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# ANTIMICROBIAL RESISTANCE CONTROL PROGRAM ON THE RATIONAL USE OF ANTIBIOTICS IN EKA HOSPITAL PEKANBARU, INDONESIA

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## ABSTRACT

**Background:** Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. Rational use of antibiotics can reduce the emergence of antimicrobial resistance, cost of treatment, length of stay in hospitals, and improve health outcomes. This study aims to analyse the output of AMR control program implementation on the rational use of antibiotics in hospitals.

**Method:** This research is a retrospective study, using descriptive analysis with Gyssens' algorithm. Data were assessed from the medical records of patients treated at Eka hospital in 2017. The number of samples 877, in the ICU wards amounted to 307 and Hopea B 570. The analysis was performed by assessing the suitability of antibiotic therapy. The results are presented in therapeutic terms: the antibiotics used and the percentage of use based on the Gyssens algorithm.

**Result:** The results of data analysis found there is an increase in the rationality of the use of antibiotics on the unit ICU (67.77%), Hopea B (67.36%). There is a decrease in Patients Length of Stay (LOS) in ICU (26%), in Hopea B (58%). The level of antibiotic use without indication in ICU (8.82%). in the Hopea B ward (5.34%). Attitude of non-compliance of doctors against hospital guidelines and inadequate monitoring of antibiotic therapy. In the case of prophylactic antibiotics remain unobserved because of the lack of pharmacists who can monitor their use.

**Conclusion:** Eka Hospital has established an AMR Control program, but it has not been implemented properly. Continuous evaluation, awareness raising and understanding of doctors, the addition of monitoring officers (pharmacists), patient screenings and hospital staff on an ongoing basis, are worthy of consideration in order to improve the implementation of the program.

**Keywords:** antimicrobial resistance, antibiotic use, Gyssens' method

## INTRODUCTION

Antimicrobial resistance (AMR) is a major global health problem.[1]An appropriate and rational use of antibiotics can lessen the burden of diseases, especially infectious diseases. On the contrary, excessive use of antibiotics in humans and animals without clear indications significantly increase the rate of antimicrobial resistance [2]. Rational use of antibiotics can reduce the emergence of antimicrobial resistance, cost of treatment, length of stay in hospitals, and improve health outcomes [3].

Factors that promote antimicrobial resistance include: 1) lack of research; 2) lack of commitment; 3) lack of infection control; 4) irrational use of antibiotics; 5) poor quality antibiotics; and 6) lack of monitoring.[3]

Antimicrobial resistance occurs when microorganisms such as bacteria, virus, fungi, and parasites undergo a transformation that causes the medications to be ineffective in treating the infections, because the microorganisms have become more difficult to eliminate. One of the examples of antimicrobial resistance is in the use of antibiotics.[4]Antibiotics are chemical substances produced by fungi and bacteria that possess a bacteriostatic or bactericidal effect, with relatively little toxicity to humans.[5]Antibiotic resistance develops more quickly due to inappropriate or excessive use of antibiotics.[6]

There are two strategies to prevent the increase of antibiotic-resistant bacteria, which include the prudent use of antibiotics to reduce selective pressure, and promoting adherence to the standard universal precaution principles.[7]Antimicrobial management refers to the rational use of antimicrobials by health care professionals, particularly in choosing the most appropriate antibiotic, duration of treatment, dosage, and delivery route for patients with infection or the suspected ones.[8]Antimicrobial resistance control programs are activities aimed to reducing and/or preventing the emergence of resistant microorganisms.[9]

With the implementation of Antimicrobial Resistance Control Program, it is expected that the hospitals can improve their quality of care, especially in managing cases of infectious diseases. In addition to that, through the Antimicrobial Resistance Control Program, hospitals are expected to minimize the risk of medical error in their patients.[10].

According to the Pharmaceutical Care Guidelines for Antibiotic Therapy, successful implementation of the antibiotic resistance control program requires collaboration among different health professions, for instance doctors, microbiologists, nurses, and pharmacists.[11]The main goal of Antimicrobial Resistance Control Program is to increase the effectivity, minimize the adverse effects and undesirable consequences of antimicrobial use, as well as to limit the spread of antimicrobial resistance.[12]

From a qualitative study on antibiotic use in SuliantiSaroso Hospital for Infectious Diseases, Jakarta in 2010, using Gyssens' method, it was reported that out of 619 patients that received antibiotics during treatment, only 40.9% showed an appropriate use of antibiotics, 14.4% had no indication of antibiotic treatment, while 43.8% used antibiotics inappropriately.[13] From the first phase of AMRIN study in 2001-2002, it was found that in the Department of Pediatrics, Kariadi Hospital, Semarang, 46% of antibiotics were prescribed without indication.[14]

Eka Hospital in Pekanbaru is a type B hospital with 160 beds. The Antimicrobial Resistance Control Committee at the hospital is responsible for limiting the spread of resistant microorganisms due to selective pressure from antibiotic use, by promoting rational use of antibiotics. The evaluation of antibiotic use in the inpatient ward was conducted both quantitatively and qualitatively. The quantitative assessment was conducted using the Anatomical Therapeutic Chemical (ATC) Classification and the measurement of antibiotic use with defined daily dose (DDD) per 100 patient-days.[15] The qualitative assessment was carried out using Gyssens' algorithm to determine the category of quality in each use of antibiotic.[14,16]

This study aims to retrospectively evaluate the use of antibiotics among the patients hospitalized in Eka Hospital Pekanbaru using Gyssens' method, and to obtain data on the quantity and quality of antibiotic use in the inpatient ward. It is to conduct analysis on the implementation of Antimicrobial Resistance Control Program and its impact on the rational use of antibiotics in the ICU and Hopea B ward in Eka Hospital Pekanbaru. Additionally, the study will inform health care quality improvement in the hospital, particularly in infectious disease case management.

## **METHODS**

This research is descriptive analytic research by using Retrospective approach that this research is back ward looking or see backward [17]. The study was conducted in ICU and Hopea B, from January to December 2017. The number of samples 877 with details, in the ICU wards amounted to 307 and Hopea

B 570. Inclusion criteria are: 1. Medical records of patients in ICU and Hopea B who received antibiotics in the 2017. 2. Complete medical records. Exclusion criteria are: 1. Patient that did not received antibiotic. 2. Patients receiving antibiotics uncompleted due to discharge without doctors approval 3. The medical record data is incomplete. 4. Patients are treated together other than Infection, Gastrohepatology, Neurology, Respiriology specialistic.

The quality of antibiotic use was assessed from the completed antibiotic use in patients' medical record to ensure the rational antibiotic use in patients according to the germs pattern and antibiotic sensitivity recommendation by microbiologist. The reviewer team of Eka Hospital Pekanbaru Antimicrobial Resistance Control Program consists of pulmonologist, internist, microbiologist, and clinical pharmacist, who used Gyssens' algorithm to determine the antibiotic use quality categories. The proposed categories are Category 0, appropriate use; Category I, inappropriate timing; Category IIA, inappropriate dose; Category IIB, inappropriate interval of use antibiotics; Category IIC, inappropriate route of use; Category IIIA, duration of therapy too long; Category IIIB, duration of therapy too short; Category IVA, a more effective alternative available; Category IVB, a less toxic alternative available; Category IVC, cheaper alternative available; Category IVD, an alternative with narrower spectrum available; Category V, no indication of use; and Category VI, medical record incomplete (insufficient data for categorization). Category 0 reflects a rational or appropriate use of antibiotics, while Category I-V are considered irrational, and Category VI is unclassifiable and unevaluable. Whenever a significant difference is found between the reviewers' cores, they would conduct a discussion to settle the case.

Analysis was carried out by assessing the appropriateness of antibiotic therapy. The results were presented in therapeutic terminologies: antibiotics used and the percentage of use based on Gyssens' algorithm. The following figure can at least provide an interpretation on the scoring categories in a diagram used for analyzing the quality of antibiotic therapy.

## RESULTS

Eka Hospital Pekanbaru had established the Antimicrobial Resistance Control Committee to implement antimicrobial resistance control program within the hospital. The team also monitors and supervises program implementation, organize forums to discuss integrated management of infectious disease cases, and conduct surveillance on the pattern of antibiotic use, microorganisms causing infectious diseases, and their sensitivity to antibiotics.

The assessment drawn in Figure 2 and 3 of antibiotic use in 307 patients in the Eka Hospital ICU who received antibiotic therapy, it was found that the average rate of rational use of antibiotics was 67.77%. Meanwhile, for 570 patients receiving antibiotic therapy in Hopea B ward, the rate was 67.36%. This was far below the target of 90% set by the hospital. In addition, the rate of antibiotic use without indication in the ICU was 8.82%, and in Hopea B ward was 9.34%.

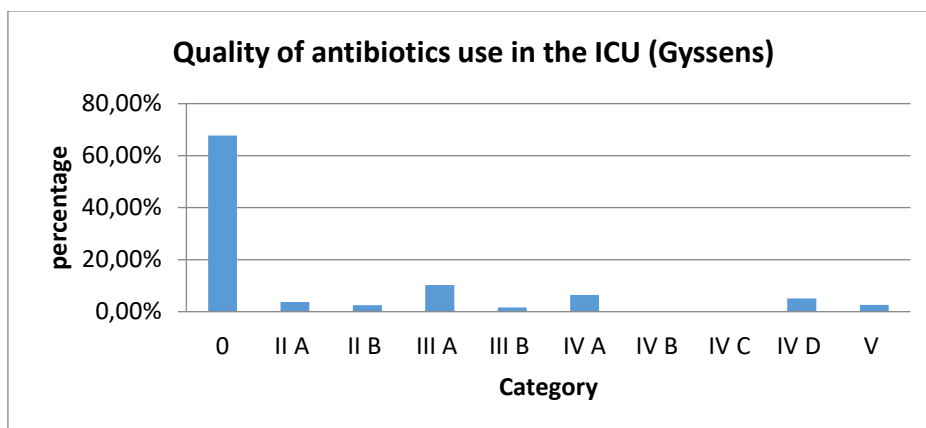


Figure2. Quality of antibiotic use in the ICU in 2017.

Figure 2 shows that Category 0 (appropriate use of antibiotics) has the highest percentage among the remaining categories (67.77%). Category IIA, inappropriate dose (3.77%). Category IIB, inappropriate interval of use antibiotics (2.54%). Category IIIA, duration of therapy too long (10.26%). Category IIIB, duration of therapy too short (1.58%). Category IVA, a more effective alternative available (6.40%). Category IVB a less toxic alternative available (0%). Category IVC, cheaper alternative available (0%). Category IVD, an alternative with narrower spectrum available (5.06%). Category V, no indication of use (2.62%) and Category VI, medical record incomplete (insufficient data for categorization) The second highest is Category IIIA (duration of the therapy too long) which is in correlation with Figure 6 that explains patients' Length of Stay.

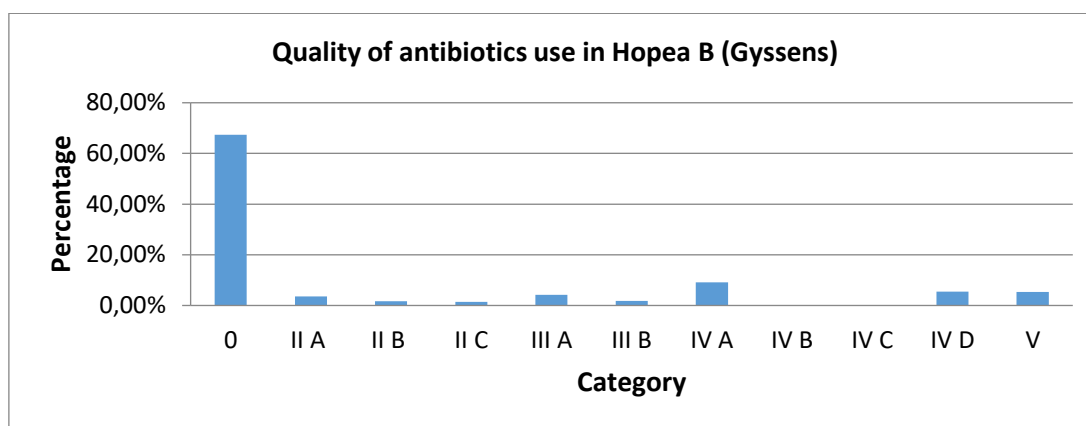


Figure3. Quality of antibiotic use in the Hopea B ward in 2017

Figure 3 shows that Category 0 (appropriate use of antibiotics) has the highest percentage among the remaining categories (67.36%). Category IIA, inappropriate dose (3.61%). Category IIB, inappropriate interval of use antibiotics (1.69%). Category IIC, inappropriate route of use (1.48%). Category IIIA, duration of therapy too long (4.16%). Category IIIB, duration of therapy too short (1.82%). Category IVA, a more effective alternative available (9.07%). Category IVB a less toxic alternative available (0%). Category IVC, cheaper alternative available (0%). Category IVD, an alternative with narrower spectrum available (5.48%). Category V, no indication of use (5.34%) and Category VI, medical record incomplete (insufficient data for categorization)

Figure 3 shows that Category 0 (appropriate use of antibiotics) also has the highest percentage among the remaining categories.

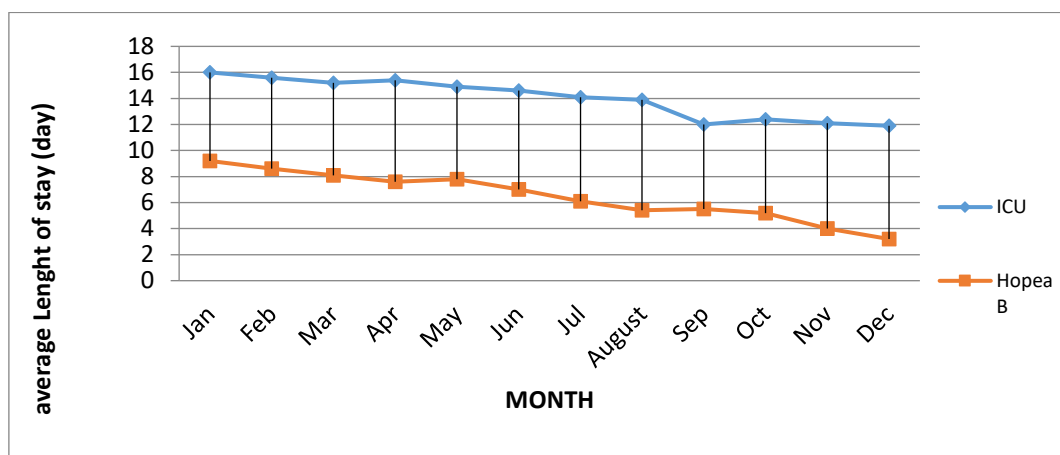


Figure 4. Average Length of Stay patient in ICU and Hopea B ward 2017

From the above figures, it shows Patients, Length of Stay (LOS) treated in ICU decreases 26%, while in Hopea B decreases 58% in 2017 after the introduction of antibiotic control program.

In November 2017, the Antimicrobial Resistance Control Committee established an empirical antibiotic restriction program as shown in Figure 5. The antibiotic restrictions were based on their classification as Broad Spectrum Antibiotic. Here are the restricted empirical antibiotics: Amikacin (Mikacin), Cefepime (Maxilan), Doripenem (Doribac), Imipenem + Enzym (Xerxes), Linezolid (Zyvox), Meropenem (Granem, Merosan, Meronem), Tigecyclin (Tygacil), and Vancomycin (vancep). The Antibiotics recommended for prophylactic use are Cefazolin (cefazol), Ceftriaxon /Starxon (for neurosurgery), and Cefuroxime (Sharox, Anbacim).

Antibiotic prescribing restriction flow: the prescribing physician should fill out the antimicrobial restriction form and get approval from the Antimicrobial Resistance Control Committee team and then the form is submitted to pharmacy, the pharmacy prepares the drug to be given to the patient. Here is the use of restriction antibiotics:

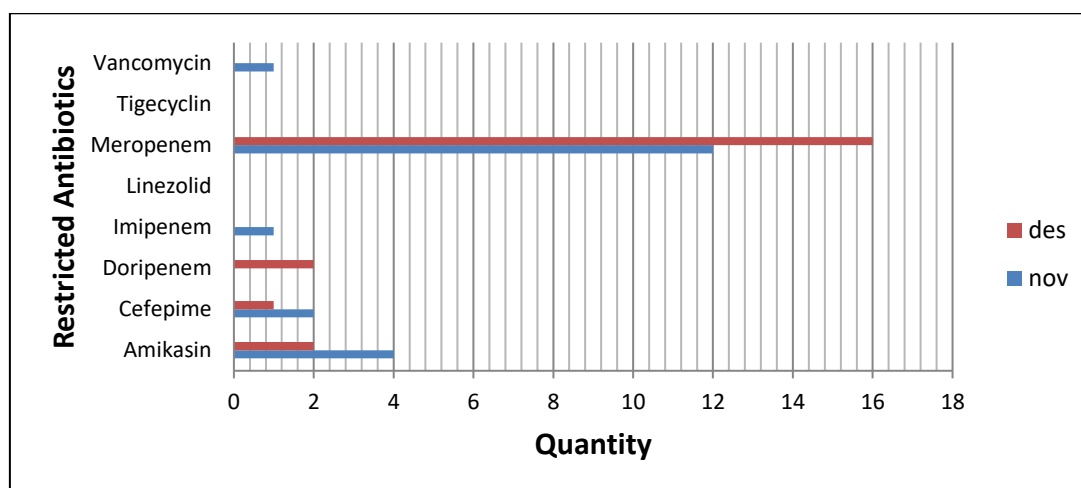


Figure 5. Use of Antibiotic Empiric Restriction

From Figure 6, it can be seen that Meropenem prescription remain high. Throughout 2017, there were some doctors who kept prescribing the restricted antibiotics despite objection by the Antimicrobial Control team.

## DISCUSSION

The average Antimicrobial Resistance Control Program in 2017 (see Figure 2 & 3) shows that Eka Hospital's target of 90% was not achieved. Through the collected data, only average of 67% Category 0 was recorded. There are some underlying factors behind the unmet target, which are antibiotic prescriptions prior to establishment of microbiological examination, in adherence to hospital's antibiotic usage guidelines despite the given reminders, and inadequate monitoring by clinical pharmacists on patients receiving empiric antibiotic therapy. Due to those issues, the evaluation process on the antibiotic use by Antimicrobial Resistance Control team will be affected.

Through the monthly observation of the antibiotic empiric restriction program in ICU from January to December 2017, it shows the constant increment of accuracy in antibiotics given to the patients. The benefits derived from the implementation of Antibiotic Empiric Restriction in Eka Hospital are the increased accuracy of antibiotics usage, which include appropriate selection, accurate dosage, and time of the antibiotic use. It is reflected in Figure 4 which visualizes the decrease in patients LOS demonstrating the positive impact of this program.



From the Figure 5, it can be seen prescription antibiotics Meropenem still often prescribed. It is found that there are doctors who remain using the antibiotic drug restriction administered even though it is prohibited by the antibiotic resistance control team. Policies and guidelines for the use of antibiotics are available in Eka Hospital Pekanbaru and those have been communicated to the relevant users. However, some of the medical personnel mentioned that they have not been informed. In case of prophylactic antibiotics is remain unobserved due to the lack of pharmacists who can monitor the usage of those.

The findings of policy documents and guidelines for antibiotic use in hospitals and inpatient installations tracing for doctors discover only a few specialists own these documents. The findings further show that the guidelines are not optimally implemented due to lack of coordination between Antibiotic Control Committee and the stakeholders in policies making process, lack of proper information distribution, and frequent unavailability of antibiotics according to the Antibiotic Guidelines .

In the implementation of the policy of antibiotics use in hospitals the role of doctors and other medical personnel are immense. While doctors' role are to determine and provide antibiotics according to the patients' needs, the paramedics should remind doctors to follow the Antibiotic Use Guidelines, such as duration of antibiotics usage, types of intravenous oral antibiotics, complete antibiotics application form filling, and medical record utilization for determining allergies, recording the duration and frequency of antibiotics, administering procedure, and mentioning possible side effects.

## CONCLUSION

Eka Hospital has established an Antimicrobial Control program since January 2017. However, it had not been properly implemented, due to doctors' incompliance to hospital guidelines and inadequate monitoring of antibiotic therapy. The assessment of antibiotic use in Eka Hospital Pekanbaru in 2017 shows rate of rational use of antibiotics in the ICU and Hopea B ward were far below the previously set target of 90%. There are a few limitations to this study. Prophylactic antibiotics remain unobserved due to the lack of pharmacists who monitors the usage of those. The study is also limited only to ICU and Hopea B ward which may show biasness and not representative of the whole Antibiotic Restriction Program in Eka Hospital.

## RECOMMENDATIONS

1. Ensure intense monitoring on patients receiving empiric antibiotic therapy by increasing the number of clinical pharmacists
2. Intensify doctors' awareness and understanding on the principles of antimicrobial resistance control and its correlation with the rational use of antibiotics by having program evaluation in timely manner and continuously communicate the policies regarding antibiotic use in the hospital
3. Support the role of infection control and prevention committee in the hospital to prevent antibiotic resistance through screening of patients and hospital staffs
4. Improve supervision, monitoring, and evaluation on the policy implementation of antibiotic use in the hospital, and apply a reward and punishment or motivation scheme whenever needed. Results from supervision, monitoring, and evaluation, including feedback and recommendations, should be communicated to hospital staffs.

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