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CLINICAL CHARACTERISTICS OF MULTIDRUG-RESISTANT *ESCHERICHIA COLI* AT A TERTIARY CARE UNIVERSITY HOSPITAL IN JAPAN

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ABSTRACT

Escherichia coli is the leading cause of various infectious diseases such as pneumonia, urinary tract and blood stream infections. Furthermore the emergenceof multidrug-resistant *Escherichia coli* has been focused worldwide. The objective of this study was to determine the clinical characteristics of multidrug-resistant *Escherichia coli* at a tertiary care university hospital in the central region of Japan. We determined the in *vitro* susceptibilities of 10 antimicrobial agents for 530 multidrug-resistant *Escherichia coli* in Japan. From antimicrobial susceptible results, these results indicated the over 60% of multidrug-resistant *Escherichia coli* had beta lactamase and fluoroquinolone resistant ability. Our results also revealed that the risk factors of multidrug-resistant *Escherichiacoli* were over 60 years, and department of urology. The emergence of multi-drug resistant *Escherichia coli* suggests that further aggressive surveillance is needed for providing useful information on the trends in antimicrobial resistance

INTRODUCTION

Escherichia coli is one of the most common pathogen bacteria that cause a variety of infections such as pneumonia, urinary tract and blood stream infections (Kang *et al.,* 2013). The use of beta-lactams has become difficult in recent years as various classes of beta-lactamases such as extended-spectrum beta-lactamase (ESBL) have found in clinical *Escherichia coli* isolates (Bush *et al.,* 1995). This result has implied to the emergence of multidrug-resistant bacteria. Although multidrug-resistant was defined as an *in vitro* resistance to one more than one antimicrobial agent previously, Magiorakos et al redefined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories(Magiorakos *et al.,* 2012). Multidrug-resistant infections with multidrug-resistant bacteria can lead to inadequate or delayed antimicrobial therapy and are associated with poorer patient outcomes (Magiorakos *et al.,* 2012). Accurate information cannot be conveyed to the public and to policy makers about the rising threat of multidrug-resistant bacteria to public health (Magiorakos *et al.,* 2012).

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The present study was conducted to find out the trend of characteristics of multidrug-resistant *Escherichia coli* isolates at a tertiary care university hospital in the central region of Japan. Our result would be useful for improving the assessment of epidemiological importance and public health impact about multidrug-resistant *Escherichia coli*.

MATERIALS AND METHODS

Strains and clinical data collection

A total of 1593 *Escherichia coli* were obtained from various clinical specimens at Nagoya City University hospital from 2008 to 2010. Nagoya City University hospital is an 808-bed tertiary care university hospital in the central region of Japan. We used medical records appended to clinical species for the analysis of clinical feature at Nagoya City University Hospital. We considered several isolates from the same region of the same patient as one isolate per one patient for the analysis in this study. All *Escherichia coli* isolates were identified by standard conventional biochemical methods or the VITEK2 system (bioMérieux, Durham NC, USA). Our experimental design was approved by the ethics committee at Nagoya City University.

Antimicrobial susceptibility analysis

Escherichia coli isolates were examined for 10 antibiotic susceptibilities as follow ABPC; ampicillin, AMPC/CVA; amoxicillin / clavulanate, CEZ; cefazolin, CTX ; cefotaxime, IPM; imipenem, AZT; aztreonam, GM; gentamicin, MINO; minocycline, CPFX; ciprofloxacin, ST; Trimethoprim-sulfamethoxazole. Minimal inhibitory concentration (MICs) were determined using broth micro dilution methodology with the VITEK2 system. Evaluation of antimicrobial resistance was based on Clinical Laboratory Standard Institute (CLSI) break point (M100-S20). Multidrug-resistance was defined as non-susceptibility to more than any three antimicrobial agents (Magiorakos *et al.,* 2012).

Statistical analysis of the data

We conducted the statistical analysis with the chi-squared test or Fisher's exact test when appropriate. Differences were considered significant when p was <0.05.

RESULTS AND DISCUSSION

In this study, we described the characteristics of multidrug-resistant *Escherichia coli* isolates from 2008 to 2010 at a tertiary care university hospital in the central region of Japan. Total one thousand five hundred ninety three *Escherichia coli* was isolated in this study. Of them, 530 (33.3%) *Escherichia coli* isolates were classified as multidrug-resistant organism. Two hundred eighty-four isolates (53.6%) were from female and two hundred forty-six (46.4%) were from male for three years (Figure 1).

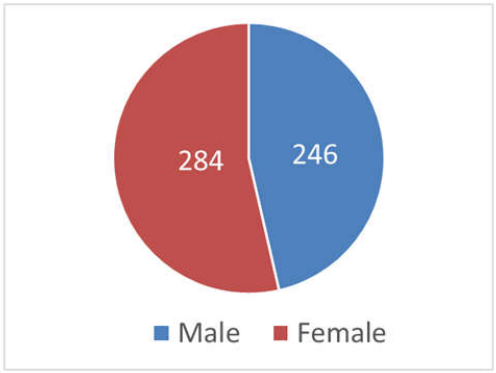

Figure 1. Gender wise distribution of multidrug-resistant Escherichia coli isolates

However, our study showed that there were no significant differences of gender group. Next, we clarified multidrug-resistant *Escherichia coli* with age distribution. The total age incidence among 0-1 years age group was 35 (6.6 %), among 1-10 years age group, 23 (4.3%), among 11-20 years age group, 3 (0.6%), among 21-30 years age group, 21 (4.0%), among 31-40 years age group, 24 (4.5%), among 41-50 years age group, 17 (3.2%), among 51-60 years age group, 52 (9.8%), among 61-70 years age group, 100 (18.9%), among 71-80 years age group, 153 (28.9%), among 81-90 years age group, 85 (16%), among 91-100 years age group, 17 (3.2%), (Figure 2).

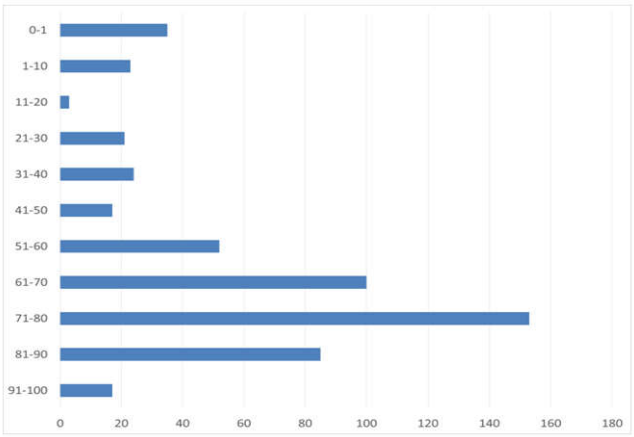

Figure 2. Age wise distribution of multidrug-resistant *Escherichia coli* isolates

The present study revealed the major prevalence of multidrug-resistant Escherichia coli were 28.9% (71-80 years age group), 18.9% (61-70 years age group), 16%(81-90years age group), 9.7% (51-60 years age group), respectively. The prevalence rate of over 60 years was about 66.7% (about two third). This result is suggested that multidrug-resistant *Escherichia coli* was serious bacterial infectious problem for aged patients. With respect to hospitalized group, two hundred forty-four isolates (46.0%) were from outpatient and two hundred eighty-six (54.0%) were from inpatient (Figure 3).

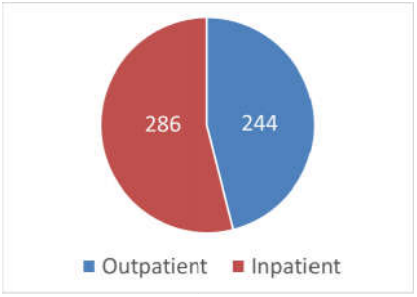

Figure 2. Age wise distribution of multidrug-resistant *Escherichia coli* isolates

There were no significant differences among hospitalization. In our study, the numbers from aseptic site were ninety-two and those from other site were four hundred thirty-eight (Figure 4).

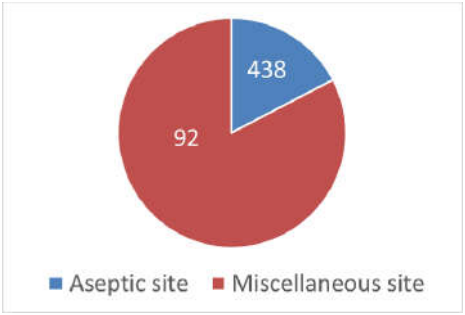

Figure 4. Site wise distribution of multidrug-resistant *Escherichia coli* isolates

Furthermore, in the analysis of clinical departments, Most of the *Escherichia coli* isolates were from the urology, surgery, general medicine, emergency room and dermatology (Figure 5). Our result showed that urinary tract disease was usually popular as *Escherichia coli* infectious diseases.

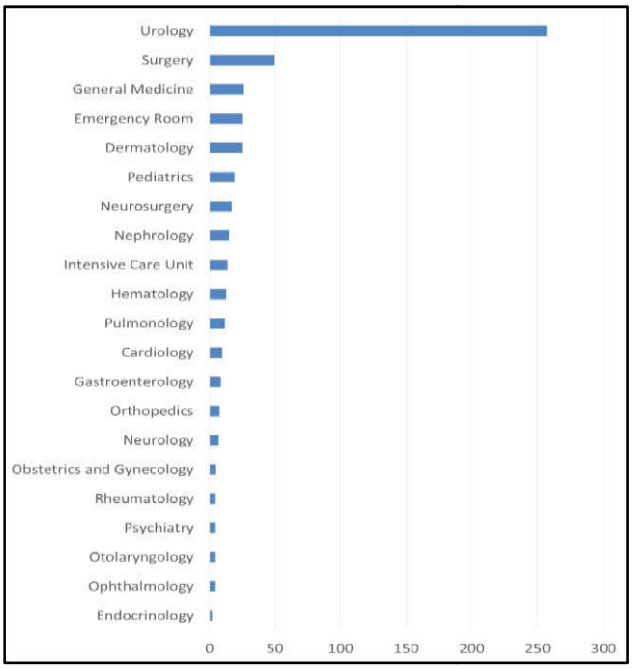

Figure 5. Clinical department wise distribution of multidrug-resistant *Escherichia coli* isolates

The results of antimicrobial susceptibility of multidrug-resistant *Escherichia coli* isolates in this study were shown in Figure 6. Significant resistant were observed in ABPC (513/96.8%), CPFX (313/59.0%), CVA/AMPC (303/57.2%), CEZ (301/56.8%), and ST (285/53.8%). The numbers of AZT-resistant and CTX-resistant isolates were one hundred ninety-eight (37.4%) and one hundred ninety-seven (37.2%), respectively. The best effective antibiotics with over 99% susceptibility rates was imipenem (525/ 99.1%).

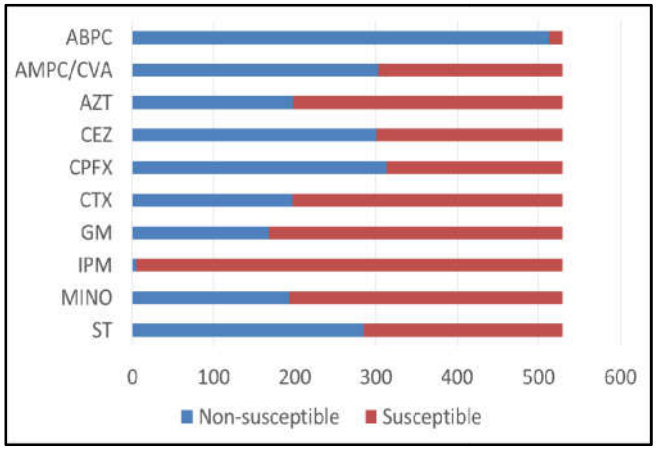

Figure 6. Antimicrobial resistant rates wise distribution of multidrug-resistant *Escherichia coli* isolates

The disease burden of multidrug-resistant including ESBL, *Escherichia coli* infections has increased due to widespread emergence of antibacterial resistance in many countries from1980s (Turner PJ. 2005). In Japan, fluoroquinolones resistant multidrug-resistant *Escherichia coli* possessed ESBL resistant (32%), or aminoglycosides aminoglycoside resistant (26.8%), respectively (Tsukamoto *et al.,* 2013).

Another Japanese report showed that 43.3% of *Escherichia coli* isolated from uropathogenicinfection were multidrug-resistant (Harada *et al.,* 2012). Our result was almost consistent with previous result of multidrug-resistant *Escherichia coli* in Japanese study. In China, the prevalence of ESBL and multidrug-resistant *Escherichia coli* were 68.8 % and 55.4%, respectively (Zhang *et al.,* 2011). In Korea, the prevalence of multidrug-resistant *Escherichia coli* was 65.4% (Lee *et al.,* 2014). In Thailand, the multidrug-resistant rates were 29.1% and most multidrug-resistant *Escherichia coli* possessed more than one tetracycline associated resistant gene (Changkaew *et al.* 2014). In Vietnam, the ESBL and multidrug-resistant rates were 40.6 and 34.9%, respectively (Le *et al.* 2015). The prevalence of multidrug-resistant *Escherichia coli* from blood stream infection was 62.3% in Cambodia study (Vlieghe *et al.* 2013).

In Malaysian hospital, the 46% of *Escherichia coli* were multidrug-resistant isolates (Ho *et al.* 2012). Indian study revealed that uropathogenic *Escherichia coli* with high producing activity of biofilm was 100% multidrug resistant isolates (Mittal *et al.,* 2015). Pakistan study showed that more than 70% of *Escherichia coli* were multidrug-resistant (Ahmad *et al.,* 2015). The prevalence rate of ESBL and multidrug-resistant *Escherichia coli* in Bangladesh were 11.8% and 11.5%, respectively (Lina *et al.* 2014). Nepal report showed that the 19% of *Escherichia coli* were multidrug-resistant (Bora *et al.,* 2014). In Iran, the 53.2 % of Enteroaggregative adherent *Escherichia coli* were multidrug-resistant (Bafandeh *et al.,* 2015). Although, the prevalence rate of multidrug-resistant *Escherichia coli* has differed geologically and increased worldwide, we need continue to assess the global prevalence of multidrug-resistant *Escherichia coli*worldwide.

Conclusion

Incidence of multidrug-resistant *Escherichia coli* infection has increased, both in healthcare institutions and throughout communities, in many countries including Asia. Further aggressive surveillance is needed for providing useful information on the trends in antimicrobial resistance in Asia including Japan.

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