KnE Life Sciences

Knowledge E
Engaging minds

Conference Paper

A Qualitative Study About Multidrug-Resistant *Acinetobacter baumannii* (MDRAB) in Healthcare-Associated Infection (HCAI) and Its Resistance Towards Carbapenem in Indonesia

W Primaningtyas[1], AAAKEN Putri[1], L Saptawati[2], J Sudarsono[3], C Cheng[4], K Rouzeus[5], and C Muntean[6]

[1]Public Health Departement of Medical Faculty of Universitas Sebelas Maret, Surakarta, Indonesia
[2]Microbiology Departement of DR Moewardi Hospital, Surakarta, Indonesia
[3]Pharmacy Departement of DR Moewardi Hospital, Surakarta, Indonesia
[4]Undergraduate student of China Medical University, China
[5]Undergraduate student of Faculty of Medicine, National and Kapodistrian University of Athens, Greece
[6]Undergraduate student of University of Medicine and Pharmacy of Târgu Mureș, Romania

Abstract

Healthcare Associated Infection (HCAI) caused by Multidrug-Resistant *Acinetobacter baumannii* (MDRAB) is one of the important public health issues worldwide. Carbapenem as the last line agents showed effectivity derivation for treating MDRAB cases. Because there is a limited data about this in Indonesia, hence the HCAI caused by MDRAB resistant to carbapenem case needs to be investigated. This was a qualitative study using a case study approach. Purposive sampling technique was chosen and applied to informants consisting of MDRAB patients and their family also healthcare providers. Data were collected from in-depth interview, direct observations, and documents review. An interactive model of Miles and Huberman was used as the study's analysis technique. We found that the MDRAB patients had favorably perceived severity and self-efficacy. They found that their treatment was beneficial for them and the existing barrier did not make them stop getting treatment. The patient's family also gave full support to get the treatment. Healthcare providers had a good experience and understand their role in the hospital. The assembling of local antibiotics guideline was not so easy due to different opinion among the doctors. We also found lack of funding for surveillance of MDRAB and lack of awareness of it's potential danger among the majority informants. In conclusion, raising awareness of the HCAI caused by MDRAB resistant to carbapenem is an urgent need. The commitment of healthcare providers in following recommended guidelines is still needed some improvement. When all the elements in the hospital reach the same understanding on this case, funding of the surveillance will no longer become a big problem.

Keywords: HCAI, MDRAB, *Acinetobacter baumannii*, Carbapenem

🔓 **OPEN ACCESS**

1. Introduction

Healthcare Associated Infection (HCAI) is known as one of major public health problem worldwide and hundreds of millions of people are diagnosed with HCAI every year[1]. HCAI prevalence keeps increasing in both developed and developing countries [1, 2]. The prevalence of HCAI in Italy was increasing in the last decade from 4.6% to 6.8%, this result also similar to other studies conducted in across Europe at the same period of time [3]. Incidence densities of HCAI among developing countries are 10 until 20 times higher compared to the US surveillance result [4].

HCAI term is made to fill the gap between Community Acquired Infection (CAI) and Hospital Acquired Infection (HAI), where a patient with HCAI presenting different micro-biological profiles compare to CAI and HAI, significantly [5]. The criteria are needed to diagnose a patient with HCAI include a patient with infection problem, 48 hours minimum length of stay in a healthcare facility, and history of contact with any healthcare provider in the last year [6, 7]. HCAI cause the longer patient length of stay, long-term disability, higher hospital cost and patient's spending on healthcare, unnecessary deaths, also higher possibility of bacteria become MDR [1].

One of the major bacteria causing HCAI is *Acinetobacter baumannii* (AB), which also become the common cause of HCAI in tropical countries compare to Europe and The United States [8]. AB is a gram-negative bacteria that has a strong surviving capabil-ity in the hospital environment [9]. Decades ago AB was also known as a commensal pathogen with low pathogenicity, but in last decade AB becomes a high pathogen bac-teria which can change themselves into multi-drug resistant bacteria (MDRAB) using more than one mechanism [10, 11]. The high use of cephalosporin antibiotics also related to the mechanism of AB become an MDRAB especially to carbapenem antibiotic due to producing of carbapenemase. Moewardi hospital's consumption of cephalosporin antibiotics during 2017 was also high especially for the 3rd generation of cephalosporins [12]. Around 45.2% (n=104) of AB isolates were resistant to carbapenem antibiotic signif-icantly, based on 2017 study's result conducted in the same hospital [13].

Based on *Permenkes* No.8 in 2015 (Indonesian Health Ministry regulations in antimi-crobial resistance), all hospital in Indonesia have to apply regular monitoring in MDR bacteria but so far only specific for Extended Spectrum Beta-Lactamase (ESBL) bacte-ria and Methicillin-Resistant *Staphylococcus aureus* (MRSA) [14]. Although the effect of the MDRAB case is huge moreover in developed countries, the emerging of MDRAB in Indonesia also it's resistance to carbapenem does not well recorded yet and get attention as much as ESBL bacteria nor MRSA.

2. Subject and Method

2.1. Study design, subject, and setting

This qualitative study aimed to investigate the cases of HCAI due to MDRAB resistant to carbapenem in Moewardi hospital with case study approach. We were analyzing this topic from patients and their family's perception, the healthcare providers role, and their collaboration to control MDRAB resistant to carbapenem cases, antimicrobial stewardship program and its application, also awareness of MDRAB resistant to carbapenem cases and it's surveillance. This study was granted full ethical approval by the medical faculty of Universitas Sebelas Maret (UNS) ethical committee.

A purposive sampling technique was chosen and applied to the informants consisting of MDRAB patients and their family, 4 doctors, 1 clinical microbiologist, 3 infection control committees and 1 pharmacist. The diagnosis of the patient with MDRAB resistant to carbapenem confirmed by the microbiology test result. Friedman criteria and medical record were used as guidelines to identified HCAI patients [13]. In-depth interviews were conducted for 15-30 minutes for each informant, audio-recorded and transcribed. Another resource used in this research was direct observations and documents review.

This study was conducted at Moewardi hospital, the main referral hospital in Surakarta, Indonesia. This study was carried out between August and October 2017. During this time, the hospital still focuses only on ESBL and MRSA.

2.2. Data collection technique

The data were collected from in-depth interviews. We listed questions based on Health Belief Model theory to analyze the perception and behavior of the patient and their family [15]. Another brief structured of questions were listed to investigate the cases. Direct observation and document review were used to strengthen the data. Observations were made to see the compliance of patients and or family, cleaning staff and healthcare providers in preventing infection by washing hands and maintaining the cleanliness of the hospital environment. Document review was conducted to determine the prevalence of HCAI due to MDRAB cases, AB cases in each hospital's ward and its resistance pattern on carbapenem also the use of cephalosporin and carbapenem in Moewardi hospital. Data validity was confirmed by the triangulation technique and interactive model of Miles and Huberman was used as the study's analysis technique.

3. Result

We were collecting interviews data from 11 informants. The authors found the main topics of this study after collecting the data and analyzed it, those topics as follows: perceptions of the MDRAB patients and their family in HCAI due to MDRAB case; the role and competency of healthcare providers in hospital related to the case; the prudent antibiotic use; surveillance of HCAI due to MDRAB and the awareness of HCAI caused by MDRAB resistant to carbapenem.

3.1. Perceptions of the MDRAB patients and their family in HCAI due to MDRAB case

All the patients already had treatment and stayed in another hospital before they were in Moewardi hospital during the last three months, all of them also had bacterial infections in that period of time. The patients and their family's perception of severity or susceptibility were positive. It meant that they understand if their condition is serious and need an intensive caring. They understood that besides the main illness they also had an infection problem and need immediate care.

The patients and their family's perception of believing or self-efficacy were positive. It meant that they believe their illness will heal as long as they follow what are the doctor suggest them to do. When they were ill the first thing they would do were getting medication to the nearest healthcare center without thinking about alternative medication or traditional one.

> "We did not think about traditional medicine. Straight away looked for medical attention, but we went to a primary health care center first…" the patient's family said.

Good service and care from the hospital made them more comfortable. They believe they were in a good hand so their illness will heal.

A positive result also found in patient's and family's perception of benefit. They had an experience before with another healthcare center that completely treated their illness, so for this illness, they also had the same perception. One of the patients felt better after a few days of treatment, meanwhile, the other patient was still in the same condition, but his family had a big hope and positive attitude according to his condition.

The patients and family had positive result for perception barriers, meant that they kept looking for medical attention from the healthcare center even if it needs long hours driving. Usually, they choose a hospital who accepts Indonesian national insurance so

they would get free medication and would save some budget. All the patients needed to be transferred to the bigger hospital and it went well without any problem because they got help and support from their family.

The patients and family had a positive result for a perception of motivation and family support. The patient's family always next to them when they were in the hospital. The patient's spouse or children were the common family members who accompany them in the hospital, but sometimes another family member such as sister, brother, daughter or son-in-law as well. When it's time to take an oral medication in the hospital, the family playing a big role to give the medication to the patient (except for the patient in the intensive care unit).

> "His wife or his kids. When they need to work, they go to work first and when it's time to drink the medicine, they go back to give it to the patient." said the patient's family.

While the patients were at home their family usually help the patients to take their oral medication and were with them when they need to go to the hospital for checking up their condition. Even the patients and family member only knew the general condition of the illness they still motivated to have a better condition after their treatment finish.

3.2. The role and competency of medics and paramedics in the hospital related to HCAI caused by MDRAB case

The healthcare providers's work experience was between 6 until 11 years in Moewardi hospital. They joined a lot of courses or workshops during those years about nosocomial and community infections, also the prudent use of antibiotics. They also already joined in a national committee for bacterial infections and resistance, called *Komite Penanggulangan Resistensi Antibiotik* (*KPRA*) since 2010. The *KPRA* consist of doctors from different specialties, pharmacists, nurses, and other paramedics. As the member of *KPRA*, they have to follow the national guideline and have an obligation to attend a meeting periodically.

Under the *KPRA*, there is an antimicrobial stewardship team called *Penjagaan dan Pengendalian Infeksi* (*PPI*). This team also consists of various healthcare providers. They do the surveillance about general bacterial counts in hospital, monitoring environmental contaminants and surveillance about hand hygiene among healthcare providers. Among all healthcare providers, they already involved in *KPRA*, or at least only as *PPI* member (1 doctor). When there were cases of nosocomial infections or any other multiple infections

in patient occur, the doctor immediately consults to the *PPI* team, but most of them straight away contacted the microbiologist to decide suitable antibiotic.

About 75% doctors recognized well the infections caused by *Acinetobacter baumannii* and it's resistance to some groups of antibiotics that lead these bacteria to become MDRAB, but 100% doctors did not recognize well the term of HCAI, since this term in Indonesia still really rare to discuss. Only the microbiologist aware enough about the MDRAB resistant to carbapenem, but the other informants still consider this as the usual or regular case only.

> "...the awareness to *Acinetobacter* cases...is not good enough,...still think that it's just a common case..." internist said.

3.3. The prudent antibiotic use

Based on microbiologist statement, the ideal way to make antibiotics guideline is through making a report about bacterial resistance pattern found in a local healthcare facility. Moewardi hospital was giving this responsibility to the microbiology department. Microbiology department made the report for Moewardi hospital yearly and made antibiotics guideline based on that report. This antibiotics guideline were then being distributed to all wards in Moewardi hospital. Problems came when applying this guideline to the patients because different doctors had different opinion.

Moewardi hospital also made a regulation about the use of empirical and prophylaxis antibiotics. When the use of those antibiotics was more than the recommendation then the pharmacist would inform "stop order" for those particular antibiotics.

> "As a pharmacist, we also joined the *KPRA* team, become part of this committee. For antibiotics, we already had rules and regulations about the use of empirical and prophylaxis antibiotics. We also had an automatic stop order mechanism for empirical antibiotics that had been used more than three times." the pharmacist said.

Pharmacist already had teams in almost every wards and intensive care unit (ICU) to record the antibiotics use and make an annual report about it. They also make some qualitative and quantitative study about the prudent antibiotic use, but all the studies only for ICU because of lack of resources. The result of those studies would be presented and reported on national scale annually and some data reported monthly. The target of prudent antibiotic use is 100%, but after the evaluation results came, is showed that Moewardi hospital did not yet achieve the 100% target. Few times Moewardi hospital

was out of stock of some antibiotics, then usually pharmacist would contact the doctor and talk about the alternative antibiotics.

3.4. The awareness of HCAI caused by MDRAB resistant to carbapenem and it's surveillance

Almost all informants did not consider HCAI case caused by MDRAB resistant to carbapenem as an urgent case, only the microbiologist did. Unlike the other case of bacterial infections such as Extended Spectrum of Beta-Lactamase (ESBL) and Methicillin-Resistant *Staphylococcus Aureus* (MRSA) bacterias, that being regularly surveyed, the MDRAB case completely did not have distinct surveillance.

PPI and the doctor in charge usually labeled a patient with an infection when it was already confirmed, or potentially infectious when it was still under investigation. When an infectious patient came, Moewardi hospital already had a special room for them, such as for airborne infection like MDR tuberculosis they prepared an isolated room. Moewardi hospital also has an isolated room with negative or positive pressure for certain infection cases. When the number of infectious patients was more than the number of isolated room, then the hospital makes an isolated chamber inside the available ward, usually, those chambers are located in the corner and only separated by a curtain from the other patients (except for VIP patient).

> "It for sure become a big source of cross-infection among the patients", said
> the internist doctor.

Based on the report of microbiology department of Moewardi hospital in 2016, AB was included in 5 biggest gram-negative bacteria (4th) found in Moewardi hospital, and generally was in the yellow zone towards carbapenem antibiotic (only 40-<70% sensitive). AB that found in Pediatric and Neonatal Intensive Care Unit (PICU-NICU) were also in the yellow zone towards carbapenem antibiotic (doripenem and meropenem) but lower rate compared to the AB found in other wards. But towards one of carbapenem group antibiotic, imipenem, AB was in the red zone (<40% sensitive). While in the pediatrics ward, AB was in the red zone towards imipenem and meropenem, and in the yellow zone towards doripenem. In the neonatal ward, AB was also in the yellow zone towards carbapenem antibiotic. The AB found in internal medicine ward were in yellow zone towards doripenem and meropenem, but towards imipenem, AB was in the red zone. The worst result found in the surgery ward, where all of the AB was in the red zone towards the carbapenem antibiotics. Unlike the surgery ward, the result from pulmonology ward for all AB was still in the green zone.

4. Discussion

The MDRAB patients in Moewardi hospital had favorably perceived severity and self-efficacy. They found that their treatment was beneficial for them and the existing barrier did not make them stop in getting treatment. Problems in Moewardi hospital came when doctor applying antibiotic guideline to the patients because each doctor has a different opinion. Some doctors do not follow hospital guidelines and formularies. The doctor from internal medicine department for example, firstly they gave an empirical antibiotic. When the empirical antibiotic work then they continue to use it, if it did not work then they would increase the dosage first. After the culture and sensitivity test finished they did not straight away follow the antibiotics suggestion written by the microbiologist. Only when it still did not work then they changed the antibiotic according to the microbiologist suggestion. If there were more than one suggestion they decided to use antibiotics from the "lower" group first. The consultant doctor of ICU chose to strictly follow the Moewardi hospital's guideline and the suggestion made by the microbiologist.

When the use of antibiotics is more than the recommended rules, the pharmacist will inform the "stop order" for certain antibiotics. In this case, the role of pharmacists is also needed to talk about alternative antibiotics. Restricting the prescription of antimicrobial agents based on the hospital's formulary is also a policy made by Moewardi hospital to prevent antimicrobial resistance. Restrictions on the use of carbapenem in the formulary such as carbapenem use only for third-line therapy for ESBL-producing bacterial infections, used for a maximum of 7 days per case and used when carbapenem is the only antibiotic that still sensitive to the bacteria based on culture results. Restricting the prescription of antimicrobial agents is important, but it is difficult to decide which regimen is the best to treat the patients for empirical therapy [16].

Cheon et al. reported that implementing an antimicrobial management program for the use of carbapenem has decreased the level of nosocomial MDRAB's incidence [17]. Another result from this antimicrobial management program was the increased use of piperacillin/ tazobactam and ciprofloxacin because this antibiotic was chosen to be an alternative to carbapenems. While in Moewardi hospital when MDRAB resistant to carbapenem, the alternatives antibiotic were amikacin that still in the green zone [18]. In other studies conducted by Huang et al. suggested that early discontinuation of carbapenem could be an effective measure in antibiotic stewardship for controlling MDRAB spreading [19].

Moewardi hospital has been equipped with isolation rooms for certain infection case also rooms with negative or positive pressure for special infection cases. The standards

of isolation rooms are: should have tight-fitting doors, glass partitions for both negative and pressure (for source isolation) and positive-pressure (for protective isolation) ventilation [20]. But these standards could not be applied when all the isolation rooms full and the patients outnumbered. This is problematic because the public hospital trapped in some rules and regulations. They are expected to receive all the incoming patients, but no suitable room available, meanwhile they do not have enough budget to build more isolation rooms.

HCAI surveillance case caused by MDRAB resistant to carbapenem needs to be a hospital priority, in addition to HCAI priority due to ESBL and MRSA. Carbapenem-resistant *Acinetobacter baumannii* (CRAB) has been shown to be a serious challenge globally so that it requires full-scale national surveillance of CRAB [21]. Based on the previous study conducted in Moewardi hospital for HCAI, all CRAB were MDRAB [13]. When the hospital run surveillance for HCAI due to MDRAB it will reduce it's prevalence and incidence also other negative impacts related to this case. The surveillance's cost is very small compared to the burden of this case, hence we hope the government will start to arrange surveillance for it.

The major cause of antibiotic resistance is irrational antibiotic use, including CRAB cases in HCAI. Differences in MDRAB resistance levels to carbapenem in each ward in Moewardi hospital describes the compliance of antibiotic prescribing by a doctor are still need to be improved. AB found mostly in pulmonology ward and all carbapenem still sensitive to combat AB (green zone), but in the surgery ward, all the carbapenem were in the red zone. This phenomenon is very interesting and a deeper investigation is needed. Based on the previous study the commitment of the doctors in following recommended guidelines is still need some improvement [22]. Furthermore, to elucidate this finding, the qualitative study of the prudent use of antibiotics in these two wards using Giessen algorithm is needed to see whether this problem occurs because of irrational antibiotics use or not. As the only prior qualitative study in Indonesia about HCAI caused by MDRAB resistant to carbapenem, this study can be based on the following research.

5. Conclusion

Rising awareness of the HCAI caused by MDRAB resistant to carbapenem is an urgent need. The commitment of healthcare providers in following the recommended guidelines still needs some improvement. When all elements in the hospital reach the same understanding on this case, the funding of the surveillance will no longer become a big problem.

Acknowledgments

References

[1] WHO 2016 *The Burden of Healthcare-Associated Infection Worldwide* http://www.who.int/entity/gpsc/en/

[2] Allegranzi B, Nejad S B, Combescure C, Graafmans W, Attar H, Donaldson L and Pittet D 2011 *Lancet* **3**(77) 228-41

[3] Charrier L, Argentero P A, Farina EC, Serra R, Mana F and Zotti C M 2014 *BMC Public Health* **14** 558

[4] Ling M M L, Apisarnthanarak A, and Madriaga G 2015 *Clin. Infect. Dis.* **60**(11) 1690-9

[5] Cardoso T, Almeida M, Carratalà J, Aragão I, Costa-Pereira A, Sarmento A E, and Azevedo L 2015 *BMC Infect. Dis.* **15** 565

[6] Cardoso T, Almeida M, Friedman D, Aragao I, Costa-Pereira A, Sarmento A E, and Azevedp L 2014 *BMC Med.* **12**(40) 1-13

[7] See I, Lessa F C, Elata O A, Hafez S, Samy K, El-Kholy A, El Anani M G, Ismail G, Kandeel A, Galal R, Ellingson K and Talaat M 2013 *Infect. Control Hosp. Epidemiol.* **34**(12) 1281-88

[8] Molton J S, Tambyah P A, Ang B S P, Ling M L and Fisher D A 2013 *Clin. Infect. Dis.* **56**(9) 1310–8

[9] Cunha B A 2016 *Acinetobacter* http://emedicine.medscape.com/article/236891-overview

[10] Nowak-Zaleska A, Wiecczor M, Czub J, Nierwicki L, Katlowski R, Mikucka A and Gospodarek E 2016 *J Glob Antimicrob Re.* **7** 145-9

[11] Peleg A Y, Seifert H and Paterson D L 2008 *Clin. Microbiol. Rev.* **21**(3) 538-82

[12] Pharmacy Departement of DR Moewardi Hospital 2017 *Rekapitulasi Pengeluaran Antibiotik Cephalosporin dan Carbapenem* (Surakarta: Dr.Moewardi Hospital)

[13] Primaningtyas W 2017 *Faktor-Faktor Penyebab Resistensi Acinetobacter baumannii terhadap Antibiotik Carbapenem pada Pasien dengan Healthcare Associated Infection (HCAI) di Rumah Sakit DR Moewardi Surakarta* (Indonesia: Sebelas Maret University) chapter 4 pp 35-36

[14] Permenkes No.8 in 2015 *Indonesian Health Ministry regulations in antimicrobial resistance*

[15] Utomo G C, Joebagyo H and Murti B 2017 *Journal of Epidemiology and Public Health* **2**(3) 186-200

[16] Chen C, Lin L, Chang Y, Chen Y, Chang C and Huang C 2015 *Int. J. Environ. Res. Public Health* **12** 8871-82

[17] Cheon S, Kim M, Yun S, Moon J Y, and Kim Y 2016 *Korean J Intern. Med.* **31** 367-74

[18] Dr Moewardi Hospital 2016 *Pola kuman dan pola kepekaan kuman periode tahun 2016* (Indonesia: Microbiology department of Dr Moewardi Hospital) p 4

[19] Huang P Y, Shie S, Ye J, Lin S, Liu T, Wu T, Wu T, Chuang S, Cheng M, Hsieh Y *et al* 2017 *BMC Infect. Dis.* **17** 598

[20] Rawajfah R N 2014 *Nurs Crit Care.* **21**(2) e20-7.

[21] Castilho S R A, Silva de Miranda G C S M, Guilarde A O, Cardoso J L, Andre M C P, Kipnis A P J, and Kipnis 2017 *PLoS ONE* **12**(5) 1-13

[22] Hasan B, Perveen K, Olsen B, and Zahra 2014 *J. Med. Microbiol.* **63** 50-5