enterobacteriaceae. Emerg Infect Dis. 2011;17:1791–8.

21. Nordmann P, Naas T, Poirel L. Global spread of Carbapenemase-producing Enterobacteriaceae. Emerg Infect Dis. 2011;17:1791–8.

22. Iredell J, Brown J, Tagg K. Antibiotic resistance in Enterobacteriaceae: mechanisms and clinical implications. BMJ. 2015;351:h6420.

23. D’Agata EM, Habtemariam D, Mitchell S. Multidrug-Resistant Gram-Negative Bacteria: Inter- and Intradissemination Among Nursing Homes of Residents With Advanced Dementia. Infect Control Hosp Epidemiol. 2015;36:930–5.

24. Blom A, Ahl J, Månsson F, Resman F, Thom J. The prevalence of ESBL-producing Enterobacteriaceae in a nursing home setting compared with elderly living at home: a cross-sectional comparison. BMC Infect Dis. 2016;16:111.

25. Yokoyama K, Uehara Y, Sasaki T, Hiramatsu K. Risk factors of fecal colonization with extended-spectrum beta-lactamase-producing Enterobacteriaceae in special nursing homes in Japan. J Gen Fam Med. 2018;19:90–96. https://doi.org/10.1002/jgf2.161