Short Communication

Proportion of Rectal Carriage of Extended-Spectrum \(\beta\)-Lactamase-Producing Enterobacteriaceae in the Inpatients of a Pediatric Tertiary Care Hospital in Japan

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SUMMARY: Extended-spectrum \(\beta\)-lactamase (ESBL)-producing-Enterobacteriaceae strains were detected in 12% (6 out of 50) of fecal samples collected from the inpatients of a Japanese pediatric hospital. All the ESBLs belonged to the CTX-M-1 group. The proportion of carriage of ESBL producers was higher among patients who had received antibiotics within the past 3 months and among those who had cardiologic diseases.

The clinical burden of extended-spectrum \(\beta\)-lactamase (ESBL)-producing pathogens has increased in pediatric care settings. Currently, the antimicrobial therapeutic options for treating infections caused by ESBL producers are limited.

To the best of our knowledge, only a few studies have reported the fecal carriage of ESBL producers in pediatric populations. Therefore, we conducted a prospective study to determine the proportion of ESBL producers in the fecal carriage of inpatients in a pediatric tertiary care hospital in Japan.

Nagano Children’s Hospital is a tertiary referral pediatric hospital located in Nagano Prefecture, Japan. It houses a Pediatric Intensive Care Unit (PICU), a neonatal ward, an obstetric ward, three pediatric wards, and a total of 160 beds.

We collected fecal samples from the inpatients on a specific day in July 2011. Patients from the neonatal and obstetric wards and the PICU were excluded from this study because of their special characteristics. Informed consent was obtained from the guardians of the patients. All study protocols were approved by the ethics committee of Nagano Children’s Hospital.

Epidemiological data were collected from medical charts to determine factors that contribute to fecal carriage of ESBL producers.

For our study, previous antibiotic use was defined as the documented use of any type of antimicrobials, either parenterally or orally, within the past 3 months.

Long-term admission was defined as an admission period of more than 14 days from the time of initiation of the study, and frequent admissions were defined as more than 2 admissions within the past 6 months and a total hospital stay of more than 14 days.

Fresh stool samples were collected from consenting patients, and were spread onto CHROMagar™ ESBL (Kanto Chemical Co., Tokyo, Japan). The plates were incubated at 35°C for 24 h. Each colony type was cultured and subjected to identification and antimicrobial susceptibility testing using the MicroScan Walk away 40 system using Neg combo 6.11J panels (Siemens Healthcare Diagnostics Inc., Tarrytown, N.Y., USA). The production of ESBLs was confirmed with the NMIC 3.31E (Siemens Healthcare Diagnostics). All the isolates that grew were screened for ESBL production using both the resistance phenotype and the double-disk synergy tests with conventional combinations (ceftaxime, cefotaxime and ceftazidime versus clavulanic acid) according to the guidelines provided by the Clinical and Laboratory Standards Institute (CLSI) (1).

We also performed a PCR assay to investigate the presence of the ESBL genes, i.e., CTX-M-1 group, CTX-M-2 group, CTX-M-9 group, and TEM and SHV \(\beta\)-lactamase genes. The bacterial colonies were first suspended in 200μl sterile water. Total DNA was extracted with the QIAamp DNA Mini Kit (Qiagen, Hilden, Germany) according to the manufacturer’s protocol. The DNA was eluted in a final volume of 100 μl to prepare DNA templates. The presence of \(\beta\)ESBL genes was determined by PCR using primers targeting \(\beta\)TEM, \(\beta\)SHV, and \(\beta\)CTX-M genes under conditions described previously (2,3).

Statistical analyses were carried out using the R software (4). The chi-square test and Fisher’s exact test were used for analysis and a P-value of <0.05 was considered significant.

From a total of 62 patients, we collected 50 fecal samples (81%). We detected 9 ESBL producers in 6 samples (6/50, 12%); 3 samples contained 2 ESBL producers; 3 samples contained 3 ESBL producers; and 1 sample contained 4 ESBL producers.
The prevalence of rectal carriage of ESBL producers in healthy Japanese adults and medical college students was reported to be 6.4% and 7.5%, respectively (6,7). The results imply that ESBL-producing bacilli are present to a certain extent even in healthy adult populations in Japan. One study conducted in Spain in 2003 reported an ESBL producer rectal carriage rate of 3.7% in healthy adult volunteers, 5.5% in outpatients, and 12% in hospitalized patients (8). Another study conducted in 2004 in an Israeli tertiary care hospital revealed an 8% ESBL rectal carriage rate on admission and a rate of 21% during hospitalization (9).

Our results implied that carriage of ESBL producers was more common in patients with previous antimicrobial use, those aged 5–9 years, and those with underlying cardiologic disease. As already reported, previous antibiotic use is one of the major risk factors for rectal carriage of ESBL producers (10).

Daily habits and the consumption of meats, vegetables, or other foods contaminated with drug-resistant bacteria might contribute to the fecal carriage of ESBL producers in Japanese children. It is known that the addition of antibiotics in the food used to feed livestock could result in the spread of drug-resistant bacteria in the environment in Japan (11).

To the best of our knowledge, cardiologic diseases have not been considered as risk factors for carriage of ESBL producers. We suspect it may be due to the unique role of our institute. Our hospital is the main center for the treatment of congenital heart diseases in Nagano Prefecture. Consequently, almost every child in Nagano with severe cardiologic diseases (for example, hypoplastic left heart syndrome and tetralogy of Fallot) is referred to our hospital. Moreover, many of them receive intensive care, are prescribed antimicrobials, and undergo repetitive examinations and operations as part of the treatment regimen. Therefore, they account for the majority of the patients in our institute.

In this study, all the isolates produced ESBLs that belonged to the CTX-M-1 group; this is consistent with the findings of recent surveys, which state that the CTX-M-1 group ESBLs are the most common and are ubiquitous in Europe (12) as well as in Japan (13). However, we cannot deny the possibility that CTX-M-1 group ESBLs may be prevalent in our hospital and horizontal transmission is ongoing. Nonetheless, further investigations are needed to clarify this hypothesis.

To control the spread of ESBL producers, active surveillance should be continued, and antimicrobial

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**Table 1. Characteristics of patients and analysis of the risk factors**

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>Sex</th>
<th>Total (n = 50)</th>
<th>ESBL + (n = 6)</th>
<th>ESBL - (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>Male</td>
<td>27 (54)</td>
<td>3 (50)</td>
<td>24 (55)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>23 (46)</td>
<td>3 (50)</td>
<td>20 (45)</td>
</tr>
<tr>
<td>1-4</td>
<td>Male</td>
<td>12 (24)</td>
<td>1 (17)</td>
<td>11 (25)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>16 (32)</td>
<td>1 (17)</td>
<td>15 (34)</td>
</tr>
<tr>
<td>5-9</td>
<td>Male</td>
<td>15 (30)</td>
<td>3 (50)</td>
<td>12 (27)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>7 (14)</td>
<td>1 (17)</td>
<td>6 (14)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>Male</td>
<td>4.6 (1 m–12 y)</td>
<td>6.1 (8 m–12 y)</td>
<td>4.4 (1 m–12 y)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>27 (4)</td>
<td>4 (1 m–12 y)</td>
<td>23 (8 m–12 y)</td>
</tr>
<tr>
<td>Long term or frequent admissions</td>
<td>Male</td>
<td>17 (34)</td>
<td>4 (67)</td>
<td>13 (30)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>7 (14)</td>
<td>1 (17)</td>
<td>6 (14)</td>
</tr>
<tr>
<td>Underlying diseases</td>
<td>Cardiologic</td>
<td>17 (34)</td>
<td>4 (67)</td>
<td>13 (30)</td>
</tr>
<tr>
<td></td>
<td>Neurologic</td>
<td>7 (14)</td>
<td>1 (17)</td>
<td>6 (14)</td>
</tr>
<tr>
<td></td>
<td>Oncologic</td>
<td>7 (14)</td>
<td>1 (17)</td>
<td>6 (14)</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>19 (38)</td>
<td>0</td>
<td>19 (43)</td>
</tr>
</tbody>
</table>
stewardship programs aimed at promoting the judicious use of broad-spectrum antimicrobials should be employed rigorously.

Conflict of interest None to declare.

REFERENCES


