DOI: 10.7860/JCDR/2020/43539.13813

Original Article

Epidemiology Section

Antimicrobial Agents Administration among Patients with Extensively Drug-resistant *Pseudomonas aeruginosa* Infection in Intensive Care Unit in Tertiary Care: A Hospital-based Study

SOMKIATTIYOS WORADET[1], BHUNYABHADH CHAIMAY[2], NUNTIPUT PUTTHANACHOT[3], NARONGCHAI SANGSA[4], PHATSARAPORN SIRISA[5]

ABSTRACT

Introduction: Infections caused by Extensively Drug-resistant *Pseudomonas aeruginosa* (XDR-PA) is a medical problem worldwide. In Thailand, the incidence of XDR-PA bacteremia remains and is continuously increasing.

Aim: To investigate an association between antimicrobial agent administration and the treatment of XDR-PA infection among patients admitted in Intensive Care Unit (ICU).

Materials and Methods: A hospital-based analytic cross-sectional study was performed from January 2014 to December 2015. Of these, 47 cases diagnosed with XDR-PA bacteremia infection and 94 controls without XDR-PA infection were enrolled. Data were retrieved and retrospectively reviewed from medical records of the patients hospitalised in the ICU at Roi-Et Hospital, Thailand. Multiple logistic regressions were used and perform to investigate an association between antimicrobial agent administrations for treatment of XDR-PA infection.

Results: Third generation Cephalosporin (OR=1.99; 95%CI: 1.22 to 4.13), Ciprofloxacin (OR=3.40; 95%CI: 1.24 to 9.49) and Carbapenem (OR=4.66; 95%CI: 2.04 to 10.64) were more likely to be administrated for treatment of XDR-PA infection among patients.

Conclusion: Antimicrobial agents associated with the treatment of XDR-PA bacteremia infection among patients were third generation Cephalosporin, Ciprofloxacin and Carbapenem.

Keywords: Bacteremia, Encephalopathy, Hospitalisation, Medicine, Respiratory tract infection

INTRODUCTION

At present, Extensive Drug Resistance (XDR) is a major therapeutic problem worldwide. It is an emergence of illness caused by bacterial pathogens. Additionally, it remains epidemologically significant because of problematic treatment [1,2]. In recent years, a rapid increase of bacterial infection has become an ongoing crisis in medical services [2]. *Pseudomonas aeruginosa* (*P.aeruginosa*) is the leading pathogen of nosocomial opportunistic infection [3] and limits in clinical treatment [4].

P.aeruginosa is a gram-negative, non-fermenting bacillus, primarily found and persists in humid environments [5]. Its ability is to survive in the diversity of environmental conditions with limited nutritional resources [2]. Moreover, it is able to colonise in human organs including; skin, respiratory tract and gastrointestinal systems related to environmental contamination [6]. XDR is defined as resistant to all, or almost all of the antimicrobial agents in particular, susceptible to Colistin [7-10].

During the last decade, the prevalence of XDR-PA infection was mostly found in Asia-Pacific countries [1]. The patterns of microbiological and antimicrobial drug resistance are varied. The prevalence of XDR-PA ranges from 1% to 2% in Northern Taiwan [11]. However, the prevalence increases up to 16% in patients with bacteremia [3,12] and causes mortality up to 67% among hospitalised patients [13]. Whereas, approximately 63% of transplant patients infected with bacteremia defined as XDR-PA in Spain [14]. In Thailand, the prevalence of XDR-PA was mostly found in tertiary care hospitals-ranged from 5% to 8% [3]. Moreover, it is up to 10% or over in university, regional and provincial hospitals [2,3]. Remarkably, the highest infection of XDR-PA was mostly found in medicinal ICU among sepsis patients (22.6%) [2]. However, a retrospective cohort study in tertiary care in Bangkok, Thailand showed that one-fifth of patients infected with Healthcare-Associated Infections (HAIs) by XDR-PA bacteremia was 22% [15].

An increasing impact of XDR-PA phenotype infections leads to the decision making of clinicians in properly prescribing antimicrobials [9], especially in patients with bacteremia, immunocompromised or immunodeficient [3-5]. It was found that 50% of sepsis patients and catheter-related infections were resistant to the third generation of Cephalosporins and 5.8% resistant to Carbapenems [16].

Roi Et Hospital located in Northeastern of Thailand, is a tertiary care hospital providing advanced health care services. The proportion of hospitalised admissions his increasing annually in particular, among patients hospitalised in the ICU. Moreover, a high prevalence of XDR-PA bacteremia infection is reported. Patients infected with XDR-PA phenotype have problematic treatment and have a higher risk of mortality. Little is known and few reports exists on the association between antimicrobial agents and XDR-PA infection among patients [17-19]. This study was a part of the research project, partial results of which has been published previously [20].

Consequently, the purpose of this hospital-based analytic cross-sectional study was to investigate an association between antimicrobial agent administration and the treatment of XDR-PA among patients in ICU.

MATERIALS AND METHODS

This hospital-based analytic cross-sectional study was performed from January 2014 to December 2015. The subjects were hospitalised patients at ICU at Roi Et Hospital, Roi Et Province,

Thailand during the study period. The outcome was retrospectively reviewed from medical records and laboratory tests that were performed at the Department of Clinical Microbiology Laboratory, Roi Et Hospital, Roi Et Province, Thailand.

This study was approved by the Ethical Committee (Ref. No. 003/2559, date of issued on November 3rd, 2017). The power of the study was calculated to be 89.10% [17-19]. The proportion of case and control was 1:2. In total, 141 cases subjects were included in this study, 47 cases and 94 controls. **The inclusion criteria** for cases were: 1) Patients diagnosed with HAIs by XDR-PA bacteremia infection [21]; 2) Duration of admission more than 48 hours; 3) Aged more than 15 years; 4) Confirmed the diagnosis by physicians with complete laboratory tests. The inclusion criteria for controls were: 1) Hospitalisation more than 48 hours; 2) Aged more than 15 years; 3) No XDR-PA infection. **The exclusion criteria** were: Patients with incomplete history of treatment and the laboratory tests were excluded.

XDR-PA bacteremia was defined as resistant to all, or almost all of the antimicrobial agents-in particular, susceptible to Colistin [7-10]. The diagnosis of XDR-PA among cases was retrospectively reviewed from the medical records and laboratory-testing database. The methods of XDR-PA laboratory testing were performed using the standards for antimicrobial susceptibility test [21,22] and is described previously by the author in a published study [20].

Demographic variables (gender, age, complications and duration of hospitalised admission) were included in this study. The independent variables were various groups of antimicrobial medication which was treated during their treatment. The first generation of Cephalosporins consisted of Cephalotin and Cephazolin. Second generation Cephalosporins is Cefuroxime, Cefamandole, and Cefoxitin. The third generation of Cephalosporins is Ceftazidime, Cefotaxime, Cefoperazone, and Ceftriaxone. In addition, the Penicillin group consisted of Ampicillin, Amoxicillin, Methicillin, Oxacillin, and Cloxacillin. The Cabapenams group was Imipenem, Meropenem, Ertapenem, and Doripenem. The Aminoglycosides group consisted of Streptomycin, Amikacin, Gentamycin, Kanamycin, Tobramycin, and Spectinomycin. The Quinolones group was Norfloxacin, Ofloxacin, Ciprofloxacin, and Levofloxacin. Finally, the Colistin group included Sulfamethoxazole/Trimethoprim and Tetracyclines (Tetracycline, Doxycycline). Variables of using antimicrobial medication were divided into dichotomous variables such as 'Yes' if using antimicrobial medication and 'No' if not using antimicrobial medication.

STATISTICAL ANALYSIS

Descriptive statistics was used to describe demographic characteristics. Test of homogeneity between cases and controls was performed by using Pearson's Chi-square test. The outcome of this study was the occurrence of XDR-PA infection among subjects. Bivariate and multivariate analysis was constructed by using logistic regression analysis to investigate an association between using antimicrobial medication and occurrence of XDR-PA infection. Initially, bivariate analysis was performed by using simple logistic regression for each interested variables and outcome. The factors with the p-value ≤0.25 by the Wald's test were considered and entered into the initial model of multivariate analysis. Using a backward elimination method, the factors with the p-value of Wald's test >0.05 were eliminated, respectively. The p-value of the partial likelihood ratio was tested by fitting model. The magnitude of using antimicrobial medication and the treatment of XDR-PA infection by presenting Odds Ratios (OR) with 95 percent confidence intervals (95% CI). The interpretation shows no association if the OR included 1, the more of using antimicrobial medication as if the OR is greater than 1 and the lower of using antimicrobial medication as if the OR is less than 1.

RESULTS

The demographic characteristics among cases and controls revealed that more than a half of them were males (55.32% and 59.57%, p-value=0.056). The average age of cases and controls was 66.51 (SD=14.76) years and 56.52 (SD=18.35) year, (p-value=0.474). However, most of the cases had complications (82.98% and 65.96%, p-value=0.035) and had duration of admission for more than seven days (82.98% and 47.87%, p-value <0.001) [Table/Fig-1]. The principle diagnosis among cases was respiratory tract infection (38.30%) and encephalopathy (19.15%) and among controls were respiratory tract infection (38.30%), encephalopathy (7.45%) and gastrointestinal infection (7.45%) [Table/Fig-2].

Variables	Cases (N=47)		Controls (n=94)		p-value
	N	%	n	%	
Gender					
Male	26	55.32	56	59.57	0.056
Female	21	44.68	38	40.43	
Age (years)					
≤60	16	34.04	54	57.45	0.474
>60	31	65.96	40	42.55	
Mean±SD (Min: Max)	66.51±14.76 (21:87)		56.52±18.35 (19:87)		
Complications					
No	8	17.02	32	34.04	0.035
Yes	39	82.98	62	65.96	
Duration of hospitalisation					
≤7 days	8	17.02	49	52.13	<0.001
>7 days	39	82.98	45	47.87	

[Table/Fig-1]: Demographic characteristic among cases and controls.
SD: Standard deviation; N: Number of patients

Principle diagnosis	Cases (N=47)		Controls (n=94)	
	N	%	n	%
Respiratory tract infections	18	38.30	36	38.30
Encephalopathy	9	19.15	7	7.45
Gastrointestinal infections	3	6.39	7	7.45
Heart diseases	2	4.25	6	6.38
Cancer	2	4.25	5	5.32
Pancreases and liver diseases	2	4.25	2	2.13
Kidney diseases	2	4.25	4	4.25
Sepsis	3	6.36	6	6.38
Others	6	12.77	21	22.34

[Table/Fig-2]: Principle diagnosis among cases and controls.
N: Number of patients

Bivariate analysis was constructed by using simple logistic regression. It revealed that there were only two antimicrobial agents that were statistically and significantly associated with the treatment of XDR-PA infection among subjects. Carbapenem was 3.12 times more likely to be administrated for treatment XDR-PA infection (OR=3.12; 95% CI:1.50-6.59). In addition, Ciprofloxacin was 3.28 times more likely to be administrated for treatment of XDR-PA infection (OR=3.28; 95% CI: 1.22–8.84) [Table/Fig-3].

Multivariate logistic regression analysis showed an association of antimicrobial agent administration for treatment of XDR-PA infection after adjustment for sex, duration of hospitalisation, and having complications. It revealed that third generation Cephalosporin was 1.99 times more likely to be administrated for treatment of XDR-PA infection (OR=1.99; 95% CI: 1.22 to 4.13). Carbapenem was 4.66 times more likely to be administrated for treatment of XDR-PA infection (OR=4.66; 95% CI: 2.04 to 10.64). As well, Ciprofloxacin was 3.40 times more likely to be administrated to treat XDR-PA infections (OR=3.40; 95% CI: 1.24 to 9.49) [Table/Fig-3].

Variables	Cases (N=47)		Controls (n=94)		Crude OR (95%CI)	Adjusted OR* (95%CI)	p-value
	N	%	n	%			
Penicillin							
No	35	74.47	76	80.86	1	1	0.352
Yes	12	25.53	18	19.14	1.45 (0.63-3.33)	1.51 (0.63-3.55)	
1st generation Cephalosporin							
No	39	82.98	79	84.05	1	1	0.678
Yes	8	17.02	15	15.95	1.08 (0.42-2.77)	1.23 (0.46-3.26)	
2nd generation Cephalosporin							
No	41	87.24	79	79.79	1	1	0.546
Yes	6	12.73	15	15.95	0.77 (0.23-2.14)	0.72 (0.25-2.08)	
3rd generation Cephalosporin							
No	22	46.81	59	62.77	1	1	0.043
Yes	25	53.19	35	37.24	1.92 (0.94-3.89)	1.99 (1.22-4.13)	
Carbapenems							
No	16	34.05	58	61.71	1	1	<0.001
Yes	31	65.95	36	38.29	3.12 (1.50-6.49)	4.66 (2.04-10.64)	
Aminoglycosides							
No	38	82.98	74	78.73	1	1	0.888
Yes	9	17.02	20	21.27	0.88 (0.36-2.11)	0.94 (0.39-2.31)	
Ciprofloxacin							
No	36	76.59	86	91.49	1	1	0.019
Yes	11	23.41	8	8.51	3.28 (1.22-8.84)	3.40 (1.24-9.49)	
Colistin							
No	37	78.73	83	88.30	1	1	0.110
Yes	10	21.28	11	11.71	2.04 (0.79-5.22)	2.24 (0.83-6.05)	
Tetracycline							
No	41	87.24	67	71.28	1	1	0.072
Yes	6	12.73	27	28.72	0.71 (0.14-1.95)	0.64 (0.44-2.05)	
Trimethoprim/Sulfamethoxazole							
No	38	80.86	78	82.98	1	1	0.416
Yes	9	19.15	16	17.02	1.15 (0.48-2.85)	1.48 (0.57-3.84)	

[Table/Fig-3]: Bivariate and multivariate analysis of antimicrobial exposure associated with extensively drug-resistant *P aeruginosa* infection.
OR: Odds Ratios; OR*: Adjusted for confounding factors; age, duration of hospitalisation and complications; N: number of patients

DISCUSSION

An association between antimicrobial agent administration and treatment of XDR-PA infection was found in this study and revealed that third generation Cephalosporin, Carbapenem, and Ciprofloxacin was more likely to be used for treatment of XDR-PA phenotype infections.

The present study was similar to the study by Pinto Pereira LM et al., (Spain, Trinidad) and showed that the prevalence of using third generation Cephalosporins was 9.5 per 1,000 admissions. The most common infections among patients were skin and soft tissue infection (20.3%), respiratory (10.9%), gastrointestinal (10.7%) and urinary (9.3%) tract infections. [23]. The study by Willmann M et al., in Germany found that haematological-oncological patients with XDR-PA bacteremia infection were administrated with Ciprofloxacin (OR=5.53, 95% CI: 1.11-27.53) [4]. Additionally, the study by Gomez-Zorrilla S et al., from Spain revealed that patients with underlying diseases infected with *P. aeruginosa* were treated with Carbapenems [21]. The study by Samonis G et al., in Greece found that cancer patients infected with XDR-PA had primary bacteremia (65%), central venous catheter placed (28%), respiratory tract infections (22%) and Urinary Tract Infections (UTI) (22%). They were treated with Fluoroquinolones (63.2%), Carbapenems (63.2%), Colistin (21.1%), Penicillins (10.5%), Aminoglycosides (5.3%), respectively [5].

The study by Pena C et al., revealed that patients who had bloodstream infection caused by XDR-PA had underlying conditions- chronic obstructive pulmonary disease (37%), malignancy (26%), diabetes (21%), chronic renal failure (16%). Total 88% of patients with XDR-PA had prior antimicrobial agent administration (Amoxicillin-clavulanic acid (42%), Piperacillin-tazobactam (37%), Fluoroquinolones (50%), Carbapenems (21%), Cephalosporins (18%) and Aminoglycosides (18%) [12]. In addition, the study by Ciofi Degli Atti M et al., (Rome, Italy) revealed that patients who had bacteremia infection and had XDR-PA phenotype infections were resistant to Carbapenems, Cephalosporins, and Penicillins plus β-lactamase inhibitors [13]. The study by Deptula A et al., in Poland showed that patients with bloodstream infection were primarily diagnosed with gastrointestinal tract or intraabdominal infection (11.8%), UTI (11.2%), respiratory tract infection (10.1%), surgical site infection (7.1%) and skin and soft tissue infections (3.6%). The infection associated with the patient department accounted to 31.91% of ICU and 53.5% of medical department. More than a half of bloodstream infection was *P. aeurugonosa* resistant to Carbapenems (55.6%) [16].

A sensitivity analysis was constructed by using multiple logistic regression analysis in present study. The significant antimicrobial agents including Carbapenem and Ciprofloxacin in bivariate analysis were selected into the multivariate model. Also, the similar confounding factors were accounted into the final model. The model yielded a smaller magnitude and a similar association of using antimicrobial agents and treatment of XDR-PA bacteremia infections as shown in the results. This revealed that Carbapenem and Ciprofloxacin were more likely to be used to treat such *P. aeruginosa* infection.

Pharmacologically, the property of antimicrobial agents is used to treat bacterial infections. Cephalosporins are the original class of β-lactam antibiotics derived from the fungus *Acremonium* known as Cephalosporium. The latest Cephalosporins are more effective against gram-negative bacteria compared to previous generation [24]. It generally has a prolonged half-life of action, in particular against *P. aeurginosa* infection [25,26]. Carbapenems are the broadest spectrum and the greatest potential against bacterial infection in both gram-positive and gram-negative bacteria [27]. Carbapenems are the β lactam antibiotics with efficacy in treatment of severe infections. Additionally, an increasing use of Carbapenems is due to its resistance to Cephalosporin [28]. While Ciprofloxacin is a broad-spectrum quinolone carboxylic acid against a wide range of gram-negative and gram-positive bacteria [29].

Limitation(s)

The principal diagnosis among patients with XDR-PA is difficult due to underlying diseases and complications, which leads to an increase in the usage and the dosage of antimicrobial agents in treatment. Besides, the doses of antimicrobial agents were unaccounted in the study that leads to dose-response bias.

CONCLUSION(S)

The present study found that third generation Cephalosporin, Carbapenem and Ciprofloxacin were more likely to be administrated for treatment in XDR-PA infections among patients. Hence, the study suggested that patients infected with XDR-PA phenotype should be intensively treated by antimicrobial agents in order to reduce the severity of disease.

REFERENCES

[1] Kiratisin P, Chongthaleong A, Tan TY, Lagamayo E, Roberts S, Garcia J, et al. Comparative in vitro activity of carbapenems against major Gram-negative pathogens: Results of Asia-Pacific surveillance from the COMPACT II study. Int J Antimicrob Agents. 2012;39(4):311-16.
[2] Kiddee A, Henghiranyawong K, Yimsabai J, Tiloklurs M, Niumsup PR. Nosocomial spread of class 1 integron-carrying extensively drug-resistant *Pseudomonas aeruginosa* isolates in a Thai hospital. Int J Antimicrob Agents. 2013;42(4):301-06.

[3] Danchaivijitr S, Judaeng T, Sripalakij S, Naksawas K, Plipat T. Prevalence of bold nosocomial infection in Thailand 2006. J Med Assoc Thai. 2007;90(8):1524-29.
[4] Willmann M, Klimek AM, Vogel W, Liese J, Marschal M, Autenrieth IB, et al. Clinical and treatment-related risk factors for nosocomial colonisation with extensively drug-resistant *Pseudomonas aeruginosa* in a haematological patient population: A matched case-controlled study. BMC Infect Dis. 2014;14:650.
[5] Samonis G, Vardakas KZ, Kofteridis DP, Dimopoulou D, Andrianaki AM, Chatzinikolaou I, et al. Characteristics, risk factors and outcomes of adult cancer patients with extensively drug-resistant *Pseudomonas aeruginosa* infections. Infection. 2014;42(4):721-28.
[6] Mayr A, Hinterberger G, Lorenz IH, Kreidl P, Mutschlechner W, Lass-Florl C. Nosocomial outbreak of extensively drug-resistant *Pseudomonas aeruginosa* associated with aromatherapy. Am J Infect Control. 2017;45(4):453-55.
[7] Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012;18(3):268-81.
[8] Li J, Zou M, Dou Q, Hu Y, Wang H, Yan Q, et al. Characterization of clinical extensively drug-resistant *Pseudomonas aeruginosa* in the Hunan province of China. Ann Clin Microbiol Antimicrob. 2016;15(1):35.
[9] Karaiskos I, Antoniadou A, Giamarellou H. Combination therapy for extensively-drug resistant gram-negative bacteria. Expert Rev Anti Infect Ther. 2017;15(12):1123-40.
[10] Strateva T, Yordanov D. *Pseudomonas aeruginosa*-A phenomenon of bacterial resistance. J Med Microbiol. 2009;58(Pt 9):1133-48.
[11] Shu JC, Chia JH, Siu LK, Kuo AJ, Huang SH, Su LH, et al. Interplay between mutational and horizontally acquired resistance mechanisms and its association with carbapenem resistance amongst extensively drug-resistant *Pseudomonas aeruginosa* (XDR-PA). Int J Antimicrob Agents. 2012;39(3):217-22.
[12] Pena C, Gomez-Zorrilla S, Suarez C, Dominguez MA, Tubau F, Arch O, et al. Extensively drug-resistant *Pseudomonas aeruginosa*: Risk of bloodstream infection in hospitalised patients. Eur J Clin Microbiol Infect Dis. 2012;31(10):2791-97.
[13] Ciofi Degli Atti M, Bernaschi P, Carletti M, Luzzi I, Garcia-Fernandez A, Bertaina A, et al. An outbreak of extremely drug-resistant *Pseudomonas aeruginosa* in a tertiary care pediatric hospital in Italy. BMC Infect Dis. 2014;14:494.
[14] Bodro M, Sabe N, Tubau F, Llado L, Baliellas C, Gonzalez-Costello J, et al. Extensively drug-resistant *Pseudomonas aeruginosa* bacteremia in solid organ transplant recipients. Transplantation. 2015;99(3):616-22.
[15] Palavutitotai N, Jitmuang A, Tongsai S, Kiratisin P, Angkasekwinai N. Epidemiology and risk factors of extensively drug-resistant *Pseudomonas aeruginosa* infections. PLoS One. 2018;13(2):e0193431.
[16] Deptula A, Trejnowska E, Dubiel G, Wanke-Rytt M, Deptuła M, Hryniewicz W. Healthcare associated bloodstream infections in Polish hospitals: Prevalence, epidemiology and microbiology-summary data from the ECDC Point Prevalence Survey of Healthcare Associated Infections 2012-2015. Eur J Clin Microbiol Infect Dis. 2018;37(3):565-70.
[17] Bernard R. Fundamentals of biostatistics. 5th Ed. Duxbery: Thomson learning, 2000: 386.
[18] Fleiss JL, Levin B, Paik MC. Statistical methods for rates and proportions. 3rd Ed. John Wiley & Sons, 2003: 76.
[19] Ngamjarus C, Chongsuvivatwong V. n4Studies: Sample size and power calculations for iOS. The Royal Golden Jubilee Ph.D. Program-The Thailand Research Fund & Prince of Songkla University, 2014.
[20] Woradet S, Putthanachot N, Chaimay B, Sangsa N, Sirisa P. Determination of factors associated with extensively drug-resistant *Pseudomonas aeruginosa* infection among intensive care unit patients at Roi Et Hospital Thailand. Southeast Asian J Trop Med Public Health. 2019;50(2):266-74.
[21] Gomez-Zorrilla S, Camoez M, Tubau F, Periche E, Canizares R, Dominguez MA, et al. Antibiotic pressure is a major risk factor for rectal colonisation by multidrug-resistant *Pseudomonas aeruginosa* in critically ill patients. Antimicrob Agents Chemother. 2014;58(10):5863-70.
[22] Clinical and Laboratory Standards Institute/NCCLS. Performance standards for antimicrobial susceptibility test: Twentieth informational supplement. CLSI document M100-S20. Clinical and Laboratory Standards Institute, Pennsylvania USA, 2010.
[23] Pinto Pereira LM, Phillips M, Ramlal H, Teemul K, Prabhakar P. Third generation cephalosporin use in a tertiary hospital in Port of Spain, Trinidad: Need for an antibiotic policy. BMC Infect Dis. 2004;4(1):59.
[24] Klein NC, Cunha BA. Third-generation cephalosporins. Med Clin North Am. 1995;79(4):705-19.
[25] Thai HB, Yu JK, Park BS, Park YJ, Min SJ, Ahn DR. A fluorogenic substrate of beta-lactamases and its potential as a probe to detect the bacteria resistant to the third-generation oxyimino-cephalosporins. Biosens Bioelectron. 2016;77:1026-31.
[26] Pruksachatvuthi S, Aswapokee N, Aswapokee P. In vitro antimicrobial activity of cefodizime, a third generation cephalosporin. J Med Assoc Thai. 1992;75(5):287-92.
[27] Papp-Wallace KM, Endimiani A, Taracila MA, Bonomo RA. Carbapenems: Past, present, and future. Antimicrob Agents Chemother. 2011;55(11):4943-60.
[28] Hawkey PM, Livermore DM. Carbapenem antibiotics for serious infections. BMJ. 2012;344:e3236.
[29] Dewart CM, Gao Y, Rahman P, Mbodj A, Hade EM, Stevenson K, et al. Penicillin allergy and association with ciprofloxacin coverage in community-onset urinary tract infection. Infection Control & Hospital Epidemiology. 2018;39(9):1127-28.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Public Health, Faculty of Health and Sports Science, Thaksin University, Pa-Phayom District, Phatthalung Province, Thailand.
2. Associate Professor, Department of Public Health, Faculty of Health and Sports Science, Thaksin University, Pa-Phayom District, Phatthalung Province, Thailand.
3. Medical Technologist, Department of Clinical Microbiology Laboratory, Roi-Et Hospital, Muang Roi-Et District, Roi-Et Province, Thailand.
4. Medical Physician, Department of Medicine, Roi-Et Hospital, Muang Roi-Et District, Roi-Et Province, Thailand.
5. Nurse, Department of Infectious Control, Roi-Et Hospital, Muang Roi-Et District, Roi-Et Province, Thailand.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Somkiattiyos Woradet,
222 Moo 2 Ban Phrao Sub-District, Pa-Phayom District,
Phatthalung Province, Thailand.
E-mail: somkiattiyos@tsu.ac.th

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Dec 31, 2019
- Manual Googling: May 12, 2020
- iThenticate Software: Jun 10, 2020 (6%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No (This research is secondary data)
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Dec 31, 2019**
Date of Peer Review: **Feb 06, 2020**
Date of Acceptance: **May 13, 2020**
Date of Publishing: **Jul 01, 2020**