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Comparison of antibiotic resistance rates and outcomes among older adult patients with urinary tract infections living in long- term care hospitals and the community

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ABSTRACT

Objective: In this study, we compared the proportion of antibiotic resistance between patients who visited the emergency department (ED) with urinary tract infection (UTI) from long-term care hospitals (LTCH), which is a type of long-term care facilities (LTCF) and the community. We assessed the resulting difference in prognosis.
Method: Older adults who visited the ED between January and December 2019 and were diagnosed with UTI were divided into community residents and LTCH residents. We investigated the antibiotics sensitivity rates, end of therapy (EOT), and the patient's outcomes were evaluated.
Results: The antibiotic resistance rate was higher in LTCH residents. LTCH residents had a higher in hospital mortality rate compared to community residents. EOT was found to be longer, and admission rate and in-hospital mortality rate were also higher in LTCH residents.
Conclusion: LTCF residents had a higher rate of antibiotic resistance and a poor prognosis.

Introduction

The number and proportion of people aged 65 or older is increasing in every country in the world. In 2019, the number of people aged 60 years or older was 1 billion. The number is expected to rise to 1.4 billion by 2030 and 2.1 billion by 2050. This ageing is occurring faster than ever before, at an unprecedented pace.[1] Like the other country, South Korea is also ageing faster than it ever has. The proportion of people aged 65 years or older in South Korea increased from 7.0% in 1999 to 16% in 2020 and is expected to rise to 39.8% in 2050, and this is the highest proportion among Organization for Economic Co-operation and Development countries.[2,3] As the ageing population has increased, many long-term care facilities (LTCFs) have also emerged. Long-term care hospitals (LTCH), a type of LTCF, are institutions that provide long-term care in Korea. They provide a variety of medical services including long-term treatment, palliative care, and rehabilitation treatment for ageing patients who have completed acute treatment. In Korea, LTCHs have almost doubled in number over 10 years, from 868 in 2010 to 1,582 in 2020.[4]

Older people living in LTCHs are more susceptible to infectious diseases. This is due to age-related changes in the immune system, functional impairment, and the effects of chronic medical diseases. The use of invasive devices such as urinary catheters and enteral feeding tubes may also be a contributory factor.[5,6] Facility-related factors such as close contact with various patients and medical staff within the facility pose a risk of spreading infectious diseases.[7,8] For this reason, antibiotics are among the most commonly prescribed medications in LTCHs.[5] However, other issues such as atypical expression of infectious diseases, uncertainty in diagnosis, failure to conduct culture tests, and the frequency of colonization of antibiotic-resistant pathogens contribute to the misuse of antibiotics.[9] In this environment, significant amounts of antibiotic use may affect antibiotic resistance development. As has been demonstrated by many

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studies, the main drivers of antibiotic resistance are the misuse and abuse of antibiotics.[10,11]

Some studies have reported that the most common use of antibiotics is in LTCFs, and that, at the same time, the most inappropriate use of antibiotics occurs with urinary tract infection (UTI).[12,13] We investigated the rate of antibiotic resistance between community residents and LTCH residents among ageing UTI patients who visit the emergency department (ED) and evaluated whether appropriate antibiotic treatment has been performed. In addition, we compared whether there was a difference in prognosis between the two groups of residents according antibiotics resistance.

Material & methods

Study design and population

This two center, retrospective study was conducted at tertiary university hospitals, located in the capital of South Korea. Data were collected from patients aged 65 or older who were diagnosed with UTI at the EDs between January and December 2019. UTI was diagnosed as patients with complaints about symptoms related UTI and patients with pyuria observed in urinalysis performed in the ED. In addition, the final diagnosis in the ED was reviewed as a patient with N10 (Acute tubulo-interstitial nephritis), N15.1 (Renal and perinephric abscess), N30 (Cystitis), N34 (Urethritis and urethral syndrome), N39.0 (Urinary tract infection, site not specified) or N41(Inflammatory diseases of prostate) in the International Classification of Diseases 10th Revision (ICD-10) codes. This enrolled group was further divided into two groups: one group of patients who visited ED from LTCHs, and the other of patients who visited from the community. We excluded patients who had not received a culture test in the ED and who had inappropriate culture results, such as contamination. We also excluded patients with an unknown prognosis because of a transfer to another hospital or discharge against medical advice (Fig. 1). This study was approved by the institutional review board of two hospitals, and the need for informed patient consent was waived.

Data collection and outcome measurement

Data were obtained from electronic medical records (EMRs) and the National Emergency Department Information System (NEDIS) database. The NEDIS is a system in which all information about patients who visit EDs nationwide in Korea is collected in real time by the National Emergency Medical Center. This study collected following variables; demographic data (age and sex), initial vital signs, mental status, qSOFA, the Korean Triage and Acuity Scale (KTAS) and disposition in the ED. The KTAS was developed based on the Canadian Emergency Department Triage and Acuity Scale for classifying the severity of patients.[14] ED disposition included discharge, revisit within 7 days, and admission. Hospital length of stay and in-hospital mortality were also obtained.

To determine antibiotic susceptibility, we investigated the antibiotic which was initially used in the ED. Antibiotics were selected empirically by ED clinicians based on the severity of the patients' symptoms. All enrolled patients gave blood and urine sample for culture before beginning antibiotic treatment. When patients had a urinalysis with $\geq$10 WBCs/field, a culture test was performed, and the positive urine culture test was defined as $>10^4$ colony forming unit (cfu)/mL or higher for gram-negative bacteria and $>10^5$ cfu/mL for gram-positive bacteria.[15] All patients were evaluated for response after treatment was completed. End of therapy (EOT) was defined as the end of the total period of antibiotics treatment with IV and PO medication from the date the antibiotic was first administered in the ED to the end of hospitalization or outpatient treatment

The primary outcomes of this study were the comparison of antibiotic resistance rate in UTI patients visiting from LTCH and the community. The secondary outcomes were the comparison of

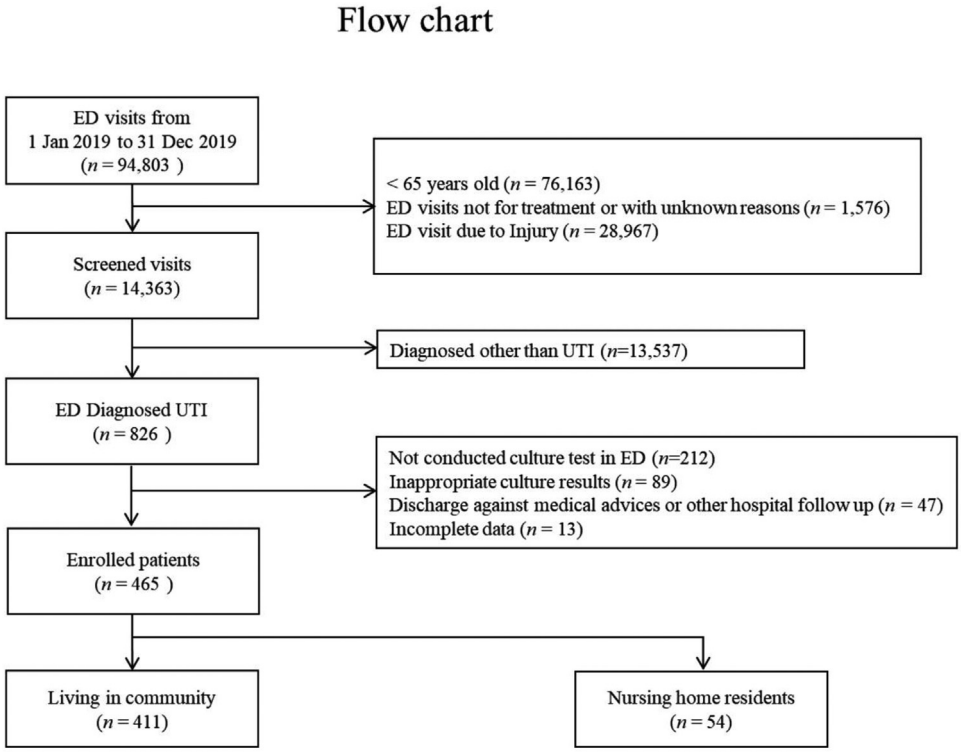

Fig. 1. Study design and patient enrollment.

prognosis, according to antibiotic resistance between the two groups of residents.

Statistical analysis

We used SPSS (version 26.0; SPSS Inc., Chicago, IL, USA) for performing statistical analyses. Continuous variables, including age, vital signs, laboratory findings, hospital LOS, and EOT were analysed using an independent t-test or the Mann-Whitney U test. Categorical variables, including sex, qSOFA score, mental status, KTAS triage category, ED disposition, and antibiotic resistance to antibiotics and cultured pathogen used were analysed using a Pearson's chi-square test. Continuous variables are described as mean ± standard deviation (SD), and categorical variables are described as count (percentage). Results were presented as statistically significant at a p-value less than 0.05.

Patient and Public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Results

Baseline characteristics

A total of 465 UTI patients aged 65 or older were registered in this study (Fig. 1). Of these patients, 411 visited from the community, and 54 visited from LTCH. The basic characteristics of the two patient groups are compared in Table 1. The mean age of two groups of UTI patients was 78.58 ± 7.58 and 79.61 ± 6.77 years, respectively (p = 0.343). The male percentage of community-living patients was 23.8%, while that of the LTCH was 38.9% (p = 0.017). In vital signs, there was a statistically significant difference in systolic and diastolic blood pressure between the two groups, but there were no other significant differences. When visiting the ED, the initial qSOFA score above 2point was 4.1% and 14.8% in the two groups, respectively (p = 0.001). The percentage of patients with 1,2 or 3 points of KTAS, which is more severe, was 70.7% in community-living patients and 81.9% in LTCH patient groups ($p < 0.001$) (Table 1).

The comparison of antibiotic susceptibility between living in the community and in long term care facilities

Of the 465 UTI patients who visited ED, 159 showed resistances to antibiotics used in urine culture result. 129 out of 411 community residents (31.4%) and 30 out of 54 LTCH residents (55.6%) showed antibiotic resistance, which was statistically significant ($p < 0.001$) (Table 2). In this study, third-generation cephalosporin was the most commonly used antibiotic in the ED, followed by fluoroquinolone, carbapenem, and amoxicillin/clavulanate. Comparing resistance according to antibiotics used showed statistically significant differences in fluoroquinolone and carbapenem, and antibiotic resistance was high in UTI patients who visited from LTCH (p = 0.010, p = 0.001).

Table 1
The baseline characteristics of patients living in the community and in long term care facilities.

Variable	Community-Living Ageing patients (n = 411)	Ageing patients in Long-Term Care (n = 54)	*p*-value
Age (y)†	78.58 ± 7.58	79.61 ± 6.77	0.343
Sex‡			**0.017**
Male	98 (23.8)	21 (38.9)	
Female	313 (76.2)	33 (61.1)	
Vital sign†			
Systolic blood pressure (mmHg)	133.61 ± 27.05	115.81 ± 29.37	<**0.001**
Diastolic blood pressure (mmHg)	71.57 ± 16.88	62.8 ± 16.44	<**0.001**
Pulse rate (beats/min)	94.62 ± 20.3	90.65 ± 18.82	0.174
Respiratory rate (breath/min)	20.1 ± 2.32	20.19 ± 1.61	0.787
Body temperature (°C)	37.47 ± 2.22	37.24 ± 0.92	0.464
qSOFA ≥2‡ (at ED admission)	17 (4.1)	8 (14.8)	**0.001**
Mental status‡			<**0.001**
Alert	393 (95.6)	45 (83.3)	
Verbal response	10 (2.4)	7 (13.0)	
Painful response	8 (1.9)	2 (3.7)	
Unresponsive	0	0	
KTAS Triage category‡			<**0.001**
Level 1	1 (0.2)	1 (1.9)	
Resuscitation			
Level 2	23 (5.6)	10 (2.2)	
Emergent			
Level 3	267 (64.9)	42 (77.8)	
Urgent			
Level 4	112 (27.3)	1 (1.9)	
Less urgent			
Level 5	8 (1.9)	0	
Non urgent			
ED Disposition			0.133
Discharge‡	189 (46.0)	19 (35.2)	
Revisit‡	23 (12.2)	1 (5.3)	0.369
Admission‡	222 (54.0)	35 (64.8)	
Hospital LOS (d)§	10 (7.00 – 20.00)	12 (7.00 – 39.00)	0.268
In-hospital mortality‡	3 (1.4)	7 (2.7)	<**0.001**

† The values are given as mean ± standard deviation.
‡ The values are given as number (%).
§ The values are given as median (interquartile range).ED: Emergency department; KTAS: Korean Triage and Acuity Scale; LOS: length of stay; qSOFA: quick Sequential (Sepsis-related) Organ Failure Assessment

Table 2
The antibiotic susceptibility between living in the community and in long term care facilities.

Antibiotics used initially in ED	Community-Living Ageing patients	Ageing patients in Long-Term Care	*p*-value
Total antibiotics used	411	54	<**0.001**
Sensitivity	282 (68.6)	24 (44.4)	
Resistance	129 (31.4)	30 (55.6)	
3rd Cephalosporin	236	23	0.080
Sensitivity	156 (66.1)	12 (52.2)	
Resistance	80 (33.9)	11 (47.8)	
Fluoroquinolone	100	4	**0.010**
Sensitivity	64 (64)	0	
Resistance	36 (36)	4 (100)	
Carbapenem	63	18	**0.001**
Sensitivity	54 (85.7)	9 (50)	
Resistance	9 (14.3)	9 (50)	
Amoxicillin/clavulanate	10	8	0.343
Sensitivity	6 (60)	3 (37.5)	
Resistance	4 (40)	5 (62.5)	
Others	3	3	

The values are given as number (%)
ED: Emergency department

The comparison of outcomes between living in the community and in LTCH

In the treatment period and prognosis comparison between all community living patients and LTCH patients, only the in-hospital mortality showed a statistically significant difference (1.4% vs. 20%, $p < 0.001$). Also, among patients with antibiotic sensitivity, only the in-hospital mortality presented a statistically significant difference (1.9% vs. 21.4%, $p < 0.001$). On the other hand, in antibiotic-resistant patients, there was a statistically significant difference in EOT, admission rate, and in-hospital mortality between two groups. Among patients with antibiotic resistance, the total treatment period of UTI patients visiting from LTCH was found to be longer (15.40 ± 11.36 vs. 20.17 ± 11.48, $p = 0.040$). The admission rate and in-hospital mortality rate were also higher in LTCH residents ($p = 0.044$, $p < 0.001$) (Table 3).

Comparison of antibiotic sensitivity according to bacteria in urine samples

The results of the urine sample cultures of UTI patients showed that *Escherichia coli* was isolated the most in the two groups. It was followed by *Klebsiella pneumoniae, Enterococcus faecium, Pseudomonas aeruginosa*, and *Proteus mirabilis. E. coli* was isolated in 298 community residents, 92 of whom were resistant to the antibiotics used, and it was isolated 25 LTCH residents, 13 of whom were resistant to antibiotics, showing statistically significant differences (30.9% vs. 52%, $p = 0.030$). Other bacteria also showed high resistance to antibiotics used in LTCH residents, but were not statistically significant (Table 4).

Discussion

In 2021, the World Health Organization (WHO) declared that antimicrobial resistance is one of the top 10 most urgent and serious threats to public health.[16] Antimicrobial resistance is the phenomenon whereby bacteria, viruses, fungi, and parasites no longer respond to common medicines used to treat them, making infections difficult to treat, and increasing the risk of spreading diseases, progression to severe diseases, and death. As a result, longer treatment periods and the use of more expensive medicines poses financial difficulties for patients.[17] The problem of antibiotic resistance to bacteria is especially urgent. Following the initial discovery of penicillin, there have been numerous improvements in the treatment of the bacterial infection that modify the morbidity and mortality rates of the population.[18] Over the decades, however, bacteria have also developed resistance to new antibiotics. The main drivers of antibiotic resistance are the misuse and overuse of antibiotics.[10,11]

About 50 to 80% of LTCF residents receive antibiotic treatment per year.[5,19] One systematic review found that antibiotics are most commonly prescribed for UTI (32–66%), respiratory tract infections (RTI) (15–36%), and skin and soft tissue infections (SSTI) (13–18%).[5] In long-term care settings such as ~~LTCF and~~ LTCH, it is difficult to diagnose infectious diseases for various reasons. Since patients are ageing, they complain of atypical symptoms, and it is difficult for them to communicate clearly due to cognitive impairment. Also, diagnosing diseases can be challenging due to the underlying medical history. Another important factor is the difficulty of proceeding with the immediate examination due to the characteristics of LTCF.[20] Therefore, antibiotic prescription is often carried out empirically in long-term care setting. However, it is not clear whether the use of antibiotics is appropriate for LTCF patients. A study carried out by Loeb et al. reported that= the proportion of antibiotic prescriptions appropriate for LTCF patients was 49%, with the least appropriate prescriptions in UTI (28%) and more appropriate prescriptions in RTI (58%) and SSTI (65%).[21]

Table 3
The outcomes of patients living in the community and in long term care facilities.

Variable	Community-Living Ageing patients	Ageing patients in Long-Term Care	*p*-value
Total visit patients	n = 411	n = 54	
End of Therapy (Day) †	13.74 ± 9.06	15.93 ± 10.73	0.104
Admission‡	222 (54.0)	35 (64.8)	0.133
In-hospital mortality‡	3 (1.4)	7 (20)	<**0.001**
Hospital LOS (Day) §	10 (7.00 – 20.00)	12 (7.00 – 39.00)	0.268
Patients with antibiotics sensitivity	n = 282	n = 24	
End of Therapy (Day) †	12.98 ± 7.69	10.63 ± 6.82	0.147
Admission‡	158 (56.0)	14 (58.3)	0.827
In-hospital mortality‡	3 (1.9)	3 (21.4)	<**0.001**
Hospital LOS (Day) §	10 (7.00 – 17.00)	12 (8.25 – 15.75)	0.592
Patients with antibiotics resistance	n = 129	n = 30	
End of Therapy (Day) †	15.40 ± 11.36	20.17 ± 11.48	**0.040**
Admission‡	64 (49.6)	21 (70.0)	**0.044**
In-hospital mortality‡	0	4 (19.0)	< **0.001**
Hospital LOS (Day) §	11.50 (6.00 – 40.25)	18 (5.00 – 80.00)	0.335

† The values are given as mean ± standard deviation.
‡ The values are given as number (%).
§ The values are given as median (interquartile range).LOS: length of stay

Table 4
Prevalence of the bacterium in urine samples between living in the community and in long term care facilities.

Bacterium in urine samples	Community-Living Ageing patients	Ageing patients in Long-Term Care	*p*-value
Escherichia coli	298	25	**0.030**
Sensitivity	206 (69.1)	12 (48.0)	
Resistance	92 (30.9)	13 (52.0)	
Klebsiella pneumoniae	26	5	0.341
Sensitivity	16 (61.5)	2 (40.0)	
Resistance	10 (38.5)	3 (60.0)	
Pseudomonas aeruginosa	18	4	0.259
Sensitivity	14 (77.8)	2 (50.0)	
Resistance	4 (22.2)	2 (50.0)	
Proteus mirabilis	12	6	0.317
Sensitivity	7 (58.3)	2 (33.3)	
Resistance	5 (41.7)	4 (66.7)	
Enterococcus faecium	20	4	0.200
Sensitivity	12 (60.0)	1 (25.0)	
Resistance	8 (40.0)	3 (75.0)	
Others	37	10	

The values are given as number (%)

In this study, antibiotic susceptibility and prognosis were compared between UTI patients who visited from LTCHs and the community to the ED. We found that patients from LTCHs had higher antibiotic resistance rates. This work supports previous studies on antibiotic resistance among LTCH residents.[22,23] In several studies, LTCH have been recognized as potential reservoirs of antibiotic-resistant bacteria as a result of multiple risk factors, catheter use, transmission opportunities, and inappropriate and unnecessary antibiotic use.[22,24] Although it was estimated that this would have a negative effect on the patient's prognosis, it only affected the in-hospital mortality rate between community and LTCH residents, but there was no difference in the overall antibiotic treatment period or admission rate. The same results were found in patients with antibiotic sensitivity. On the other hand, in targeting patients with antibiotic resistance, the overall antibiotic treatment period was extended (20.17 ± 11.48 vs. 15.40 ± 11.36, $p = 0.040$), the admission rate increased (70.0% vs. 49.6%, $p = 0.044$), and the mortality rate in the hospital was also higher among ~~LTCF~~ LTCH residents (18 (5.00 − 80.00) vs. 11.50 (6.00 − 40.25, $p < 0.001$).

The results from our study suggest that it may be caused by the detection of more antibiotic-resistant bacteria in urine culture of UTI patients visiting from ~~LTCF~~ LTCH. Inappropriate empirical antibiotic treatment will have a negative effect on all ages, but the negative impact on older people is greater than that of younger adults.[25] The prognosis comparison between all community residents and LTCH residents enrolled in our study was not significant, but the prognosis of LTCH residents was found to be worse in antibiotic-resistant patients using inappropriate antibiotics. This means that the choice of antibiotics in UTI patients visiting from LTCHs should be made with care, and urine culture should be performed to evaluate for antibiotic resistance bacteria.

Third-generation cephalosporin and fluoroquinolone are the antimicrobial agents that can be recommended for empirical treatment of UTI.[26] However, a lot of resistance to fluoroquinolone, which has been widely used as an empirical antibiotic in the past, has been shown among LTCH residents.[23,27] This study showed similar results. Fluoroquinolones are no longer recommended as an empirical treatment for UTI, due to fluoroquinolone resistance levels exceeding 10% in several countries.[28,29] Recently, ceftriaxone has been the first recommended empirical antibiotic for UTI and acute pyelonephritis, with no risk factors for resistant organisms.[30] In our study, third-generation cephalosporin was the most frequently selected empirical antibiotic. And there was no significant difference in resistance to cephalosporin between community residents and LTCH residents.

This study has some limitations. The main limitation is its retrospective design and small sample size of patients visiting from LTCHs (n = 54) compared with community residents (n = 411), therefore, caution is required when generalizing the results of the study due to confounding and selection bias. In an effort to reduce bias, we conducted the study at two centers. Also, we have not investigated whether patients who may have an effect on prognosis took antibiotics before visiting the ED, or their past medical history. This may have affected the entire treatment period or the patient's prognosis; therefore, there is a limitation in applying this result to all older patients. Lastly, patients who visit the ED from LTCHs are often not treated with early empirical antibiotics; thus, it can be biased toward resistance. In addition, the use of empirical antibiotics before the visit to the ED may have affected the urine sample.

Conclusion

Our findings showed that LTCF residents had higher antibiotic resistance rates in UTI compared to community residents. In addition, we found that due to resistance, inappropriate use of empirical antibiotics led to a poor prognosis for LTCF residents. Therefore, consideration should be given to prescribing effective and appropriate antibiotics to older patients with UTI living in LTCFs.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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