

Title	STUDY OF EXTENDED-SPECTRUM β -LACTAMASE-PRODUCING ENTEROBACTERIACEAE AMONG ASYMPTOMATIC PEOPLE
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Citation	大阪大学, 2013, 博士論文
Version Type	VoR
URL	https://hdl.handle.net/11094/54702
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Note	

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博士の専攻分野の名称	博士（保健学）
学位記番号	第 26123 号
学位授与年月日	平成25年3月25日
学位授与の要件	学位規則第4条第1項該当 医学系研究科保健学専攻
学位論文名	STUDY OF EXTENDED-SPECTRUM β -LACTAMASE-PRODUCING ENTEROBACTERIACEAE AMONG ASYMPTOMATIC PEOPLE (健常人が保菌する基質特異性拡張型 β -ラクタマーゼ産生腸内細菌の 研究)
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論文内容の要旨

The prevalence of and risk factors associated with extended-spectrum β -lactamase (ESBL)-producing microorganisms have not been well studied among asymptomatic individuals in communities. Therefore, the aim of this study was to determine this in healthy individuals in Thailand and Japan.

We collected 445 stool samples during 2008-9, and 417 samples in 2010 from Thailand; and 443 samples from Japan during 2009-10. Stool samples were screened for ESBLs using MacConkey agar supplemented with cefotaxime. Results were confirmed using cefotaxime and ceftazidime with and without clavulanic acid. The *bla*_{CTX-M} genes were identified and genotyped using PCR. Multivariate analysis was performed to investigate risk factors associated with the faecal carriage of CTX-M producers.

We identified high prevalence of CTX-M-type ESBL-producing *Enterobacteriaceae* in the three provinces of Thailand: 29.3% in Nan, 29.9% in Nakhon Si Thammarat and 50.6% in Kanchanaburi. Genotyping of *bla*_{CTX-M} revealed that most CTX-M producers harboured genes belonging to the CTX-M-9 group, followed by the CTX-M-1 group. *Escherichia coli* was the predominant member of the *Enterobacteriaceae* producing CTX-M-type ESBLs. No statistically significant association was observed between the presence of ESBL-producing bacteria and gender, age, education, food habits or antibiotic usage. However, the provinces that had the highest prevalence of ESBL-producing *Enterobacteriaceae* also had the highest prevalence of use and purchase of antibiotics without a prescription.

After 2 years since the initial study we conducted another study in Kanchanaburi province with a more detailed questionnaire and increased number of the participants. The prevalence of CTX-M-type ESBL-producing *Enterobacteriaceae* was increased to 65.7%. Genotyping and bacterial identification results were similar to previous findings. In a multivariate logistic regression model, better education status, history of hospitalization and the use of antibiotics within the last 3 months were independently associated with faecal carriage.

In contrast, faecal carriage of CTX-M producers among asymptomatic Japanese people was very low (6.0%). CTX-M-9 group was dominant, followed by CTX-M-2 group. *E. coli* was predominantly identified among CTX-M producers. Statistical analysis did not reveal any significant association between ESBL production and antibiotic usage or hospitalization experience. However, the prevalence of CTX-M-producers in nursing homes of Japan was much higher (19.6%). In multivariate logistic regression analysis, inability to turn over in bed, diabetes, and invasive procedures within the last 2 years were the only variables independently associated with fecal carriage of CTX-type ESBL producers among nursing home residents.

In summary, faecal carriage of CTX-M-type ESBL-producing *Enterobacteriaceae* among asymptomatic individuals in rural Thailand is alarmingly high, and previous antibiotic use and a history of hospitalization may contribute to its dissemination. It is also increasing among healthy Japanese people, with nursing homes acting as a possible reservoir for community spread of CTX-M producers.

論文審査の結果の要旨

The prevalence of and risk factors associated with extended-spectrum β -lactamase (ESBL)-producing microorganisms have not been well studied among asymptomatic individuals in communities. Therefore, the aim of this study was to determine this in healthy individuals in Thailand and Japan.

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hospitalization may contribute to its dissemination. It is also increasing among healthy Japanese people, with nursing homes acting as a possible reservoir for community spread of CTX-M producers.

The study sufficiently fulfills the requirements for a PhD degree.