

Prevalence of *Escherichia coli* in the Community Acquired Bacteremic UTI in Southeast Asian Countries: A Mini-Review

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ABSTRACT

Urinary tract infection due to *E. coli* is common among Southeast Asian countries. However, there is limited research available providing the prevalence of *E. coli* in Urinary Tract Infection in Southeast Asia. With 94%, Myanmar, among the other Southeast Asian Countries had the highest prevalence rate of *E. coli* that causes Urinary Tract Infection. Brunei, on the other hand, had the lowest prevalence rate of 1.18%. Further, Vietnam accounts for more than 48% of the *E. coli* isolates in different SEA. Meanwhile, there is no data available at Timor-Leste making it difficult to know the prevalence of *E. coli* in the country. Despite having the most number of *E. coli* isolate among other region, there's still limited data among Southeast Asian countries that could mean: (1) researchers had little interest in this field, or (2) clinicians and researchers would still not acknowledge its high prevalence rate. Despite the limited data, clinician and researchers should be encouraged more to conduct study about the said topic to further widen the knowledge and to create permanent solutions to halt the infection brought by *E. coli*. Further, it is also highly suggested to create an organization that would monitor the prevalence of *E. coli* in different countries in Southeast Asia as this may be beneficial in order to prevent other severe cases of infections.

Key words: *Escherichia coli* or *E. coli*, Urinary Tract Infection or UTI, Bacteremic Urinary Tract Infection, Southeast Asia, Community-acquired

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INTRODUCTION

Urinary Tract Infection is caused by the invasion of microorganisms that rapidly multiplies at the organs located at the urinary tract. It is said to be the most common severe public health problem and is responsible for countless mortality and morbidity worldwide.^[1] However, despite the severity of UTI it is yet one of the most neglected infections due to the limited data. This infection can be due to various community- and

hospital- acquired bacteria like *Escherichia coli*, *Klebsiella* spp., *Staphylococcus aureus*, coagulase negative *Staphylococci*, *Proteus mirabilis*, *Enterococcus* species, *Pseudomonas aeruginosa*, and *Enterobacter* spp.^[2]

Most common causative agent of urinary tract infection is uropathogenic *Escherichia coli* (UPEC). It came from the family *Enterobacteriaceae* that are commonly found inhabiting in the lower gastrointestinal tract of humans.^[3] In general, *Escherichia coli* can be both found and acquired in community and hospital cases. Due to the low prevalence rate of community acquired UTI, there is only a limited data available. With that, this mini-review aims to investigate the prevalence of community acquired *E. coli* in UTI in Southeast Asian countries to increase awareness regarding the severity of *E. coli* and to compare the available data in SEA countries.

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MATERIALS AND METHODS

Literature Search

The literature search was performed using the database: PubMed, Google Scholar and PubMed Central (PMC). The keywords used includes the combination of *Escherichia coli* + Urinary tract Infection + Bacteremic urinary tract infection + Southeast Asia + Community-acquired. The search filter did cover the year the articles are published from the year 2010 up to the present year 2021. The following are the inclusion criteria; [1] published journals and articles written in English language, [2] people reported having Urinary Tract Infection in Southeast Asia, [3] causative agent of the said infection is *Escherichia coli*. While the exclusion criteria include; [1] journals and articles that do not specify *Escherichia coli* as the causative agent, [2] articles/journals not translated or written in English language, [3] articles/journals that do not specify methods.

Eligibility Criteria

This study is limited to the data related to the cases of Urinary Tract Infection to the countries around Southeast Asia, such as Indonesia, Vietnam, Thailand, Singapore, Philippines, Malaysia, Myanmar, Cambodia, Laos, Brunei, Timor-Leste. Data, articles, journals, and research studies that were written in English were the only one included in this study. Published studies that were written in other languages were excluded to avoid misinterpretation of the data. The articles must be published from year 2010 to present to be eligible for the study. Any other publications older than the said years are not accepted. This will also limit to those UTI that are community acquired with the cases of both symptomatic and asymptomatic. This study will include both male and female in all ages that were reported to have Urinary Tract Infection. Cases of Urinary tract infection will only be limited to those with the causative agent of the bacteria *Escherichia coli*. Other strains of bacteria that cause UTI such as *K. pneumoniae*, *Staphylococcus aureus* and *Enterobacter* spp. was excluded from the study.

RESULTS

A ten (10) year comparison of the prevalence of *E. coli* that cause bacteremic UTI

The prevalence of extended spectrum beta lactamase-producing *E. coli* has increased vastly before and after 2010. Out of the countries that been mentioned, South Asia has the most number of community acquired urinary tract infections *E. coli* with 21.7 % before 2010 to 33.2% after 2010 followed by Far East Asia with

4.8 ~ 7.55% before 2010 to 7.6 ~ 10.7% after 2010. (Table 1)

Comparison of the prevalence of *E. coli* that cause bacteremic UTI in Southeast Asian Countries

Philippines

Escherichia coli is a common isolate in the Philippines that affects both gender regardless of the patients age. From the studies collated, majority of the isolates were *Escherichia coli* that causes urinary tract infection followed by: *Proteus mirabilis* and *Pseudomonas aeruginosa* (5.7%),^[4] *Enterobacter* sp. (16.7%),^[5] *Klebsiella pneumoniae* (8.7%),^[6] *Pseudomonas aeruginosa* (31.1%),^[7] and other gram-positive (15.8%)^[6] (Table 2). In addition, various study showed that most of these organisms are antibiotic resistant. Further, most of these micro-organisms were collected from tertiary hospitals from different age and gender.

Table 1: The Prevalence of Extended Spectrum beta lactamase-producing *E. coli* has increased vastly before and after 2010. Retrieved from "Community-Acquired Urinary Tract Infection by *Escherichia coli* in the Era of Antibiotic Resistance".^[6]

	Before 2010	After 2010
South Asia	21.7%	33.2%
Far East Asia	4.8 ~ 7.55	7.6 ~ 10.7%
Latin America	1.7%	7.1 ~ 12.5%
US and Canada	7.4	1.8 ~ 8%

Table 2: Pathogens present in patients with Urinary Tract Infection.

Organism	Percentage
Encarnacion (2012)	
<i>Escherichia coli</i>	75.5 %
<i>Proteus mirabilis</i> and <i>Pseudomonas aeruginosa</i>	5.7%
Bay & Anacleto (2010)	
<i>Escherichia coli</i>	44.4%
<i>Klebsiella pneumoniae</i>	5.6%
<i>Enterobacter</i> sp.	16.7%
Ganguangco et al. 2015	
<i>Escherichia coli</i>	76.2%
<i>Klebsiella pneumoniae</i>	3.4%
other gram positive	15.8%
Suwantarat & Carroll (2016)	
ESBL – producing	36.8%
<i>Escherichia coli</i>	59.4%
<i>Klebsiella pneumoniae</i>	46.7%

Singapore

The gathered results in Singapore showed that *E. coli* had the most number of isolates that causes the urinary tract infection. Generally, adult woman had been diagnosed with the positive urinary tract infection and most of the men result had a medical history with other underlying disease such as diabetes mellitus, genitourinary abnormalities, use of antibiotics within last four (4) weeks and hospitalize within the last six (6) months.^[8,9] The biggest group of patients that results with positive urine culture is the women aged 13-65 years old followed by the women with > 65 years of age.^[9]

Thailand

Escherichia coli is the most common cause of Urinary Tract infection in the country accounting for almost half of the results from the studies gathered in Thailand followed by *K. pneumoniae* and other ESBL-producing bacteria. Enterococcus faecium had the most number of isolates only followed by *E. coli*.^[10] In addition, urinary tract infection caused by *E. coli* is common in women than in men. Underlying illnesses and diseases, such as hypertension, diabetes, dyslipidemia, are common among men with *E. coli* isolates.^[11] A study conducted in Southern Thailand collected 254 urine specimens from patients with UTI in Maharaj Nakhon Si Thammarat Hospital, Southern Thailand. These specimens tested for bacterial isolates during a time frame of July 2014 to December 2014. The PCR conducted as confirmatory study confirmed that the uropathogenic *Escherichia coli* (UPEC) is the causative agent in UTI in patients at the tertiary hospital in Southern Thailand.^[12] (Table 3)

Vietnam

Antibiotic resistant uropathogenic *Escherichia coli* is common in Vietnam.^[13] 39.4% of 436 isolates were ESBL-producing microorganisms in which Vietnam has the highest rate with 55.1% of the said isolates followed by Thailand.^[7] In addition, *E. coli* accounts for more than 48.1% of the isolates making it the most collected ESBL-producing species in the country.^[7]

Malaysia

E. coli is one of the comorbidities present in Diabetes Mellitus. However, *E. coli* is not only prevalent in

patient with Diabetes Mellitus. It is also common in children and other age group. Further, it is the leading bacterial pathogen in children that causes Urinary Tract Infection with a prevalence rate of 41.6%, and there is high antibiotic resistance to the commonly used antibiotic in children, especially ampicillin.^[14] Prevalence rate of *E. coli* in all ages was 40.2%.^[15] This data showed that *E. coli* is the common cause of UTI in Malaysia. (Table 4)

In Kuala Lumpur, Malaysia, it was found that the positivity rate of UTI was 23.25 % (326 out of 1402 patients).^[16] The bacterial strain analysis demonstrated that most patients with UTI were infected with *Escherichia coli* with a positivity rate of 50.3%. and from ages 36 and above. Enterococci had a positivity rate of 24.23% and had infected the age range of 22 to 28 year. Staphylococci isolates had a positivity rate of 17.17% and infected people ages 15 to 21 years. *Klebsiella* showed a positivity rate of 5.52% and from people with the age range of 22 to 28 years. Proteus isolates showed a positivity rate of 2.14% and people who were infected were in the ages 15 to 21 years old. Lastly, Enterobacter only showed a positivity rate of 0.61%.

Myanmar

During the period of June 2019 and December 2019, the frequency of ESBL *E. coli* from the clinical samples of pediatric patients in Yangon Children's Hospital, Myanmar were investigated.^[17] They were able to collect a total of 3462 clinical specimens, for which blood, sputum, urine, CSF fluid, and pus swabs, were collected from the pediatric patients. A total of 123 *E. coli* was isolated and 100 of *E. coli* isolates were resistant to cephalosporins, also 94% *E. coli* isolates were confirmed to be Extended Spectrum Beta-Lactamase producers by PCR.

Indonesia

One study in Jakarta, Indonesia investigated the susceptibility pattern of Urinary Tract Infections among 715 pregnant women in their community health centers between the period of 2015 to 2017.^[18] Based on the results of their investigation, 73 out of 715 women had

Table 3: Prevalence Rate of UTI Caused by *E. coli* from different studies in Thailand.

No. of samples	Gender	Age	Prevalence Rate of <i>E. coli</i> causing UTI			Reference
			Total	ESBL	Non-ESBL	
408	M/F	>15 yrs. old	408	159 (39%)	249 (61%)	Savatmongkornkul et al. 2016 ^[12]
166	M/F	≤15 - ≥61 yrs. old	113	52 (46%)	61 (54%)	Themphachana et al. 2014
127	M/F	≥ 18 yrs. old	27	8 (30%)	19 (70%)	Kotikula & Chaiwarith, 2018

Table 4: List of studies that showed the prevalence rate of UTI caused by *E. coli*.

Population (n)	Gender	Age	Prevalence Rate of <i>E. coli</i> in UTI	Reference
721	M/F	1 day – 13 years old	41.6%	Mohd et al. 2015
348	M/F	All ages	40.2%	Shah et al. 2019

Table 5: List of accepted articles in the study showing the reported cases of *E. coli* that caused UTI Indonesia.

Population (n)	Gender	Reported UTI	<i>E. coli</i> as causative agent	Duration of data collection	Reference
715	F	73	26.7%	2015 – 2017	[18]
110	M/F	20	0.09%	June 2011- December 2011	[19]

asymptomatic bacteriuria and it was found that *E. coli* was the major causative agent Table 5.^[18]

In a study conducted by the Department of Child Health at CMH, Pediatric Polyclinic at Budi Kemuliaan, and Thamrin Hospitals during the time frame of June to December 2011, it was found that the prevalence of UTI was 18.2% and *E. coli* was the most common isolates found in the subjects.^[19]

Cambodia

Some studies gathered showed that *E. coli* is one of the most common causative agents for various infections in different tertiary hospitals in Cambodia.^[20] A study conducted in Angkor Hospital for Children (AHC) in Cambodia showed that among the 217 isolates, 78% were *E. coli* followed by *Klebsiella pneumoniae*. With that, it is the most commonly isolated organism in Children with Urinary tract infection.^[21]

Laos

Laboratory reports from Mahosot Hospital in Vientiane, Laos were reviewed in retrospective approach during the time course of five year, from 2010 to 2014.^[22] A total of 18,319 blood cultures from 15,665 patients were examined, it was found that both *E. coli* and *K. pneumoniae* accounted for 34.8% (360/1,032) of all clinically significant isolates.

Since their study approach was retrospective, they admitted that they have several limitations, which include the retrieval of hospital charts which were considered to be crucial particularly in investigating

the clinical outcomes of the organism that they were able to isolate. However, it was mentioned in their paper that both *E. coli* and *K. pneumoniae* isolated from the patients were associated in the disease.

Brunei

A study conducted at Reja Iseri Pengiran Anal Saleha (RIPAS) Hospital in Brunei showed that out of the 170 pregnant women visiting for prenatal and antenatal care there were 163 (95.88%) who had normal urine samples with no organisms detected. However, there were seven (7) who had infected samples in which both *Klebsiella* spp. (2.94%) and *Escherichia coli* (1.18%) were present. Both organisms are causative agents for urinary tract infections. The implication of this is that the microorganism seen in the urine sample is the most probable cause for the risk of having acute episodes of *E. coli*.^[23]

Timor – Leste

There are no existing studies about the prevalence of *E. coli* in Urinary Tract Infection in this country.

DISCUSSION

Prevalence of *E. coli* that causes Urinary Tract Infection

Escherichia coli is known to be the main causative agent for most diarrhea and urinary tract infection cases. There are numerous studies available about its etiology, clinical manifestations, laboratory diagnosis, and treatment. However, uropathogenic *E. coli* that causes urinary tract infection in Southeast Asian countries still lacks popularity making it the least chosen topic to study. After 10 years of gathering data, results showed that *E. coli* is prevalent in Southeast Asian countries compared to other regions.^[24]

There are various data available regarding isolation, antimicrobial resistance, and clinical disease and infections related to Enterobacteriaceae. Among the species that belongs to the family, *Escherichia coli* is mostly isolated and tested.^[7] It was estimated that 250 million people a year were affected by UTI.^[25] Developing countries like the United States showed great interest in producing more studies and developing more facilities in order to better widen the knowledge and information that is currently available at various research journal publications. Main causative agent for most UTI cases among the Asian geographic region alone was identified to be *E. coli*.^[26] However, despite it being prevalent in Asian countries,^[24] there is still limited data available produced in the said countries due to limited resources.

Comparison of Results among Southeast Asian Countries

Most countries in Southeast Asian regions are developing countries. It lacks resources in producing studies that will help prevent further infection. Among the 11 countries of Southeast Asia, Timor-Leste presents no journal article about *Escherichia coli* making it difficult to track its prevalence. On the other hand, Thailand has the most journal articles available [seven (7) journal articles]. In the study conducted in Singapore, data showed that among the patients in the studies 74% were Chinese, 10% were both Malay and Indian, and the remaining 6% were from unknown ethnicity.^[8] The prevalence of *Escherichia coli* causing Urinary Tract Infection is high in South Asia, having 21.7% before 2010 and increased to 33.2% after 2010.^[24] It implies that the infection rate due to *E. coli* causing UTI increases. Further, urinary tract infection due to *E. coli* is the most common problem in Singaporean hospitals^[7] as well as in tertiary hospital at Southern Thailand,^[11] and Cambodia.^[20] Meanwhile, Vietnam accounts for more than 48.1% of *E. coli* isolates in a study conducted in Southeast Asian countries except Timor-Leste.^[7] The result of the data is very alarming for South Asia as the percentage of infection increases each year.

Researchers from different Southeast Asian countries mostly conduct studies about urinary tract infection in female and pregnant women. In the Philippines, most of urine sample showed *E. coli* isolates with huge percentage.^[6] In a retrospective analysis of cases involving children aged one to thirteen years old with culture-proven UTI at Selayang Hospital in Malaysia, the most common organism isolated was *E. coli*, which accounted for 41.6 percent of the total population. As a result, *E. coli* remains the most common bacterial pathogen responsible for UTI in children.^[27] In addition, UTI is also present and rampant among patient with Diabetes mellitus making it one of the few underlying disease and infection brought by UTI caused by *E. coli*.^[14] However, in a study conducted in Indonesia, most of the patients were male (59.9%). Among the 3380 patients from the study, 70% were UTI caused by *E. coli*.^[28] Aside from female and pregnant women, researchers in Myanmar conducted a pediatric study that revealed that *E. coli* is also commonly isolated with pediatric patients with urinary tract infection.^[17] A study of medical case reports analysed in Singapore.^[9] Every patient who had a UTI diagnosis and were given a urine culture were examined. The most common organism identified for all genders and age groups was *Escherichia coli*, which accounted for 74.5 percent of all UTI-causing species. Also, in a research in Cambodia, 161 samples

or 74% from outpatients and 56 samples which is 26% from inpatients were submitted. Gram-negative bacteria were present in 97 percent of isolates (210/217), and *E. coli* is by far the most common organism with a total of 78% (170/217) that caused UTI among Cambodian children.^[21] With that, this confirmed that regardless of age and gender, UTI caused by *E. coli* is rampant in Southeast Asian countries.

CONCLUSION

This narrative review showed high prevalence among patients with Urinary Tract infection due to *E. coli*. Gender, age, and ethnicity are not the factors that could rule someone out from acquiring the infection. Despite its high prevalence in Southeast Asian countries, there are still limited journals available due to the reason that most countries in this region are developing countries. It is also highly suggested to build a team or organization that would monitor the prevalence of not just *E. coli* but as well as other pathogenic microorganisms. Clinicians and researchers need to recognize the high prevalence could later be a cause of even severe cases of infections.

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CONFLICT OF INTEREST

The authors declare that there are no conflict of interests.

Declaration

Study Limitations

This study was limited to the prevalence rate of community-acquired *E. coli* that causes Urinary Tract Infection in Southeast Asian Countries. This did not cover the presence of hospital-acquired *E. coli* in other regions aside from Southeast Asia, for making their papers available online and their contribution into the writing of the review.

Authors' Contributions

Rosero, J.B., Alvarez, J.G, Soriano, H.B., Raymundo, J.D. Batisla-on, C.E., Morales, K.O, and Lirio, M.R. partici-

pated in literature searches, data analysis, and writing of the paper. All authors read and approved the paper.

ABBREVIATIONS

UTI: Urinary Tract Infection; ***E. coli:*** *Escherichia coli*; **UPEC:** Uropathogenic *Escherichia coli*; **SEA:** Southeast Asia; **ESBL:** Extended Spectrum Beta Lactamase.

SUMMARY

Urinary tract infection caused by *Escherichia coli* is rampant in Southeast Asian countries. Among of which, Myanmar has the highest prevalence with 94% while Timor-Leste had little to no data about *Escherichia coli*. Further, it is also evident that despite the prevalence rate of *Escherichia coli* in Southeast Asian countries there are little to no data available due to lack of researches. It is alarming considering that UTI caused by *E. coli* can cause other comorbidities such as hypertension, diabetes, and dyslipidemia. With that, researchers should focus more in providing more data regarding *Escherichia coli* particularly with its underlying comorbidities.

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