

Epidemiology of Antibiotic Use and Antimicrobial Resistance in Selected Communities in Thailand

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Objective: To generate epidemiological information regarding antibiotic use and antimicrobial resistance (AMR) in targeted communities for use by the Thailand AMR Containment and Prevention Program.

Material and Method: A survey of antibiotics sold by 215 grocery stores and retail shops located in the target communities was done by the local people who were instructed to purchase specified antibiotics and to present to such stores and shops with symptoms of sore throat, backache, common cold, acute diarrhea, inflamed uterus, and dysuria. The purchased drugs were then identified and recorded. Contamination of extended-spectrum β -lactamase (ESBL)-producing *E. coli* was identified in 174 samples of foods and open water sources collected from the target communities. Carriage of ESBL-producing *E. coli* in gastrointestinal tracts of 534 adults living in the target communities was performed by stool sample culture. One thousand three hundred one patients with upper respiratory infection (URI) and 235 patients with acute diarrhea who attended the tambon health promoting hospitals located in the target communities were monitored for their clinical outcomes of treatments. The patients with URI and acute diarrhea with no indication of antibiotic received symptomatic treatments as appropriate and they were followed via telephone contact every few days until all symptoms related to URI and acute diarrhea disappeared. The data were analyzed by descriptive statistics.

Results: Antibiotics were sold to the local people who were presenting with common ailments at many grocery stores and retail shops in their respective communities. In almost all cases, antibiotics were inappropriately given. Overall prevalence of ESBL-producing *E. coli* contamination in foods and open water sources was 26.4%. ESBL-producing *E. coli* was isolated from fresh meat and open water sources in many samples. Overall prevalence of ESBL-producing *E. coli* carriage in gastrointestinal tracts of the adults cultured was 66.5%. All patients with URI and acute diarrhea who had no indication of antibiotics and did not receive antibiotics had either cure or favorable response within seven days of start of symptomatic treatment.

Conclusion: Antibiotics are widely available and are inappropriately sold and given by grocery stores and retail shops located within local communities in Thailand. Antibiotic-resistant bacteria commonly and freely circulate within the community. Patients with URI and acute diarrhea with no indication for antibiotic therapy can be treated without antibiotics. Findings and observations from this study will be used as part of a social marketing campaign on prevention and containment of AMR to educate people living within communities in Thailand.

Keywords: Antimicrobial resistance, Antibiotic use, Community, Thailand

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Antimicrobial resistance (AMR) has been an urgent health threat in Thailand over the past several decades. One of the most common and important AMR bacteria causing infections in Thailand is extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae. The health and economic burdens

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associated with AMR in Thailand are estimated to be at least 87,751 hospitalizations due to AMR infections, resulting in an estimated 3.24 million days of hospitalization and 38,481 deaths⁽¹⁾. The cost of antibiotics used for treatment of AMR infections was US\$202 million and the total cost, including the cost of morbidity and mortality associated with premature deaths related to AMR, was at least US\$1,300 million⁽¹⁾. AMR-related health and economic burdens comprise at least 0.6% of Thailand's gross national product.

The Thailand AMR Containment and Prevention Program was established in 2011 to help contain and prevent the emergence and spread of key AMR bacterial infections in Thailand. The program has been implemented as a “One Health” approach, which involved multidisciplinary participation to control and prevent AMR since 2012. The program is supported by the Thai Health Promotion Foundation, Health Systems Research Institute (Thailand), Faculty of Medicine Siriraj Hospital, Government Pharmaceutical Organization, and International Development Research Center (Canada). The program’s core campaign is entitled, STOP Being Victims of AMR, as defined by the three pillars of the campaign, 1) stop the production of AMR by promoting responsible use of antibiotics, 2) stop the acquisition of AMR, and 3) stop the transmission of AMR by promoting good sanitation and hygiene, as well as compliance with infection control and prevention practices⁽²⁾. The key operational strategies of the program include creating an AMR containment and prevention package and implementing the AMR containment and prevention package in each of the target groups (healthcare personnel, farmers, and people) in the pilot communities for purposes of determining the required resources, benefits, key success factors, obstacles, and barriers to the implementation of such a program.

The AMR containment and prevention package to be used should contain key messages relevant to the beliefs, attitudes, knowledge, and practices of those living in the target communities. The program intends to use social marketing to reach people in the target communities. The surveys conducted in healthcare personnel and people living in the target communities revealed the following key findings: 1) people usually referred to antibiotics as anti-inflammatory drugs and they believed that both drugs were the same, 2) people took anti-inflammatory drugs when they experienced any symptoms that they considered to be “inflammation” and/or other related symptoms, 3) people usually purchased drugs from grocery stores and retail shops located near their homes for minor ailments and they would go to other healthcare facilities if they did not get better within several days, and 4) most people indicated that they had never heard of or about AMR, did not believe that AMR was real, were not afraid of AMR, and were not involved in producing and/or spreading AMR. It is, therefore, necessary and important for the Thailand AMR Containment and Prevention Program to generate

and disseminate information locally regarding the epidemiological impact of AMR and antibiotic use via a social marketing campaign in the respective target communities.

Material and Method

Studies were conducted in selected districts in Lumphun and Cholburi provinces, both of which are pilot communities for the Thailand AMR Containment and Prevention Program for 2014 and 2015.

Survey of antibiotics sold by grocery stores and retail shops

Local people living in each community were instructed to present to 215 grocery stores and retail shops located in their community with requests for 1) amoxicillin and norfloxacin, 2) anti-inflammatory drugs for sore throat and backache, 3) drugs to treat common cold, acute diarrhea, inflamed uterus, and dysuria. The purchased drugs were identified according to the names shown on the packages. If drug names were unknown, they were sent to pharmacists at Siriraj Hospital for identification. The data were analyzed by descriptive statistics.

Survey of contamination of antibiotic-resistant bacteria in foods and environment

One hundred sixteen samples of fresh foods and 44 samples of cooked foods were purchased from local markets in the target communities. Fresh food samples included chicken, pork, beef, fish, shrimp, chicken eggs, spring onions, parsley, bean sprouts, and other vegetables. Cooked food samples included chicken with rice, grilled chicken, grilled pork, spicy green papaya salad, spicy minced meat, spicy grilled meat, and chili sauce. Each food sample was thoroughly swabbed with a sterile cotton swab. Swabs were placed in Cary-Blair transport medium. Water samples were collected from 14 open water sources including canals. Unspun water sample was used for culture. All cultures were performed at the Infectious Disease Laboratory, Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital. Sample was inoculated onto MacConkey agar supplemented with ceftriaxone (4 mg/L) in order to detect antibiotic-resistant Gram-negative bacteria, particularly ESBL-producing *Escherichia coli*. Bacteria grown on MacConkey antibiotic supplemented agar were further identified. ESBL-producing bacteria were detected by double-disk diffusion method for

antibiotic susceptibility testing⁽³⁾. The data were analyzed by descriptive statistics.

Survey of antibiotic-resistant bacteria colonization in people

Adult aged 18 years and older was asked to collect a stool sample directly from stool before it touched the floor of the toilet by a swab and it was put in Cary-Blair transport medium, as well as to provide information regarding demographics, underlying diseases, occupation, food consumption habits, and drugs used over the previous three months. Five hundred thirty four individuals voluntarily provided stool samples. Bacterial culture of stool samples was performed at the Infectious Disease Laboratory, Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital. Sample was inoculated onto MacConkey agar supplemented with ceftriaxone (4 mg/L) in order to detect antibiotic resistant Gram-negative bacteria, particularly ESBL-producing *E. coli*. Bacteria grown on MacConkey antibiotic supplemented agar were further identified. ESBL-producing bacteria were detected by double-disk diffusion method for antibiotic susceptibility testing⁽³⁾. The data were analyzed by descriptive statistics.

Monitor of clinical responses of the patients with upper respiratory infection (URI) and acute diarrhea who received no antibiotics

One thousand three hundred one patients with URI and 235 patients with acute diarrhea with no indication of antibiotic who received only symptomatic treatments as appropriate at the tambon health promoting hospitals located in the target communities between June and August 2015 were followed via telephone contacts every few days until all symptoms related to URI and acute diarrhea disappeared. The data were analyzed by descriptive statistics.

Results

Antibiotics sold and given by 215 grocery stores and retail shops

Amoxicillin and norfloxacin were sold at the request of customers in 31.6% and 14.0% of customer visits, respectively. The cost of each tablet or capsule of each drug was normally 5 baht (US\$ 0.20). Antibiotics sold by grocery stores and retail shops and the respective complaints/ailments for which they were given are shown in Table 1. Tetracycline was the most common antibiotic sold and it was given for all

specified complaints, especially for inflamed uterus. The amount of tetracycline dispensed was 2 to 40 capsules, with a median of 10 capsules. Amoxicillin and ampicillin were given for sore throat and common cold. The amount of amoxicillin/ampicillin given was 4 to 20 capsules, with a median of 10 capsules. Norfloxacin was given for acute diarrhea and dysuria, with a range of 1 to 10 tablets and a median of four tablets. A combination of diiodohydroxyquinoline, furazolidone, neomycin sulfate, phthalylsulfathiazole, and light kaolin was also commonly given for diarrhea by some grocery stores and retail shops.

Contamination of antibiotic-resistant bacteria in foods and open water sources

Among 174 samples collected from foods and open water sources, 46 samples (26.4%) were positive for at least one isolate of ESBL-producing *E. coli*. ESBL-producing *E. coli* was isolated from 93.3% of fresh pork meat samples, 38.5% of fresh chicken meat samples, and 35.4% from open water sources. Rate of ESBL-producing *E. coli* contamination in fresh vegetables and cooked foods was 8.1%.

Antibiotic-resistant bacteria colonization in people

Among 534 adults who voluntarily provided stool samples for culture, 33.2% were males with mean

Table 1. Antibiotics sold by 215 grocery stores and retail shops for each complaint

Antibiotic	Number of grocery stores and retail shops
Sore throat	
Tetracycline	89 (41.4%)
Amoxicillin/ampicillin	46 (21.4%)
Backache	
Tetracycline	9 (4.2%)
Common cold	
Amoxicillin/ampicillin	28 (13.0%)
Tetracycline	20 (9.3%)
Acute diarrhea	
Norfloxacin	59 (27.4%)
Tetracycline	11 (5.1%)
Combination*	42 (19.5%)
Inflamed uterus	
Tetracycline	155 (72.1%)
Dysuria	
Tetracycline	58 (27.0%)
Norfloxacin	23 (10.7%)

* Combination of diiodohydroxyquinoline 250 mg, furazolidone 50 mg, neomycin sulfate 50 mg, phthalylsulfathiazole 250 mg, light kaolin 250 mg

(SD) age of 50.4 (13.8) years. Most of the participants were laborers, housewives, or farmers (13% were pig and/or chicken farmers). Sixty-five percent of participants had no underlying diseases. Hypertension, diabetes mellitus, and dyslipidemia were common health problems in those with underlying diseases. Regular consumption of raw meat, semi-cooked food, and water from natural water sources was reported in 30.1% of participants. Consumption of any kind of drugs over the past three months was reported in 59.9% of the participants, with 28% of drugs being either anti-inflammatory drugs or antibiotics. Of 534 individual stool samples, ESBL-producing *E. coli* strains were isolated from 355 (66.5%) individuals.

Clinical responses of the patients with URI and acute diarrhea who received no antibiotics

Among 1,301 patients with URI and 235 patients with acute diarrhea attending the tambon health promoting hospitals located in the target communities who had no indication of antibiotic therapy and did not receive antibiotics, 57% were females and the mean, median, and range of age were 34.5, 37, and 1 to 69 years, respectively. Thirty-two percent of the patients were children aged 13 years and younger. The patients with URI were clinically diagnosed with common cold (65.0%), pharyngotonsillitis (29.1%), and acute bronchitis (5.9%). Clinical responses on day 3 after treatment revealed that 36.9%, 56.7%, 6.0%, and 0.4% of the patients were cured, improved, unchanged, and worse, respectively. Clinical responses on day 7 after treatment revealed that 83.6% and 16.4% of the patients were cured and improved, respectively. For the patients with acute diarrhea, their clinical responses on day 3 after treatment revealed that 74.9%, 21.7%, and 3.4% of the patients were cured, improved, and unchanged, respectively. Clinical responses on day 7 after treatment revealed that 96.6% and 3.4% of the patients were cured and improved, respectively.

Discussion

Social marketing is an approach used to develop activities aimed at changing or maintaining peoples' behavior for the benefit of both individuals and communities. One of the aims of the Thailand AMR Containment and Prevention Program is to change the behavior of people in the community regarding responsible use of antibiotics and appropriate sanitation and hygiene practices. The present study was conducted in response to observations from a survey conducted in these communities as mentioned in the

introduction part. The findings from the present study confirm that 1) antibiotics, the main driver of AMR, were easily accessed by customers and were inappropriately sold and given by grocery stores and retail shops located in the community, 2) antibiotic-resistant bacteria commonly circulate among people, food, and the environment in communities, similar to observations from a previous studies in other areas of Thailand, Laos, and Vietnam^(4,5), and 3) many patients with URI and acute diarrhea can be treated without antibiotics and their clinical responses were similar to those observed from a previous study conducted in other healthcare settings⁽⁶⁾. The observations made from this study will be useful in producing key messages, media, tools, and activities for the development of a social marketing campaign to correct the beliefs, attitudes, knowledge, and practices of people in these communities in order to prevent and contain AMR. Additional campaigns for combating AMR in the community will include the following key messages, 1) antibiotics are not anti-inflammatory drugs, 2) antibiotics are beneficial only in bacterial infections, 3) overuse and misuse of antibiotics will create AMR, 4) overuse and misuse of antibiotics (most notably purchasing antibiotics from a grocery store, retail shop, or drug store) must be stopped, and 5) consumption of clean water and hygienically prepared and thoroughly cooked food, as well as good personal sanitation and hygiene, are essential to avoiding acquisition and transmission of antibiotic-resistant bacteria. The people who had URI and acute diarrhea with no indication for antibiotic therapy successfully treated without antibiotics will be invited to give testimonial accounts to others as a strategy for convincing people to stop taking antibiotics for illnesses that are not caused by bacteria. Grocery stores and retail shops will be encouraged to stop selling antibiotics since it is illegal and it is likely to result in the development of AMR, and to sell alternative remedies instead (such as herbal medicines) that do not contain antibiotics. Genotyping of antibiotic-resistant bacteria isolated from several sources in the same community is being conducted to determine an association of antibiotic resistance among these isolated antibiotic-resistant bacteria.

What is already known on this topic?

Most people in community indicate that they have never heard of or about AMR, do not believe that AMR is real, are not afraid of AMR, and are not involved in producing and/or spreading AMR.

What this study adds?

People in community are actually involved in producing and/or spreading AMR.

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Potential conflicts of interest

None.

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ระบาดวิทยาของการใช้ยาต้านจุลชีพและเชื้อยาด้านจุลชีพในบางชุมชนในประเทศไทย

สมพงศ์ คำสาร, ยุพิน นำปุ่นศักดิ์, สุพรรณิ บุษมาโร, วีระวิทย์ ตั้งก่อสกุล, จักรพงศ์ สีนามะ, ภิญโญ รัตนอัมพวัลย์, อธิรัฐ บุญญาศิริ, วิษณุ ธรรมลิขิตกุล

วัตถุประสงค์: เพื่อทราบระบาดวิทยาของการใช้ยาต้านจุลชีพและเชื้อยาด้านจุลชีพในบางชุมชนในประเทศไทยสำหรับนำไปใช้รณรงค์ การควบคุมและป้องกันการดื้อยาด้านจุลชีพในชุมชนเป้าหมายของโครงการควบคุมและป้องกันการดื้อยาด้านจุลชีพในประเทศไทย **วัสดุและวิธีการ:** สืบหาการขายยาของร้านชำและร้านค้าปลีกในชุมชนเป้าหมายจำนวน 215 ร้าน โดยคนในชุมชนไปซื้อยาชื่อเฉพาะ และซื้อยาสำหรับอาการเจ็บคอ ปวดหลัง หัวดี อุจจาระร่วง มดลูกอักเสบ และปัสสาวะแสบ-ขัด แล้วนำยาที่ได้รับมาวิเคราะห์ชนิด ยาต้านจุลชีพ เก็บตัวอย่างอาหารสด อาหารปรุงสำเร็จ และน้ำจากแหล่งน้ำในชุมชนเดียวกันจำนวน 174 ตัวอย่าง มาตรวจหาเชื้อแบคทีเรียดื้อยาที่ปนเปื้อนอยู่ เก็บอุจจาระผู้ใหญ่ในชุมชนเดียวกันจำนวน 534 คน มาตรวจหาเชื้อแบคทีเรียดื้อยาที่อยู่ในอุจจาระ และเก็บข้อมูลผลการรักษาผู้ป่วยติดเชื้อที่ระบบการหายใจช่วงบน 1,301 คน และผู้ป่วยอุจจาระร่วงเฉียบพลัน 235 คน ที่ไม่มีข้อบ่งชี้ของการรักษาด้วยยาต้านจุลชีพซึ่งมารับการรักษาที่โรงพยาบาลส่งเสริมสุขภาพตำบลในชุมชนเดียวกันโดยไม่ได้รับยาด้านจุลชีพ ด้วยการโทรศัพท์สอบถามอาการทุก 2-3 วัน จนกว่าอาการจะหาย ข้อมูลที่ได้นำมาวิเคราะห์ด้วยสถิติเชิงพรรณนา

ผลการศึกษา: ร้านชำและร้านค้าปลีกในชุมชนเป้าหมายส่วนมากขายยาด้านจุลชีพให้ประชาชนที่มีอาการป่วยที่พบบ่อย ยาด้านจุลชีพเกือบทั้งหมดที่ขายให้ประชาชนไม่เหมาะสม ความชุกของเชื้ออีโคไล ดื้อยาด้านจุลชีพในอาหารสดและแหล่งน้ำในชุมชนร้อยละ 26.4 โดยเชื้อดื้อยาดังกล่าวมักแยกได้จากเนื้อสดและแหล่งน้ำ ผู้ใหญ่ในชุมชนร้อยละ 66.5 มีเชื้ออีโคไล ดื้อยาด้านจุลชีพในอุจจาระ ผู้ป่วยโรคติดเชื้อที่ระบบการหายใจช่วงบนและผู้ป่วยอุจจาระร่วงเฉียบพลันที่ไม่มีข้อบ่งชี้ของการรักษาด้วยยาด้านจุลชีพทุกรายหาย หรืออาการดีขึ้นมากภายใน 7 วันหลังการรักษา โดยไม่ต้องใช้ยาต้านจุลชีพ

สรุป: ประชาชนในชุมชนเข้าถึงยาด้านจุลชีพได้ง่ายมากโดยการซื้อจากร้านชำและร้านค้าปลีกในชุมชน เชื้ออีโคไล ดื้อยาด้านจุลชีพมักปนเปื้อนในอาหารสดและแหล่งน้ำในชุมชน คนส่วนมากในชุมชนมีเชื้อดื้อยาดังกล่าว ผู้ป่วยโรคติดเชื้อที่ระบบการหายใจช่วงบน และผู้ป่วยอุจจาระร่วงเฉียบพลันที่ไม่มีข้อบ่งชี้ของการรักษาด้วยยาด้านจุลชีพสามารถหายได้โดยไม่ต้องใช้ยาต้านจุลชีพ ข้อมูลที่พบดังกล่าวมีประโยชน์มากในการใช้เป็นแนวทางรณรงค์การควบคุมและป้องกันการดื้อยาด้านจุลชีพในชุมชนด้วยการตลาดเชิงสังคม
