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A 5-Year-Retrospective Review: The Clinical Outcome between Adequate and Inadequate of Initial Antibiotics Treatment in Pediatric Patients, Vajira Hospital

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ABSTRACT

OBJECTIVE: The results of adequate and inadequate empirical antibiotics remain unclear. This study aimed to evaluate the results of using adequate and inadequate empirical antibiotics.

METHODS: A retrospective cohort analysis that covered January 2017 and December 2021 was conducted. At Vajira Hospital, we enlisted pediatric patients with bacteremia and urinary tract infections (UTIs). Patient attributes, empirical antibiotics, therapeutic results, financial expenditures, and antibiotic susceptibility patterns were assessed.

RESULTS: In total, 286 pediatric patients were enrolled. There were 230 (80.4%), and 56 (19.6%) patients with UTIs and bacteremia, respectively. The organism that was found the most frequently was *Escherichia coli* (53.5%), while third-generation cephalosporin was the most often used empirical antibiotic (74.5%). Only 78.4% of *Escherichia coli* were vulnerable to third-generation cephalosporin. Of 220 patients (76.9%) were treated with adequate empirical antibiotics. The outcomes in the adequate empirical antibiotics group revealed better-improved symptoms than inadequate empirical antibiotics group (96.4% VS 84.8%, p = 0.002).

CONCLUSION: Clinical outcomes among pediatric patients from adequate initial antibiotics groups were reported the better outcomes. The mortality rates were not different. Nonetheless, appropriate empirical antibiotics are needed. In UTI patients, amikacin is preferable options for empirical antibiotics.

KEYWORDS: adequate, empirical antibiotics, inadequate, pediatrics

INTRODUCTION

Infections are to blame for one-third of all fatalities globally[1]. Bacteremia, and urinary tract infections (UTIs) each had in-hospital death rates of 23.4%, and 11.9%, respectively[2]. Bacteremia is linked to higher rates of morbidity, death, and costs[3]. Additionally, bacteremia has a mortality rate that ranges from roughly 28 to 55%[4]. In addition to bacteremia, major and frequent issues include UTIs. Each year, 8.1 million UTIs diagnoses were recorded in the United States. If the condition was not treated properly, renal failure would result[5-7]. In order to address and avoid complications from bacteremia, and UTI, appropriate antibiotics are required.

Antibiotic-resistant microorganisms are now more prevalent, which increases costs, lengthens hospital stays, and boosts fatality rates[8]. The World Health Organization promotes awareness of microbes that are resistant to antibiotics[8]. However, the use of inferior empirical antibiotics is rising. Information on adequate and

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inadequate empirical antibiotics varies. Inadequate empirical antibiotics have been shown to promote catastrophic outcomes in the past, but another investigation found there was no distinction in the results between inadequate and adequate empirical antibiotics[9-13]. In order to determine if appropriate empirical antibiotics are necessary, data on outcomes between adequate and inadequate empirical antibiotics as well as antimicrobial susceptibility patterns in the pediatric ward at Vajira Hospital require examination. The primary objective is to approve the mortality rate between adequate and inadequate initial antibiotics.

METHODS

We carried out a 5-year retrospective cohort analysis at a single location. When bacteremia and UTIs were determined to be caused by bacteria on hemoculture, and urine culture ($\geq 10^5$ CFU per milliliter of urine), respectively with the relevant symptoms, we enrolled pediatric patients under the age of 15 who had these diagnoses [14-15]. Therapy was determined to be adequate or inadequate empirical antibiotics treatment based on the in-vitro susceptibility of an isolated organism. Adequate empirical antibiotics are referred to as in-vitro susceptibility of the isolated pathogen to at least one of the antibiotics administered and inadequate empirical antibiotics are referred to as in-vitro resistance of the isolated pathogen to at least one of the antibiotics administered that administration in the first 24 hours[16].

We collected all data from 1 January 2017 to 31 December 2021 at the Pediatrics outpatient and inpatient departments at Vajira Hospital, Navamindradhiraj University. Vajira Hospital is a tertiary care facility that serves over 700,000 outpatient visits and 30,000 inpatient admissions per year. Demographic information, organisms, antimicrobial susceptibility patterns, treatment results between sufficient and inadequate empirical antibiotics, and expenditures were gathered. Institutional review board ethics clearance was received from the Faculty of Medicine at Vajira Hospital, Navamindradhiraj University.

The sample size for the comparison results between adequate and inadequate empirical antibiotics was determined using an unmatched cohort study. Kelsey et al. described the sample size formula for the present method.

$$n_1 = \frac{(Z_{\alpha/2}+Z_{1-\beta})2\bar{p}\bar{q}\ (r+1)}{r(p_1-p_2)^2}$$

$$n_2 = rn_1$$

where n_1 = amount of inadequate empirical antibiotics (exposed group), n_2 = amount of adequate empirical antibiotics (unexposed group), α = 0.05, $1-\beta$ = 0.8, p_1 = correlation between inadequate empirical antibiotics and death, p_2 = link between the segment of adequate empirical antibiotics and death.

According to an earlier study, inadequate empirical antibiotics resulted in 67.8% in-hospital mortality, whereas adequate empirical antibiotics resulted in 28.7% in-hospital deaths[17]. Additionally, data from a month at the pediatric department of Vajira Hospital showed that the number of patients receiving an appropriate course of empirical antibiotics was more than three times higher than that of the inadequate group. As a result, we aimed to gather samples from unexposed and exposed groups at a ratio of 3 to 1.

At least 66 participants in total, comprising at least 17 in the exposed group and 49 in the unexposed group, made up the overall sample size. This study was approved by the Institutional Review Board Faculty of Medicine (COA 069/2565).

Interquartile range (IQR) and percentage were used in descriptive statistics to determine the mean. The Independent Samples T-test, Mann-Whitney U Test, Chi-Square Test, or Fisher's Exact Test, as applicable, were correlated to the p-value. IBM SPSS Statistics 28.0 was used to examine the data.

RESULTS

From January 1, 2017, to December 31, 2021, we enrolled 286 pediatric patients who had been diagnosed with UTIs, and bacteremia. Age was 7.16 months on average (IQR 2.21-30.66).

159 (55.6%) of the patients were male. Furthermore, genitourinary tract illness was the most prevalent underlying condition in 90 (31.5%) patients (n = 39, 13.6%) such as vesicoureteral reflux, chronic kidney disease, and renal cysts. From the sample, 236 were inpatients (82.5%). UTIs, and bacteremia were identified in 230 (80.4%), and 56 (19.6%) patients, respectively. The most prevalent empirical antibiotic (74.5%) was third-generation cephalosporin. Septic shock was the most prevalent complication, occurring in 14 (4.9%) patients. Both adequate and inadequate empirical antibiotics can cause complications (10.5% vs. 16.7%, p = 0171). The improved clinical showed that 208 patients in adequate empirical antibiotics, and 60 patients in inadequate empirical antibiotics (p = 0.002). Still, 18 patients (6.3%) died, 12 patients received appropriate empirical antibiotics, and 6 patients received inadequate empirical antibiotics (p = 0.099). (table 1)

Table 1 Patient characteristics of adequate and inadequate empirical antibiotics

Patient profile	Total patients (N = 286)		Adequate empirical antibiotics (N = 220)		Inadequate empirical antibiotics (N = 66)		P-value
Age; months*	7.16	(2.21-30.66)	7.16	(2.11-34.06)	7.16	(2.41-19.66)	0.945
Sex							
Male	159	(55.6%)	116	(52.7%)	43	(65.2%)	0.075
Female	127	(44.4%)	104	(47.3%)	23	(34.8%)	
Underlying disease	90	(31.5)	65	(29.5%)	25	(37.9%)	0.201
Genitourinary tract	39	(13.6%)	25	(11.4%)	14	(21.2%)	0.041
Neurological	18	(6.3%)	11	(5.0%)	7	(10.6%)	0.143
Cardiovascular	17	(5.9%)	14	(6.4%)	3	(4.5%)	0.770
Hematological	13	(4.5%)	12	(5.5%)	1	(1.5%)	0.311
Respiratory	8	(2.8%)	6	(2.7%)	2	(3.0%)	1.000
Endocrine	6	(2.1%)	6	(2.1%)	0	(0.0%)	0.342
Gastrointestinal	6	(2.1%)	3	(1.4%)	3	(4.5%)	0.138
Delay development	1	(0.3%)	1	(0.5%)	0	(0.0%)	1.000
Type of care							
Inpatient care	236	(82.5%)	185	(84.1)	51	(77.3%)	0.201
Outpatient care	50	(17.5%)	35	(15.9%)	15	(22.7%)	
Diagnosis							
UTI	230	(80.4%)	176	(80%)	54	(81.8%)	0.739
Bacteremia	56	(19.6%)	44	(20%)	12	(18.2%)	
Initial antibiotics							
third-generation cephalosporin	213	(74.5%)	169	(76.8%)	44	(66.7%)	0.097
aminoglycosides	81	(28.3%)	70	(31.8%)	11	(16.7%)	0.017
carbapenems	28	(9.8%)	22	(10.0%)	6	(9.1%)	0.827
Complication	34	(11.9%)	23	(10.5%)	11	(16.7%)	0.171
septic shock	14	(4.9%)	9	(4.1%)	5	(7.6%)	0.325
seizure	11	(3.8%)	7	(3.2%)	4	(6.1%)	0.285
acute kidney injury	9	(3.1%)	8	(3.6%)	1	(1.5%)	0.690
respiratory failure	4	(1.4%)	2	(0.9%)	2	(3.0%)	0.229
others	4	(1.4%)	2	(0.9%)	2	(3.0%)	0.229
Transferred to ICU	25	(8.7%)	20	(9.1%)	5	(7.6%)	0.702
Length of stay; days*	81.5	(13-161)	88	(11-163)	58	(17-130)	0.609
Cost expenses; Baht*	26,230	(11,269-152,156)	25,898	(11,625-175,017)	31,128	(9,473-109,044)	0.723
Status of discharge							
Improved	268	(93.7%)	208	(94.5%)	60	(90.9%)	0.002
Death	18	(6.3%)	12	(5.5 %)	6	(9.1%)	0.099

Abbreviations: ICU, intensive care unit; N, number; UTI, urinary tract infection

*Data are presented as median (interquartile range)

Klebsiella pneumoniae and *Escherichia coli* were the frequent organisms in bacteremia, and UTI patients. (table 2)

Third-generation cephalosporin (84.8%) was the most often utilized empirical antibiotics for UTI patients. With adequate and inadequate empirical antibiotics, 175 patients (99.4%) and 53 patients (96.4%), respectively, recovered symptoms significantly in adequate empirical antibiotics ($p = 0.001$). However, 0.6% of patients receiving adequate empirical antibiotics and 3.6% receiving inadequate empirical antibiotics perished ($p = 0.142$) from UTIs. (table 3)

Table 2 Prevalence of pathogens by diagnosis

Pathogen	Total (N=286)		Adequate empirical antibiotic (N=220)		Inadequate empirical antibiotic (N=66)	
	N	(%)	N	(%)	N	(%)
Bacteremia	47	(100)	37	(78.7)	10	(21.3)
Klebsiella pneumoniae	8	(17.0)	7	(18.9)	1	(10.0)
Escherichia coli	6	(12.8)	4	(10.8)	2	(20.0)
Enterobacter cloacae	4	(8.5)	4	(10.8)	0	(0.0)
Pseudomonas aeruginosa	3	(6.4)	3	(8.1)	0	(0.0)
Staphylococcus epidermidis	3	(6.4)	2	(5.4)	1	(10.0)
Acinetobacter baumannii	2	(4.3)	0	(0.0)	2	(20.0)
Staphylococcus capitis	2	(4.3)	1	(2.7)	1	(10.0)
Staphylococcus hominis	2	(4.3)	1	(2.7)	1	(10.0)
Streptococcus agalactiae	2	(4.3)	2	(5.4)	0	(0.0)
Acinetobacter calcoaceticus complex	1	(2.1)	1	(2.7)	0	(0.0)
Acinetobacter pittii	1	(2.1)	1	(2.7)	0	(0.0)
Acinetobacter spp.	1	(2.1)	1	(2.7)	0	(0.0)
Aeromonas hydrophilia	1	(2.1)	1	(2.7)	0	(0.0)
Burkholderia cepacia	1	(2.1)	1	(2.7)	0	(0.0)
Burkholderia species	1	(2.1)	1	(2.7)	0	(0.0)
Enterococcus faecium	1	(2.1)	0	(0.0)	1	(10.0)
Pantoea species	1	(2.1)	1	(2.7)	0	(0.0)
Proteus mirabilis	1	(2.1)	1	(2.7)	0	(0.0)
Pseudomonas putida	1	(2.1)	1	(2.7)	0	(0.0)
Salmonella group D	1	(2.1)	1	(2.7)	0	(0.0)
Salmonella species	1	(2.1)	1	(2.7)	0	(0.0)
Serratia marcescens	1	(2.1)	1	(2.7)	0	(0.0)
Staphylococcus coagulase negative	1	(2.1)	1	(2.7)	0	(0.0)
Staphylococcus haemolyticus	1	(2.1)	0	(0.0)	1	(10.0)
UTI	231	(100)	176	(76.2)	55	(23.8)
Escherichia coli	144	(62.3)	112	(63.6)	32	(58.2)
Klebsiella pneumoniae	33	(14.3)	22	(12.5)	11	(20.0)
Enterococcus faecium	9	(3.9)	4	(2.3)	5	(9.1)
Pseudomonas aeruginosa	9	(3.9)	8	(4.5)	1	(1.8)
Enterococcus faecalis	8	(3.5)	7	(4.0)	1	(1.8)
Proteus mirabilis	8	(3.5)	7	(4.0)	1	(1.8)
Enterobacter cloacae	6	(2.6)	5	(2.8)	1	(1.8)
Morganella morganii	3	(1.3)	2	(1.1)	1	(1.8)
Staphylococcus haemolyticus	3	(1.3)	2	(1.1)	1	(1.8)
Kluyvera ascorbata	2	(0.9)	2	(1.1)	0	(0.0)
Streptococcus agalactiae	2	(0.9)	2	(1.1)	0	(0.0)
Enterobacter kobei	1	(0.4)	0	(0.0)	1	(1.8)
Pseudomonas putida	1	(0.4)	1	(0.6)	0	(0.0)
Staphylococcus hominis	1	(0.4)	1	(0.6)	0	(0.0)
Staphylococcus saprophyticus	1	(0.4)	1	(0.6)	0	(0.0)

Abbreviations: N, number; UTI, urinary tract infection

Table 3 Patient treatment and outcome in urinary tract infection patients

Patients	Total (N = 231)		Adequate empirical antibiotic (N = 176)		Inadequate empirical antibiotic (N = 55)		P-value
Initial antibiotic treatment							
third-generation cephalosporin	195	(84.4%)	152	(86.4%)	43	(78.2%)	0.144
aminoglycosides	58	(25.1%)	50	(28.4%)	8	(14.5%)	0.038
Piperacillin/tazobactam	15	(6.5%)	11	(6.3%)	4	(7.3%)	0.759
Complication	19	(8.2%)	13	(7.4%)	6	(10.9%)	0.406
Length of stay (days)*	65	(10-153)	71	(8-159)	51	(15-129)	0.959
Cost expenses (Baht)*	20,114	(8,569-45,946)	19,768	(9,342-46,193)	21,774	(2,246-44,536)	0.918
Status of discharge							
improved	228	(98.7%)	175	(99.4%)	53	(96.4%)	0.001
death	3	(1.3%)	1	(0.6%)	2	(3.6%)	0.142

Abbreviations: N, number

*Data are presented as median (interquartile range)

With respect to treatment and results, bacteremia did not differentiate between adequate and inadequate empirical antibiotics. (table 4)

The most often used empirical antibiotics were third-generation cephalosporin, although only *Acenitobacter spp., Burkholderia spp., Enterobacter spp., Escherichia coli, and Klebsiella pneumoniae* were susceptible to them, with respective susceptibilities of 60%, 50%, 45.5%, 78.4%, and 43.9%. Coagulase-negative *Staphylococcus* was shown to be sensitive to *trimethoprim/sulfamethoxazole* in 73.3%, but only 46.7% to vancomycin. (table 5)

Table 4 Patient treatment and outcome in bacteremia patients

Patients	Total (N = 56)		Adequate empirical antibiotic (N = 44)		Inadequate empirical antibiotic (N = 12)		P-value
Initial antibiotic							
aminoglycosides	23	(41.7%)	20	(45.5%)	3	(25.0%)	0.154
carbapenems	20	(35.7%)	14	(31.8%)	6	(50.0%)	0.460
third-generation cephalosporin	16	(28.6%)	15	(34.1%)	1	(8.3%)	0.131
vancomycin	3	(5.4%)	3	(6.8%)	0	(0.0%)	1.000
Complication	14	(29.8%)	9	(24.3%)	5	(50.0%)	0.137
Length of stay (days)*	97	(48-213)	97	(49-214)	100	(30-189)	0.582
Cost expenses (Baht)*	231,071	(118,561-530,180)	279,322	(128,619-619,972)	180,373	(103,221-260,005)	0.274
Status of discharge							
improved	45	(80.4%)	37	(84.1%)	8	(66.7%)	0.186
death	11	(19.6%)	7	(15.9%)	4	(33.3%)	0.186

Abbreviations: N, number

*Data are presented as median (interquartile range)

Table 5 Antimicrobial susceptibility pattern from urine, blood, and cerebrospinal fluid specimens

Pathogens	Penicillin	Third-generation cephalosporin	Carbapenems	Piperacillin/ tazobactam	Quinolones	Trimethoprim/ sulfamethoxazole	Aminoglycosides	Vancomycin	Macrolides
Acinetobacter spp.	0%	60%	60%	60%	60%	0%	60%	-	-
Aeromonas hydrophilla	100%	100%	100%	100%	100%	100%	100%	-	-
Burkholderia spp.	50%	50%	100%	50%	50%	100%	50%	-	-
Enterobacter spp.	0%	45.5%	100%	72.7%	63.6%	63.6%	90.9%	-	-
Enterococcus faecalis	88.9%	0%	0%	0%	22.2%	0%	66.7%	100%	-
Enterococcus faecium	0%	0%	0%	0%	8.3%	0%	16.7%	100%	-
Escherichia coli	13.1%	78.4%	98.7%	97.4%	60.1%	40.5%	88.9%	-	-
Klebsiella pneumoniae	2.4%	43.9%	97.6%	65.9%	53.7%	43.9%	75.6%	-	-
Kluyvera ascorbata	0%	100%	100%	100%	100%	100%	100%	-	-
Morganella morganii	0%	100%	100%	100%	100%	100%	100%	-	-
Pantoea species	0%	100%	100%	100%	100%	100%	100%	-	-
Proteus mirabilis	33.3%	88.9%	100%	88.9%	66.7%	44.4%	66.7%	-	-
Pseudomonas spp.	0%	92.9%	85.7%	85.7%	85.7%	7.1%	78.6%	-	-
Salmonella spp.	50%	100%	50%	50%	100%	100%	0%	-	-
Serratia marcescens	0%	100%	100%	0%	100%	100%	100%	-	-
Staphylococcus coagulase negative	20%	-	-	-	6.7%	73.3%	46.7%	40%	6.7%
Streptococcus spp.	100%	100%	-	-	-	-	40%	100%	-

(-) is not done for drug susceptibility

DISCUSSION

The results of adequate and inadequate empirical antibiotics differed according to past studies. According to previous research, using inadequate empirical antibiotics was linked to higher 28-day death rates, higher inpatient mortality rates, and increased treatment failure rates[9-13,17-20]. Other research on people with bacteremia found a lack of evidence of higher fatality rates and longer hospital stays due to inadequate empirical antibiotics[17,20-22]. Inadequate empirical antibiotics did not increase the risk of 30-day death or UTIs recurrence in UTI patients[23]. Adults made up the majority of the comparative results between adequate and inadequate empirical antibiotics. There was less indication of a correlation among children. Thus, the purpose of this study is to examine the results of groups of children who received adequate and inadequate empirical antibiotics. According to this analysis, pediatric patients responded much better to adequate empirical antibiotics compared to inadequate empirical antibiotics. Additionally, patients who received inadequate empirical antibiotics experienced more complications, higher costs, and more in-hospital deaths, although this did not provide any conclusive information on the effects of these treatments on outcomes for a large group of patients. The duration of stay and frequency of transfers to the ICU, however, were the same for both groups. In this study, the bacteremia subgroup had a higher rate of complications, a longer duration of stay, and in-hospital deaths, but there was no definitive proof. The UTIs category only had clinically meaningful improvements when receiving adequate empirical antibiotics. This grouping also experienced higher complications, financial hardships, and in-hospital deaths but lacked conclusive proof. Aminoglycosides were the suitable option for UTI patients with a narrow spectrum antibiotic and strong sensitivity to *K. pneumoniae* and *E. coli*, according to this study, which showed that adequate empirical antibiotics improved clinical outcomes in pediatric patients with UTIs.

The data gathered for bacteremia, and UTIs, which are serious and frequent illnesses, were the study's main strengths. In addition, this study found that the present knowledge of pediatric patients was scant. The study's main drawback, though, was the small patient population, particularly in cases of bacteremia. Therefore, more research should be done to compare the outcomes of pediatric patients with each disease who are given adequate and inadequate antibiotics.

Furthermore, antimicrobial susceptibility patterns at the pediatric ward of Vajira Hospital had few different from antibiotic susceptibility patterns from the National Antimicrobial Resistance Surveillance Center, Thailand (NARST) [24] such as *Acinetobacter spp., Burkholderia spp., Enterobacter spp., E.coli, and Salmonella spp.* is susceptible to third-generation cephalosporin about 60%, 50%, 45.5%, 78.4%, and 100%, respectively in Vajira Hospital, but in NARST, is susceptible to third-generation cephalosporin 35-63%, 87-97%, 64-72%, 55-65%, and 87-89%, respectively. The dissimilar antimicrobial susceptibility patterns between Vajira Hospital and NARST can be attributed to the fact that this study solely gathered data from the pediatric ward, which exclusively represents a tertiary care hospital. Hence, antimicrobial susceptibility patterns should be collected in each hospital.

CONCLUSION

Clinical outcomes among pediatric patients from adequate empirical antibiotics groups were reported the better outcomes. The mortality rates were not different. Nonetheless, appropriate empirical antibiotics are needed. To choose the best empirical antibiotics, antimicrobial susceptibility trends in hospitals must be observed. In UTI patients, amikacin is preferable options for empirical antibiotics.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest.

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DATA AVAILABILITY STATEMENT

The data that support this study are available on request from the corresponding author, Thiraporn Kanjanaphan.

REFERENCES

1. Michaud CM. Global burden of infectious diseases. In: Schaechter, editor. Encyclopedia of Microbiology. 3rd ed. Academic Press; 2009. p. 444–54.
2. Abe T, Ogura H, Kushimoto S, Shiraishi A, Sugiyama T, Deshpande GA, et al. Variations in infection sites and mortality rates among patients in intensive care units with severe sepsis and septic shock in Japan. J Intensive Care 2019;7:28-36.
3. Wenzel RP, Edmond MB. The impact of hospital-acquired bloodstream infections. Emerg Infect Dis 2001;7(2):174-7.
4. Dellinger RP. Cardiovascular management of septic shock. Crit Care Med 2003;31(3):946-55.
5. Centers for Disease Control and Prevention. Urinary tract infection [internet]. 2021 [cited 2021 November 10]. Available from: https://www.cdc.gov/antibiotic-use/uti.html
6. Urology Care Foundation. Urinary tract infections in adults [internet]. 2021 [cited 2021 November 10]. Available from: https://www.urologyhealth.org/urology-a-z/u/urinary-tract-infections-in-adults
7. Swanson D. Meningitis. Pediatr Rev 2015; 36(12):514-24.
8. World Health Organization. Antibiotic resistance [internet]. 2020 [cited 2021 November 10]. Available from: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance
9. Fraser A, Paul M, Almanasreh N, Tacconelli E, Frank U, Cauda R, et al. Benefit of appropriate empirical antibiotic treatment: thirty-day mortality and duration of hospital stay. Am J Med 2006;119(11):970-6.
10. Kang CI, Kim SH, Park WB, Lee KD, Kim HB, Kim EC, et al. Bloodstream infections caused by antibiotic-resistant gram-negative bacilli:

risk factors for mortality and impact of inappropriate initial antimicrobial therapy on outcome. Antimicrob Agents Chemother 2005;49(2):760-6.

11. Marquet K, Liesenborgs A, Bergs J, Vleugels A, Claes N. Incidence and outcome of inappropriate in-hospital empiric antibiotics for severe infection: a systematic review and meta-analysis. Crit Care 2015;19(1):63.
12. Lambregts MMC, Wijnakker R, Bernards AT, Visser LG, Cessie SL, Boer MGJ. Mortality after delay of adequate empiric antimicrobial treatment of bloodstream infection. J Clin Med 2020;9(5):1378.
13. Savage RD, Fowler RA, Rishu AH, Bagshaw SM, Cook D, Dodek P, et al. The effect of inadequate initial empiric antimicrobial treatment on mortality in critically Ill patients with bloodstream infections: a multi-centre retrospective cohort study. PLoS One 2016;11(5): e0154944.
14. Hagel S, Pletz MW, Brunkhorst FM, Seifert H, Kern WV. Bakteriämie und sepsis [bacteremia and sepsis]. Internist (Berl) 2013;54(4):399-407.
15. Bates B. Interpretation of urinalysis and urine culture for UTI treatment. US Pharm 2013; 38(11):65-8.
16. Hung YP, Lee CC, Ko WC. Effects of inappropriate administration of empirical antibiotics on mortality in adults with bacteraemia: systematic review and meta-analysis. Front Med (Lausanne) 2022;9:869822.
17. Garnacho-Montero J, Ortiz-Leyba C, Herrera-Melero I, Aldabó-Pallás T, Cayuela-Dominguez A, Marquez-Vacaro JA, et al. Mortality and morbidity attributable to inadequate empirical antimicrobial therapy in patients admitted to the ICU with sepsis: a matched cohort study. J Antimicrob Chemother 2008;61(2):436-41.
18. Retamar P, Portillo MM, López-Prieto MD, Rodríguez-López F, de Cueto M, García MV, et al. Impact of inadequate empirical therapy on the mortality of patients with bloodstream infections: a propensity score-based analysis. Antimicrob Agents Chemother 2012;56(1): 472-8.
19. Davey PG, Marwick C. Appropriate vs. inappropriate antimicrobial therapy. Clin Microbiol Infect 2008;14 Suppl 3:15-21.
20. Bassetti M, Rello J, Blasi F, Goossens H, Sotgiu G, Tavoschi L, et al. Systematic review of the impact of appropriate versus inappropriate initial antibiotic therapy on outcomes of patients with severe bacterial infections. Int J Antimicrob Agents 2020; 56(6):106184.
21. Schuttevaer R, Alsma J, Brink A, van Dijk W, de Steenwinkel JEM, Lingsma HF, et al. Appropriate empirical antibiotic therapy and mortality: conflicting data explained by residual confounding. PLoS One 2019; 14(11):e0225478.
22. Lambregts MMC, Wijnakker R, Bernards AT, Visser LG, Cessie SL, Boer MGJ. Mortality after delay of adequate empiric antimicrobial treatment of bloodstream infection. J Clin Med 2020;9(5):1378-87.
23. Zhu H, Chen Y, Hang Y, Luo H, Fang X, Xiao Y, et al. Impact of inappropriate empirical antibiotic treatment on clinical outcomes of urinary tract infections caused by Escherichia coli: a retrospective cohort study. J Glob Antimicrob Resist 2021;26:148-53.
24. National Antimicrobial Resistant Surveillance Center, Thailand. Antibiograms [internet]. 2019 [cited 2022 May 10]. Available from: http://narst.dmsc.moph.go.th/antibiograms.html