Retrospective Analysis on Antibiotic Resistance among Clinical Bacterial Isolates in the General Hospital Sanjiwani, Gianyar Bali

Anak Agung Gede Indraningrat[1*], Dewa Ayu Putri Sri Masyeni[1,2], I Made Sila Darmana[1,2]
[1]Faculty of Medicine and Health Sciences, Warmadewa University, Denpasar-Bali, Indonesia
[2]General Hospital Sanjiwani, Gianyar-Bali, Indonesia
*Corresponding author: anak.indraningrat@gmail.com

Abstract
Resistensi antibiotik saat ini merupakan ancaman kesehatan global yang muncul akibat penggunaan antibiotik yang salah dan berlebihan sehingga meningkatkan angka mortalitas dan morbiditas. Informasi tentang resistensi antibiotik sangat penting untuk menentukan pengobatan yang ideal bagi pasien. Ketersedian data terkait resistensi antibiotika di Bali masih cukup rendah. Studi ini bertujuan untuk menganalisi profil kerentanan antibiotik pada isolat bakteri klinik di RSUD Sanjiwani Gianyar Bali menggunakan metode retrospektif tahun 2018. Data tersebut meliputi jenis antibiotik yang diuji, nama isolat bakteri klinis, sumber isolasi. dan profil resistensi antibiotik. Diantara 65 isolat bakteri klinis, ditemukan keragaman bakteri patogen yang tinggi dan dikelompokkan menjadi 22 spesies, dimana Escherichia coli, Klebsiela pneumoniae, Acinetobacter baumanii dan Staphylococcus aureus merupakan empat isolat dominan yang diidentifikasi. Paparan terhadap 17 jenis antibiotika menunjukkan bahwa isolat bakteri dominan resisten terhadap levofloxacin, ciprofloxacin, dan gentamycin. Sedangkan isolat dominan tersebut rentan terhadap meropenem, amikacyin dan ampicillin-sulbactam. Surveilans rutin untuk mengetahui profil resistensi antibiotik penting dilakukan dan direkomendasikan untuk menghasilkan antibiotikogram lokal sebagai pedoman untuk mengatasi infeksi patogen.

Kata kunci: Resistensi antibiotik, Resistensi, Bakteri klinis

Introduction

The development of penicillin in the early 1940s have paved way to combat bacterial infections, which subsequently were followed by introduction of different type of antibiotics (1, 2). However, in recent decade overused and misused of antibiotics on the society have led to resistance among pathogenic bacteria (1-3). In addition, the emerging rate of antibiotic resistance pathogens are also triggered by several other factors including: insufficient of research, limited of infection control, low quality of antibiotics and weak health policies (4). The emerging of pathogenic bacteria that develop resistance against antibiotics is currently serious global health issues with a rough estimation predict that antibiotic resistance will contribute to economic loss globally approximately 100 trillion USD in 2050 as the reduced of Gross Domestic Bruto (5). Therefore, immediate and comprehensive actions are required in order to tackle this antibiotic crisis including introduction of novel antibiotics, increased awareness on antibiotic used and routine surveillance on antibiotic resistance in the society (3, 5, 6).

In Indonesia, antibiotic resistances have been suspected to spread throughout the country (4). This situation occurs since most of the people can easily access antibiotics without prescriptions from physicians (4). Furthermore, many of hospitals in Indonesia, as many other developing countries, are lack of facilities to conduct microbiological examination (4, 6). As a consequence, physicians often have limited data and knowledge on the susceptibility pattern of pathogenic bacteria against antibiotics (6). Therefore, surveillance on antibiotic resistance should be done regularly in order to provide proper medication to threat pathogenic infections (6-9).

Bali is one of the province in Indonesia and like many other provinces, the data on antibiotic resistance among clinical patients among hospitals in Bali is rather scarce (6), Therefore, this study provided additional information in term of antibiotic resistance among clinical patients in a public hospital in Bali. In this study, assessment on antibiotic resistance was focused on retrospective data obtained from the General Hospital

Sanjiwani, Gianyar, Bali. It is expected the outcome of this analysis will provide basis information to develop an effective medication for patient with bacterial infection in the General Hospital Sanjiwani and in a bigger frame could serve as a stepping stone in order to generate antibiotic resistance pattern among clinical patients in Bali.

Methods

Retrospective data on antibiotics susceptibility was collected from the Laboratory of Microbiology of Sanjiwani Hospital Gianyar Bali from January to December 2018 after receiving ethical clearance from the Medical Research Ethics Committees of Faculty of Medicine, Udayana Universityno 2203/UN14.2.2.VII.14/LT/2020. Data was generated from the Laboratory of Microbiology Log Book of 65 patients which were distributed over 30 females and 35 males. The culture identification and antibiotic susceptibility tests were performed following a procedure as previously described (6) against 25 antibiotics namely Ceftriaxone, Ciprofloxacin, Augmentin, Bactrim, Ceftazidime, Ampicillin, Gentamicin, Meropenem, Amikacin, Ampicillin/sulbactam, Aztreonam, Cefepime, Cefoperazone-Sulbactum, Chloramphenicol, Fosfomycin, Levofloxacin, Piperacillin-Tazobactam, Erythromycin, Clindamycin, penicillin G, Tetracycline, Cefoxitin, Cephazolin, Cefaloglycin, Minocycline, Tobramycin, Cefotaxime and Linezolid. The retrospective data was analysed univariately using Microsoft Excel 2010.

Results

In total 65 bacterial species were isolated from clinical patients and these bacteria were tested against panel of antibiotics discs. These isolates came mainly from pus (42%, n = 28), urine (18%, n = 12), blood (9%, n = 6) and sputum (8%, n = 5) and other sources as presented in Figure 1. These isolates were identified into 22 species and among all isolates, the most frequent Gram-negative bacteria found was *Escherichia coli* (23%, n = 15), and the Gram-positive bacteria represented by *Klebsiella pneumoniae* and *Staphylococcus aureus* (12%, n = 8). Furthermore, the top four bacterial isolates found were *Escherichia coli* (23%), *K. pneumoniae* (12%), *S. aureus* (12%) and *Acinetobacter baumanii* (8%) as shown in Figure 2.

Escherichia coli was predominantly isolated from pus (40%), urine (33%), and blood (13%). *S. aureus* were dominantly isolated from pus (75%), wound swab (12.5%) and basic wound (12.5%). Isolates belong to *K. pneumoniae* were isolated from pus (75%), blood (12.5%) and sputum (12.5%). While, majority of *A.baumanii* isolates came from pus (75%), swab basic wound (12.5%) and urine (12.5%).

Of the 65 isolates tested against 28 antibiotics, the top four species displayed resistance against six antibiotics as shown in Table 1. More than half of isolates belong to *E. coli* displayed resistance against Bactrim, Ciprofloxacin and Levofloxacin. Similarly, 63% of *S. aureus* were resistant against Gentamycin and Levofloxacin. Likewise, 63% of *K. pneumoniae* isolates were resistance against Ciprofloxacin and Levofloxacin. While, all isolates belong to *A. baumanii* were resistance against Aztreonam, Ciprofloxacin, Cefotaxime and Levofloxacin.

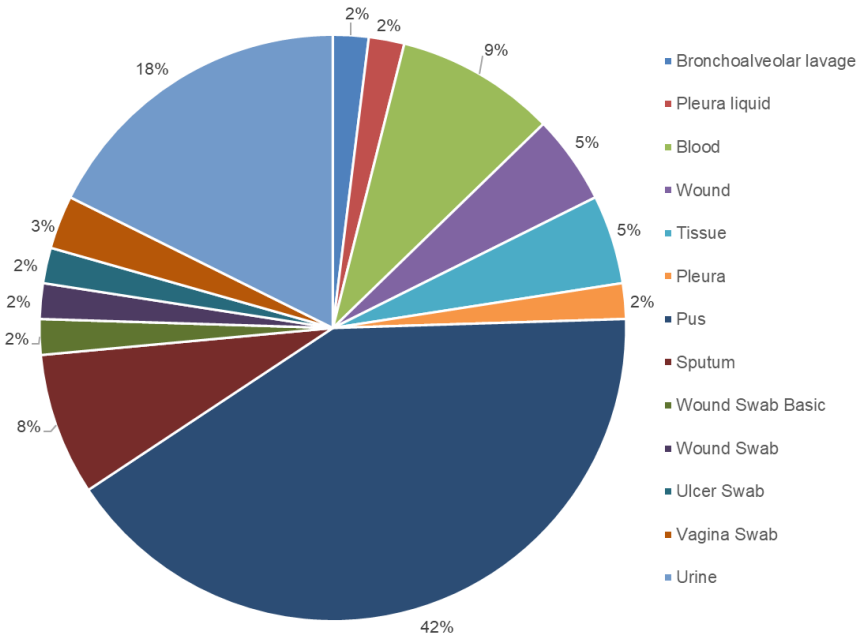

Figure 1. Source of bacterial isolates among patients during retrospective study

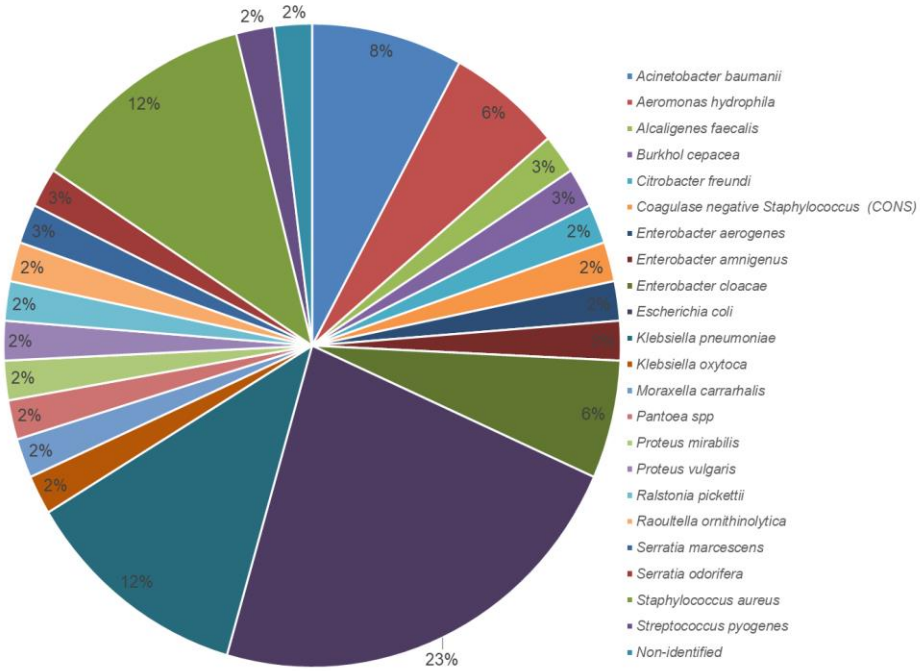

Figure 2. The percentages of bacterial species isolated for antibiotic susceptibility test from clinical patients at the General Hospital Sanjiwani, Gianyar-Bali in 2018

Table 1. Percentages of antibiotic resistance among the top four bacterial isolates. Note: abbrevations of antibiotics are bactrim (bact), gentamycin (genta), aztreonam (aztreo), ciprofloxacin (cipro), cefotaxime (cefotax), and levofloxacin (levo). The remaining isolates were not included in the table due to low number of samples (n < 5). ND (not detected).

Pathogen (n)	Antibiotic susceptibility (%)					
	merop	amika	ampi-sulb	cefox	cephazo	cefope-sulb
E. coli (n = 15)	80	87	73	ND	ND	93
K. pneumoniae (n = 8)	100	100	38	ND	ND	75
S. aureus (n = 8)	13	13	13	50	50	13
A. baumanii (n = 5)	20	60	80	ND	ND	100

Table 2. Percentages of antibiotic susceptibility among the top four bacterial isolates. Note: abbrevations antibiotics are Meropenem (merop), Amikacyin (amika), Ampicillin-Sulbactam (ampi-sulb), Cefoxitin (cefox), Cephazolin (cephazo), and Cefoperazone-Sulbactum (cefope-sulb). The remaining isolates were not included on the table due to low number of samples (n < 5). ND (not detected).

Pathogen (n)	*Antibiotic resistance (%)*					
	bact	*genta*	aztreo	cipro	cefotax	levo
E. coli (n = 15)	*67*	*33*	47	60	40	67
K. pneumoniae (n = 8)	50	25	38	63	25	63
S. aureus (n = 8)	ND	63	13	13	13	63
A. baumanii (n = 5)	20	60	100	100	100	60

Discussion

Bacterial infections are one of the prominent health problem in many developing countries including in Indonesia, which mainly occur due to low standard of sanitation and hygiene (4, 6-9). In most of cases, treatments to cure bacterial infections often hamper by limited knowledge on bacterial susceptibility on antibiotics given that the emerging rate of antibiotic resistance in the society. Furthermore, the rapid rate of bacterial mutations require routine assessment on how the antibiotic resistance profile have changed over a period of time. Up to now, several studies have reported antimicrobial resistance of bacterial isolates in Indonesia which were generated from burn patients (10), urine (11), and various clinical patients (6).

The top four main sources of microbial isolation from clinical patients at the General Hospital Sanjiwani in 2018 were pus, urine, blood and sputum. This finding is in line with a previous report from Masyeni et al that underlined urine, pus and sputum were the main source of bacterial isolation for antibiotic susceptibility test in two clinical laboratories in Denpasar (6).

Our result indicated that meropenem, amikacyin and ampicillin-sulbactam are rather effective to inhibit the growth majority of bacteria. These three antibiotics have been regarded to have broad spectrum of activity, thus effectively inhibit both Gram positive and Gram negative bacteria. Conversely, high percentage of resistance was evident when isolates were exposed against Levofloxacin, Ciprofloxacin, and Gentamycin.

We reported the presence of multidrug resistance *S. aureus* and extended-spectrum ß-lactamases (ESBL) as shown in representative isolates of *E. coli*, *K.*

pneumoniae and *A. baumanii*. These ESBL strains have been reported to be resistant against third generation of Cephalosporin e.g. Cefotaxime and Ceftazidime (6, 12, 13). In addition, the presence of EBSL strain may indicate that isolates confer resistant gene CTX-M-15 that encode resistance against ß-lactamases (12, 13). However, in this study we could not confirm the presence of the CTX-M-15 gene since analysis on gene level was not conducted. Furthermore, these bacterial species are in particular belong to the member of ESKAPE (*Enterococcus faecium, Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species) and these group of pathogens have been recognized as prominent agent of nosocomial infections (14).

Conclusion

In conclusion, the most predominant bacterial isolates from patients in the General Hospital Sanjiwani, Gianyar displayed high resistance to levofloxacin, ciprofloxacin, and gentamycin but they were predominantly susceptible to Meropenem, Amikacyin and Ampicillin-Sulbactam. The observed ESBL and multi drug resistance strains among these isolates have given alarming signal that antibiotics resistance must be treated urgently. These finding suggest the importance of routine surveillance of antibiotic susceptibility test in order to obtain an up-to-date information on antibiotic resistance pathogen which will be beneficial for physicians to provide proper antibiotic medication to treat patients due to microbial infections.

Acknowledgment

We would like to thank the Unit of Research and Community Service (UPPM) of Faculty of Medicine and Health Sciences, Warmadewa University for financial support to conduct this study.

References

1. Bottery, M.J., Pitchford, J.W., Friman, V.P. Ecology and Evolution of Antimicrobial Resistance in Bacterial Communities. *The ISME Journal*. 15(4): 939-948; 2021.
2. Shallcross, L.J., Howard, S.J., Fowler, T., Davies, S.C. Tackling the Threat of Antimicrobial Resistance: from Policy to Sustainable Action. *Philos Trans R Soc Lond B Biol Sci*. 370(1670): 20140082; 2015.
3. Ventola, C.L. The Antibiotic Resistance Crisis: Part 1: Causes and Threats. *P&T*. 40(4): 277-283; 2015.
4. Hadi, U., Kuntaman, Qiptiyah M., Paraton, H. Problem of Antibiotics Use and Antimicrobial Resistance in Indonesia: Are We Really Making Progress? *Indonesian Journal of Tropical and Infectious Disease*. 4(4): 5-8; 2013.
5. O'Neill, J. *Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations*. London: Review on Antimicrobial Resistance; 2014.
6. Masyeni, S., Sukmawati, H., Siskayani, A.S., Dharmayanti, S., Sari, K. Antimicrobial Susceptibility Pattern of Pathogens Isolated from Various Specimens in Denpasar-Bali: A Two Years Retrospective Study. *Biomedical and Pharmacology Journal*. 11(1): 493-502; 2018.
7. Alabi, A.S., Frielinghaus, L., Kaba, H., Kösters, K., Huson, M.A.M., Kahl, B.C., *et al*. Retrospective Analysis of Antimicrobial Resistance and Bacterial Spectrum of Infection in Gabon, Central Africa. *BMC Infect Dis.* 13: 455; 2013.
8. Mohammed, J., Hounmanou, Y.M.G., Thomsen, L.E. Antimicrobial Resistance among Clinically Relevant Bacterial Isolates in Accra: A Retrospective Study. *BMC Research Notes*. 11(1) :254; 2018.
9. Moolchandani, K., Sastry, A.S., Deepashree, R., Sistla, S., Harish, B.N., Mandal, J. Antimicrobial Resistance Surveillance among Intensive Care Units of a Tertiary Care Hospital in Southern India. J Clin Diagn Res. 11(2): DC01-DC7; 2017.
10. Wardhana, A., Djan, R., Halim, Z. Bacterial and Antimicrobial Susceptibility Profile and the Prevalence of Sepsis among Burn Patients at the Burn Unit of Cipto Mangunkusumo Hospital. *Annals of Burns and Fire Disasters*. 30(2):107-115; 2017.
11. Warganegara, E., Apriliyana, E. The Determining Type of Extended-Spectrum B-Lactamase Enzyme (ESBL) from Escherichia coil Resistance Cephalosporine of Third Generation in

RSUD Abdoel Moeloek Bandar Lampung. *Jurnal Kedokteran*. 4(7); 2014.
12. Bora, A., Sanjana, R., Jha, B.K., Narayan Mahaseth, S., Pokharel, K. Incidence of Metallo-Beta-Lactamase Producing Clinical Isolates of *Escherichia coli* and *Klebsiella pneumoniae* in Central Nepal. *BMC Research Notes*. 7(1): 557; 2014.
13. Perez-Lopez, A., Sundararaju, S., Al-Mana, H., Tsui, K.M., Hasan, M.R., Suleiman, M., *et al*. Molecular Characterization of Extended-Spectrum β-Lactamase–Producing *Escherichia coli* and *Klebsiella pneumoniae* among the Pediatric Population in Qatar. *Front Microbio*l. 11: 5817; 2020.
14. Mun, S.J., Kim, S.H., Kim, H.T., Moon, C., Wi, Y.M. The Epidemiology of Bloodstream Infection Contributing to Mortality: The Difference between Community-Acquired, Healthcare-Associated, and Hospital-Acquired Infections. *BMC Infect Dis*. 22(1): 336; 2022.