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Case Report

PROBLEM OF ANTIBIOTIC USE AND ANTIMICROBIAL RESISTANCE IN INDONESIA: ARE WE REALLY MAKING PROGRESS?

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ABSTRACT

Background: Based on the results Antimicrobial Resistance in Indonesia: prevalence and prevention-study (AMRIN-study), the Ministry of Health of Indonesia in 2005 began a program antibiotic resistance control (PPRA) in some government hospitals, and is currently developing to all government teaching hospitals in Indonesia. Aim: The core activities of the PPRA are to implement standardized surveillance emergence of antibiotic resistant bacteria, and the surveillance of antibiotic use in terms of quantity and quality. Method: Our research in the years 2003 showed the proportion of antibiotic use 84% of patients in a hospital. The use of inappropriate antibiotics was very high, 42% no indication. Result: In 2012 the results of surveillance showed decline of inappropriate use of antibiotic, but prevalence extended-spectrum β-lactamase (ESBL)-producing K.pneumoniae (58%), and E.coli (52%) and methicillin-resistant S.aures (MRSA) (24%) were increasing. Conclusion: It was needed to implement the most appropriate programs to prevent the growth and development of bacteria resistant to antibiotics.

Key words: *Indonesia, K.pneumoniae, E.coli, methicillin-resistance S.aureus, surveillance*

ABSTRAK

Latar belakang: Berdasarkan hasil penelitian Antimicrobial Resistance di Indonesia: prevalensi dan pencegahan (AMRIN-studi), Kementerian Kesehatan Republik Indonesia tahun 2005 memulai program pengendalian resistensi terhadap antibiotik (PPRA) di beberapa rumah sakit pemerintah, dan saat ini diperluas untuk semua rumah sakit pendidikan pemerintah di Indonesia. Tujuan: Kegiatan inti dari PPRA adalah untuk melakukan surveilance kuman kebal antibiotik, dan monitoring penggunaan antibiotik dalam hal kuantitas dan kualitas secara terstandar. Metode: Penelitian kami di tahun 2003 menunjukkan proporsi penggunaan antibiotik dari pasien di rumah sakit sebanyak 84%. Penggunaan antibiotik yang tidak tepat sangat tinggi, 42% tidak ada indikasi pemberian antibiotik. Hasil: Hasil surveilance tahun 2012 menunjukkan penurunan penggunaan dari antibiotik yang tidak tepat, tetapi prevalensi extended-spectrum β-laktamase (ESBL) K.pneumoniae (58%), dan E.coli (52%) dan methicillin-resistant S.aures (MRSA) (24%) meningkat. Kesimpulan: Untuk memperbaiki kondisi ini diperlukan program lain yang paling tepat untuk mencegah pertumbuhan dan perkembangan bakteri resisten terhadap antibiotik.

Kata kunci: *Indonesia, K.pneumoniae, E.coli, methicillin-resistance S.aureus, survailans*

INTRODUCTION

World Health Organization has announced that the issue of antibiotic-resistant bacteria is a global problem that threatens human being. This happens because of a deficiency in 6 issues: 1) lack of research, 2) lack of commitment, 3) lack of infection control, 4) Irrational use of antimicrobials, 5) poor quality antibiotics, 6) weak oversight. To cope with these conditions, all countries should participate actively.

Efforts to suppress the development of antibiotic-resistant bacteria have been implemented throughout the world including Indonesia. A scientific research on Antimicrobial Resistance in Indonesia: Prevalence and

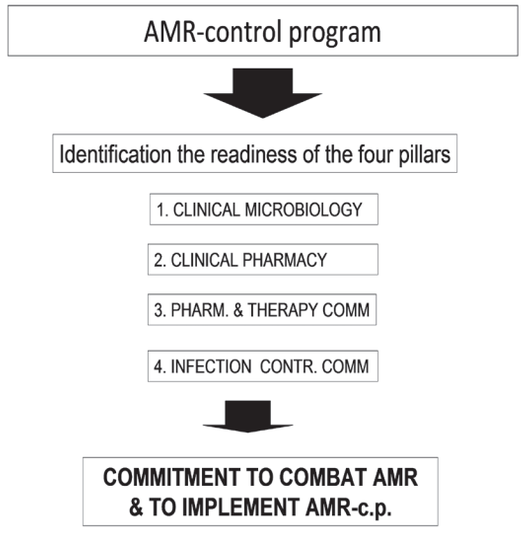
Prevention (AMRIN) study was conducted between 2001 and 2005. It aimed to create a program of scientifically based guidelines for the assessment of antimicrobial resistance, the pattern of antibiotic use, infection control and the implementation of interventions in the home hospital in Indonesia. The results of AMRIN study show that the problems also occur in Indonesia. It means that integrated handling of the various stakeholders in the hospital is required (AMRIN study group, 2005). To overcome this problem, the Ministry of Health has taken an action by developing a program of antimicrobial resistance control program (AMR-control program) for Hospital in Indonesia. The program was first implemented in teaching hospitals in Indonesia and it is expected to further evolve to all hospitals in Indonesia (AMRIN-study, 2005).

The problem in Indonesia is that not all hospitals have the facilities to conduct microbiological examination or culturing of bacteria, antibiotic resistant bacteria so that the surveillance can not be performed. AMR-control program is expected to be able to make the use of antibiotic more rational, to improve the implementation of infection control measures, and to inhibit the development of antibiotic-resistant bacteria. Hospitals that do not have a complete facility are expected to realize it because without good microbiology laboratory, the control of antimicrobial resistance is not possible to be done.

This paper describes the implementation AMR-control program so as to give an idea whether the program works well or whether it is still necessary to make some improvements to the program in order to achieve the program objectives.

Implementation Method of AMR-control Program

AMR-control program was implemented in stages. First, identifying the readiness of the hospital management to implement this program. Hospital is considered ready to execute this program when it has four supporting pillars, namely: 1) clinical microbiology, 2) clinical pharmacy, 3) pharmacy and therapy committee, 4) infection control committee. Once the four pillars had been identified, they were then assessed to know whether they were already running as they should. It was then followed by performing training to the 4 pillars so as they had the same understanding of this program as shown in Scheme 1.



Scheme 1. The concept of AMR-control program (AMRIN study group, 2005)

Second, creating a team consisting of the four pillars responsible for the execution of AMR-control program.

Each pillar has a function in accordance with its respective field.

The Role of Clinical Microbiology in the Management of Infectious Diseases

In Indonesia most of clinical microbiology laboratories are not yet well developed. Hence, the hospital management has to upgrade microbiology laboratory to meet the actual standard.

The clinicians usually treat infectious disease patients with a clinical diagnosis and they give antibiotic empirically. To improve collaboration between clinicians and the clinical microbiologists, the two sides should enhance the quality of their work.

We do the following recommendations to improve the cooperation between clinicians and microbiologists.

1. Holding regular (weekly) meetings between clinicians and microbiologists to discuss current infectious disease cases in hospital.
2. Holding routine evaluation of adherence to clinical guidelines by clinicians and giving feed back of adherence figures.
3. Enhancing the involvement of the clinical microbiologist in patient care such as by instituting a 24 hour service for advice concerning diagnostics and treatment of patients with infectious diseases.

Clinical Pharmacy

Clinical pharmacy has an important role to control antibiotic prescribed in the hospital. In addition, clinical pharmacists have to meet the needs of antibiotics prescribed by a clinician. They should have the signs made by the pharmacy and therapeutics committee to control the excessive use of antibiotic.

Pharmacy and Therapeutics Committee

Pharmacy and Therapeutics Committee is obliged to make the antibiotic guidelines and policies for the use of antibiotics.

They have to revise guidelines for the use of antibiotics and antibiotic use policies when needed.

Another task of this committee is to conduct surveillance of antibiotic use quantitatively and qualitatively particularly in the ward where antibiotic-resistant bacteria emerge.

Infection control committee

This committee is responsible for the prevention of AMR organism spreading. Besides, this committee also has to increase infection control implementation in hospital consisting of:

- Standard precautions
- Isolation of patients
- Source control
- Surveillance of AMR organisms

Implementation steps of AMR-control program

1. Forming a team of AMR-c.p. in hospital.
2. Choosing one department or unit as a pilot project, e.g. department of Internal Medicine or pediatric.
3. Updating or developing antibiotics guideline.
4. Socializing antibiotics guideline.
5. Conducting baseline data collection for 1–3 months respectively.
6. Implementing the antibiotics guideline.
7. Conducting surveillance data collection post intervention.
8. Evaluating and discussing.
9. Presenting the result: e.g. workshop
10. Getting antibiotics guideline updates.
11. Conducting surveillance (monitoring and evaluating).
12. Getting back to point number 3.

Results of AMRIN-study (period of study 2002–2005)

Our study of quantity and quality of antibiotic usw showed that the percentage of antibiotic prescribed in hospitalized patients was quite high (85%). As many as 90% of patients staying for 5 or more days in the department of Surgery and Pediatrics used antibiotics while in the Gynecology & Obstetrics Department and Internal Medicine Department, there were as many as 87% and 67% of the patients respectively using antibiotics (Hadi, 2008). 53% out of 2058 prescriptions was classified as therapy, 15% as prophylaxis, and 32% as unknown indication.

The quality of antibiotic use was assessed by two Indonesian reviewers and one foreign reviewer. Almost 60% of the assessed prescriptions was classified as incorrect either unjustified (42%) or inappropriate (15%) by at least two of the three reviewers (Hadi, 2008).

Our study of bacterial resistance from normal flora gastro-intestinal tract showed that Escherichia coli had been isolated from 781 hospitalized patients and all data were available for analysis. Eighty-one percent of the hospitalized patients carried Escherichia coli resistant to one or more antibiotics. Ampicillin resistance was seen most frequently (570 isolates, 73%), followed by trimethoprim/sulfamethoxazole resistance in 434 isolates (56%), chloramphenicol resistance in 334 isolates (43%), ciprofloxacin resistance in 173 isolates (22%) and gentamicin resistance in 141 isolates (18%) (Duerink, 2007).

In the community group of 2996 individuals, 2494 information cases regarding carriage of Escherichia coli were available. Forty-three percents of the population carried resistant Escherichia coli. Ampicillin resistance was observed in 851 (34%) isolates, trimethoprim/sulfamethoxazole resistance in 716 (29%) isolates and chloramphenicol resistance in 369 isolates (15%) (Duerink, 2007).

Surveillance of Post Implementation of AMR-control Program

Because of limited funds and facilities, surveillance could not be implemented fully in all hospitals in Indonesia. We only present the results of surveillance in a hospital in Surabaya.

The results of surveillance of antibiotic use in the department of internal medicine in 2012 showed that 50.22% of patients was treated with antibiotics. It was lower compared to the percentage of antibiotic use in 2005 which was 67%.

In terms of the quality of antibiotic use, there was also an improvement in which a more rational usage of antibiotics was found compared to the use of antibiotics in 2005. On the one hand, there was a decline regarding no indication of antibiotic therapy from 42% to 30.6%, and inappropriate antibiotic therapy from 15% to 7.3%. On the other hand, there was a change in the pattern of antibiotic use between 2005 and 2012. In 2005 the use of ampicillin was dominant whereas in 2012 3rd generation cephalosporin was more widely used.

We conducted AMR surveillance in the period from January to June 2010 by looking back to the medical records performed in the microbiology laboratory. 4359 bacteria were found consisting of 3115 negative gram and 1244 positive gram bacteria isolates. Among these bacteria, 456 (22%) were ESBL positive isolates and 45 (18%) were MRSA isolates from total of 250 *S aureus* isolates. Of these ESBL isolates, 107 specimens of *E.coli* ESBL(+) (17%) were obtained from a total of 633 *E. Coli* isolates and 196 isolates of *K. pneumonia* ESBL(+) (23%) were obtained from a total of 196 *K pneumonia*.

While the surveillance conducted in the period from July to December 2012 showed that there were *K.pneumoni* ESBL(+) 202 (58%) specimens from a total of 351 *K pneumonia* specimens and *E. coli* ESBL(+) 327 (52%) specimens from a total of 629 *E.coli* specimens.

63 (24%) MRSA specimens were obtained from a total of 259 *S.aureus* specimens while the prevalence of ESBL was (53%).

Table 1. Comparison of prevalence of ESBL and MRSA between 2010 and 1012

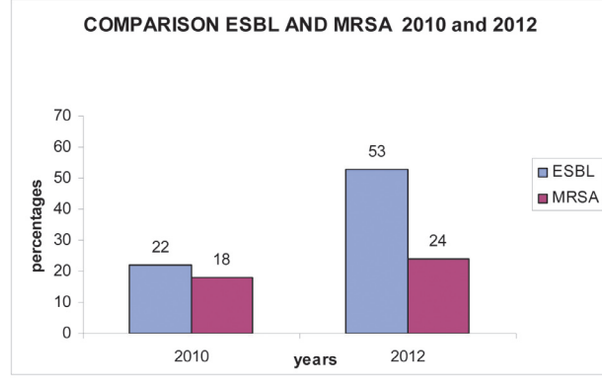


Table 2. Comparison between *K pneumonia* and *E.coli* ESBL producing bacteria's

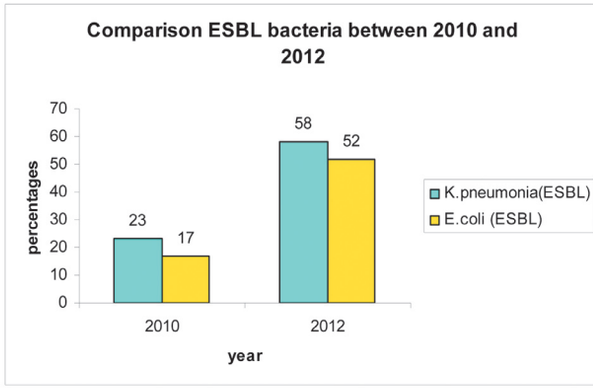


Table 3. Comparison of quality of antibiotic use between 2005 and 2012

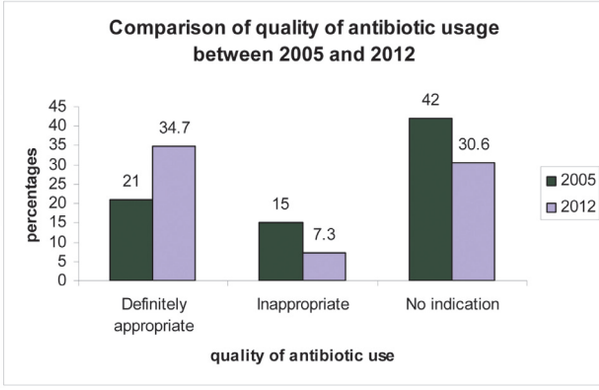


Table 2 shows that the quality of antibiotic use is improved in which there is an increase in the appropriate use of antibiotics and a decrease in the inappropriate use and no indication.

CONCLUSION

This program could not be implemented fully because there were many limitations in many hospitals in Indonesia. Our study in Surabaya showed that the results of surveillance of antibiotic use demonstrated an improvement compared to that between 2005 and 2012. Yet, in terms of the development of antibiotic-resistant bacteria e.g. ESBL producing bacteria, the prevalence increased. In addition, MRSA also increased. This could occur because the possibility of the use of antibiotics in the community outside the hospital was still very high or excessive.

Both improvement of health facilities especially microbiology laboratory and the addition of experts in the field of microbiology are required.

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