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Evaluation of standard operating procedure in Tabanan regional general hospital (RSUD Tabanan): usage of restricted antimicrobials

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Abstract

Background: The healthcare sector, specifically hospitals, is vulnerable to antimicrobial resistance due to diverse services and patient populations, alongside continuous intensive antimicrobial use. This resistance presents a significant national and global health threat. Therefore, implementing an antimicrobial stewardship program is crucial for reducing resistance development and spread in hospitals. Pharmacists, as healthcare professionals, have an essential role in upholding stewardship through pharmaceutical services in line with Standard Operating Procedure (SOP).

Objective: This study aimed to evaluate Restricted Antimicrobial Standard Operating Procedure (SOP-A) at Tabanan Regional General Hospital (RSUD Tabanan) to enhance the quality of pharmaceutical services.

Method: A qualitative method was used in SOP evaluation, comparing data from interviews with the Head of Pharmacy Installation at RSUD Tabanan and observations of implementation. The data were then contrasted with recent literature and regulations to identify discrepancies necessitating improvements. Moreover, data were analyzed using the descriptive method and presented in narrative, figure, and table formats.

Results: The results showed that based on interviews and observations of SOP-A implementation, several revisions were needed. These revisions include adding restricted antimicrobials from the reserve categories (cefepime, cefpirome, and carbapenems), establishing a protocol for eligible patients without waiting for culture results, outlining a process for obtaining approval from the Head of the Antimicrobial Resistance Control Program (PPRA) and Hospital Director, as well as incorporating antimicrobial usage history into the restricted antibiotic use application form.

Conclusion: SOP-A at RSUD Tabanan requires four key additions, namely a list of reserve category antimicrobials, a protocol for administering restricted antimicrobials to eligible patients without waiting for culture results, a process for obtaining approval from the Head of the PPRA and Hospital Director, as well as inclusion of antimicrobial usage history in the restricted antibiotic use application form.

Keywords: Antimicrobials, antimicrobial resistance, qualitative, restricted, standard operating procedure (SOP)

1. Introduction

The improper use of antimicrobial agents is a key contributor to the increasing incidence of antimicrobial resistance (CDDEP, 2021). For example, bacteria have various mechanisms facilitating resistance to antimicrobial activity, including genetic mutations that modify the active components of antimicrobials, thereby reducing efficacy. Additionally, certain bacteria can alter the outer membrane structures and receptors, preventing the binding of antimicrobials (Habboush & Guzman, 2023). These adaptive mechanisms allow survival of antimicrobial treatment and acquisition of resistance, which can be disseminated across species through horizontal gene transfer (Read & Woods, 2014). Antimicrobial-resistant infections represent a significant global health threat (ECDC, 2022), with this challenge being of particular concern in Indonesia.

The development of antimicrobial resistance is influenced by several factors, including widespread self-medication, unequal access to quality healthcare, a rising incidence of infectious diseases, and insufficient regulation of antimicrobial use (Parathon *et al.*, 2017). At the healthcare facility level, resistance is strongly associated with patterns of antimicrobial consumption, the accuracy of prescriptions, antimicrobial stewardship practices, and the perceptions of both consumers and healthcare providers concerning antimicrobial use (Limato *et al.*, 2022).

The high incidence of antimicrobial resistance frequently occurs in healthcare settings and is particularly common among patients with compromised immune systems, elderly individuals, and young patients who require frequent medical interventions (Pulingam *et al.*, 2022). Hospitals, as major providers of healthcare services, serve as potential hubs for the transmission of antimicrobial-resistant bacteria. This is attributable to the wide range of medical procedures performed, the diverse patient population, as well as the potential for prolonged and intensive use of antimicrobial agents (Knobler *et al.*, 2003).

World Health Organization (WHO) has implemented antimicrobial stewardship program that engages all healthcare workers in facilities, including hospitals, to mitigate the development of antimicrobial resistance (WHO, 2019). This program is designed to ensure that healthcare professionals follow appropriate antimicrobial usage protocols, thereby reducing the development and dissemination of resistance in healthcare environments (Bankar *et al.*, 2022). Pharmacists play a critical role in the implementation of antimicrobial stewardship in hospitals, with one of the key responsibilities being the development of local guidelines, such as Standard Operating Procedure (SOP) (Jantarathaneewat *et al.*, 2022).

SOP should be used by hospital pharmacists to enhance the delivery of pharmaceutical services. It serves as comprehensive guidelines that outline operational procedures in an organization, ensuring all decisions, actions, and the use of facilities are conducted effectively, consistently, and systematically by personnel (Tambunan, 2013). Technical, administrative, and procedural SOP are essential for guiding the implementation of healthcare services in hospitals (Taufiq, 2019). In particular, SOP related to antimicrobial use is critical for minimizing the incidence of resistance arising from antimicrobial treatment in healthcare settings, specifically hospitals. SOP must be continuously evaluated, taking into account the internal conditions of the hospital, the evolution of relevant policies in the region, and should be consistent with global health regulations to ensure the delivery of high-quality pharmaceutical services and enhance patient safety.

Tabanan Regional General Hospital (RSUD Tabanan) has established antimicrobial stewardship program in Pharmacy Installation, incorporating this initiative into SOP for restricted

antimicrobials issued in 2022. However, as new regulations regarding antimicrobial use develop over time, it is imperative to update SOP. Previous studies have assessed SOP related to the pharmaceutical supply planning process in Hospital X (Noviyani & Purnamasari, 2023), but there has not been an evaluation for restricted antimicrobials in hospitals. Therefore, this study aimed to evaluate Restricted Antimicrobial Standard Operating Procedure (SOP-A) in Pharmacy Installation of RSUD Tabanan to enhance the effectiveness and compliance with current standards.

2. Method

2.1. Data collection and processing methods

This qualitative study was conducted over 2 months, with permission (Number: 445/649/TIMKORDIK/RSUD/2023) and ethical clearance (Number: 445/634/TIMKORDIK/RSUD/2023) obtained from RSUD Tabanan. Data were collected through interviews with the Head of Pharmacy Installation at RSUD Tabanan and direct observations of SOP-A. The assessment was guided by current literature and regulations concerning restricted antimicrobials and pharmaceutical services in hospitals. The results from the interviews and observations were analyzed descriptively, using narratives, images, and tables to identify any compliance or non-compliance of activities or information in SOP-A relative to established guidelines. Any discrepancies identified indicate areas requiring improvement in SOP-A. This study concluded with the formulation of a revised SOP consistent with contemporary literature and regulations.

2.2. Tools and materials

Tools and materials used for data collection included SOP-A from RSUD Tabanan, a structured interview questionnaire, an observation sheet for documenting activities, an interview data collection form, informed consent forms, and relevant literature. These include *Peraturan Pemerintah Republik Indonesia No. 28 Tahun 2024 tentang Peraturan Pelaksanaan Undang-Undang No. 17 Tahun 2023 tentang Kesehatan* (Government Regulation No. 28 of 2024 regarding the Implementation Regulation of Law No. 17 of 2023 on Health), *Undang-Undang No. 17 Tahun 2023 tentang Kesehatan* (Law No. 17 of 2023 on Health), *Peraturan Menteri Kesehatan Republik Indonesia No. 28 Tahun 2021 tentang Pedoman Penggunaan Antimikroba* (Indonesia Minister of Health Regulation No. 28 of 2021 on Guidelines for Antimicrobial Use), and *Peraturan Menteri Kesehatan No. 8 Tahun 2015 tentang Program Pengendalian Resistensi Antimikroba* (Indonesia Minister of Health Regulation No. 8 of 2015 on the Antimicrobial Resistance Control Program (PPRA)). The results of

the interviews recorded using audio and video devices were subsequently analyzed descriptively with Microsoft Office software on a computer.

3. Result and discussion

In this study, an evaluation of SOP-A was carried out based on the results of interviews, observation of activities, and literature studies of applicable laws and regulations in Indonesia. Interviews with resource persons (the Head of Pharmacy Installation at RSUD Tabanan) and direct observation of antimicrobial service activities by RSUD Tabanan Pharmacy Installation have been carried out to obtain detailed information and a complete picture of SOP-A as well as the application. The results of interviews and observations of these activities are presented in **Table 1**.

Table 1. The results of interviews and observations of the implementation of sop-a

No.	Question	Resource person answer	Observation (appropriate/ inappropriate)
1.	Who are the parties engaged and responsible for preparing SOP-A?	The PPRA Team at RSUD Tabanan.	Appropriate
2.	Is there a set schedule for updating SOP-A? How long is the time?	Currently, there is no specific time for updating SOP-A. However, in every routine meeting at RSUD Tabanan, it is necessary to revise SOP-A and other applicable SOP, based on the current situation.	Appropriate
3.	Does SOP-A only cover the use of ceftazidime, meropenem, and vancomycin? Is there a possibility of adding other antimicrobials to the list of restricted antimicrobials in SOP-A?	At the time of SOP-A development, only ceftazidime, meropenem, and vancomycin were included based on the conditions at RSUD Tabanan and the current regulations. New regulations regarding restricted antimicrobials or other antimicrobials used in the hospital will be added to SOP-A.	Inappropriate
4.	Other than ceftazidime, meropenem, and vancomycin, what antimicrobials are currently used at RSUD Tabanan based on the newest list of restricted antimicrobials?	Cefepime, cefpirome, and the carbapenem class.	Appropriate
5.	Are there any additional documents required besides restricted antimicrobial form for prescribing and administering restricted antimicrobials at RSUD Tabanan? If yes, what documents are required?	Yes, in addition to restricted antimicrobial form, an additional document required is the culture result of the patient sample from the laboratory, which must be attached as part of the form. Culture sampling is a mandatory requirement for every patient who will receive restricted antimicrobials at RSUD Tabanan.	Appropriate
6.	What are the specific situations referred to in SOP-A that allow for the	Certain situations that require the administration of restricted antimicrobials without culture sampling include urgent	Inappropriate

No.	Question	Resource person answer	Observation (appropriate/ inappropriate)
	submission of restricted antimicrobials without culture sampling?	situations, such as in post-chemotherapy patients who show febrile neutropenia symptoms, but we have not included this situation in SOP-A.	
7.	What is the procedure for reporting the use of restricted antimicrobials by pharmacists to the PPRA?	Reporting has been performed through in-person meetings, phone calls, or electronic messages when the PPRA cannot meet. Culture results will be submitted later. This is carried out to ensure decisions on the administration of restricted antimicrobials can be made immediately according to the patient's condition.	Inappropriate
8.	Is there a special handling procedure when bacteria resistance is detected after administering restricted antimicrobials to the patient?	There have not been any cases of bacteria resistance after the administration of restricted antimicrobials, no special handling procedures have been designed for this situation. However, when this occurs in the future, there will be an evaluation and development of operational procedures according to current guidelines and recommendations.	Appropriate
9.	How is SOP-A implementation efficient in improving the quality of patient health services at RSUD Tabanan?	SOP-A plays an important role in controlling the use of antimicrobials at RSUD Tabanan, specifically in reducing the incidence of antimicrobial administration errors. For patients with certain conditions, restricted antimicrobial administration can be carried out without waiting for culture results, according to SOP-A guidelines. This allows for faster management of the patient health condition.	Appropriate
10.	Is the submission of restricted antimicrobial form to the PPRA required to provide information on the history of antimicrobial use?	Information on the history of antimicrobial use is essential for restricted antimicrobial application form, but it is currently not included.	Inappropriate

Description:
SOP-A: Restricted Antimicrobial Standard Operating Procedure in RSUD Tabanan

As shown in **Table 1**, four factors are not in accordance with the latest regulations, including no inclusion of other types of restricted antimicrobials, the absence of complete information about certain conditions where antimicrobials can be given before culture sampling, the absence of procedures or flows governing approval by the Head of the PPRA before pharmacists administer antimicrobials to patients, and the incomplete restricted antimicrobials form. Therefore, these four factors need to be added in making the new SOP for the Use of Restricted Antimicrobials. The results of these interviews and observations are then used as a reference to evaluate SOP-A.

According to *Peraturan Pemerintah No. 34 Tahun 2018 tentang Sistem Standardisasi dan Penilaian Kesesuaian Nasional* (Government Regulation No. 34 of 2018 concerning the National

Standardization and Conformity Assessment System), standards are optimized technical or appropriate requirements, including procedures and methods that are prepared based on the consensus or related government or international decisions by taking into account the requirements of safety, security, health, environment, development of science and technology, experience, as well as current and future developments to obtain the maximum benefit. Standards are made to direct service delivery and expected results. To produce performance in accordance with the established standards, a standardized set of procedures is needed, also known as SOP. In general, SOP in hospitals is a guideline or reference for carrying out tasks or work in line with the functions and performance assessment tools based on technical, administrative, and procedural indicators of the work procedures concerned (Wiraya and Haryati, 2022). In the implementation, SOP must always be reviewed to accommodate and anticipate changes related to the technical, administrative, and procedural indicators concerned.

One of SOP that has been implemented at RSUD Tabanan is SOP-A made by RSUD Tabanan on August 29, 2022. It was prepared based on Indonesia Minister of Health Regulation No. 8 of 2015 and *Surat Keterangan Direktur Rumah Sakit No.422/SK.RSUD/2022 tentang Penggunaan Antimikroba pada Rumah Sakit Umum Daerah Kabupaten Tabanan* (Hospital Director's Statement Letter No. 422/SK.RSUD/2022 concerning the Use of Antimicrobials at RSUD Tabanan) that refers to *Undang-Undang Republik Indonesia No. 36 Tahun 2009 tentang Kesehatan and Peraturan Menteri Kesehatan No. 72 tahun 2016 tentang Standar Pelayanan Kefarmasian di Rumah Sakit* (Indonesian Law No. 36 of 2009 concerning Health and Regulation of the Minister of Health No. 72 of 2016 concerning Standards of Pharmaceutical Services in Hospitals).

According to Indonesia Minister of Health Regulation No. 8 of 2015, antimicrobial resistance refers to resistance to antimicrobials that are usually effective in treating infections caused by bacteria, fungi, viruses, and parasites. Currently, the increase in cases of antimicrobial resistance continues to rise, while the rate of drug development has not been able to keep up with the development of this resistance. An optimal antimicrobial use management strategy is needed to prevent the development of resistance and improve patient outcomes. Restriction is a control effort by limiting the use of antimicrobials (Bardani, Andriani, and Rahmadevi, 2021). Grouping Restricted antimicrobials aims to prevent a more severe increase in resistance, considering the many bacteria that have developed resistance. On the other hand, the discovery of new, more effective antimicrobials has not been able to keep up with the rate of resistance development (Basavaraju *et al.*, 2021).

Following Indonesia Minister of Health Regulation No. 8 of 2015, antimicrobial groups that can be used in hospitals are divided into those free to be used by all clinicians (non-restricted), and others restricted to expert team approval (restricted and reserved). The regulation does not explain what types of antimicrobials are included in these groups. Therefore, to prepare SOP, the types of reserved antimicrobials have been determined based on the availability which is the last line to overcome bacteria infections in the hospital (Saleem *et al.*, 2020). Three types of antimicrobials that have been listed in SOP restricted antimicrobials category include ceftazidime, meropenem, and vancomycin. Based on Indonesia Minister of Health Regulation No. 28 of 2021 on Guidelines for Antimicrobial Use, there is a grouping of antimicrobials in line with the AWaRe (access, watch, and reserve) category also recommended by WHO (WHO, 2023), The existence of the latest regulations is then taken into consideration in improving SOP.

Access category antimicrobials are used for common bacteria infections and can be prescribed by doctors, dentists, specialists, and reviewed by pharmacists. Access category antimicrobials consist of amoxicillin, ampicillin, amoxicillin-clavulanic acid, ampicillin sulbactam, benzathine benzylpenicillin, doxycycline, erythromycin, phenoxymethyl penicillin, gentamicin, kanamycin, clindamycin (oral), cloxacillin, chloramphenicol, metronidazole, oxytetracycline injection, thiamphenicol, pyrimethamine, procaine penicillin, cefadroxyl, cephalexin, cefazolin, ciprofloxacin (oral), spiramycin, streptomycin, sulfadiazine, and tetracycline (Kemenkes RI, 2021).

Watch category antimicrobials are used for special indications or when access groups are ineffective and can be prescribed by specialist doctors, dentists, reviewed by pharmacists, and approved by an infection consultant doctor. When no infection consultant doctor is available, approval is given by a member of Antimicrobial Resistance Control Committee (KPRA). Antimicrobial watch category consists of amikacin, azithromycin, fosfomycin, clarithromycin, levofloxacin, moxifloxacin, netilmicin, ofloxacin, cefixime, cefoperazone-sulbactam, cefotaxime, cefpodoxime proxetil, cefazidime, ceftriaxone, cefuroxime, and ciprofloxacin injection (Kemenkes RI, 2021).

Reserve category antimicrobials reserved to treat bacteria infections caused by Multiple Drug-Resistant Organisms (MDRO) are the last resort in severe life-threatening infections and only prescribed by specialist doctors and dentists, reviewed by pharmacists, and approved for use by Antimicrobial Stewardship (PGA) team which is part of the Hospital KPRA. Antimicrobials in the reserved category consist of aztreonam, daptomycin, carbapenems, cotrimoxazole injection, linezolid, nitrofurantoin, piperacillin-tazobactam, polymyxin b, polymyxin e, cefepime, cefpirom, cefarolin, teicoplanin, tigicycline, vancomycin, cefolozane-tazobactam, and cefazidime-avibactam (Kemenkes RI, 2021).

SOP-A has been regulated regarding what types of antimicrobials are included in restricted antimicrobials, namely ceftazidime, meropenem, and vancomycin. However, following Indonesia Minister of Health Regulation No. 28 of 2021, there are still discrepancies. Three types of reserve category antimicrobials are still used at RSUD Tabanan which should be classified as restricted antimicrobials but have not been included in SOP, namely cefepime, cefpirome, and other carbapenem groups besides meropenem. This was discovered from the results of interviews delivered directly by the Head of Pharmacy Installation: "Cefepime, cefpirome, and carbapenems such as ertapenem, doripenem, and imipenem are also used as a treatment for infections at RSUD Tabanan but we have not included them in SOP". Therefore, the results of SOP evaluation indicate that the three types of antimicrobials need to be included in the new SOP-A, as shown in Appendix 1.

In reviewing the previous SOP-A, there are two types of flow for the administration of restricted antimicrobials, differentiated by the patient treatment room. In the first flow, when the prescription and drug request form originates from the attending physician for a patient in intensive care (ICU, HCU 1, HCU 2, Isolation ICU, NICU, Hemodialysis, or Declining Immune Room), pharmacy staff can prepare and dispense the prescribed restricted antimicrobials without requiring approval from the Head of the PPRA Team or Hospital Director. The evaluation shows that this first flow of SOP is appropriate and does not necessitate any changes. However, there are a few considerations for pharmacy staff. Before drug administration, the medical team should be consulted to obtain samples for complete blood tests when necessary. Interviews showed instances of non-compliance with culture testing before antimicrobial administration. Cultures are the gold standard for detecting and identifying bacteria infections, and the results are crucial for making informed decisions regarding the appropriate use of specific antimicrobials based on the infection source, thereby preventing the development of antimicrobial-resistant bacteria (Herman *et al.*, 2019).

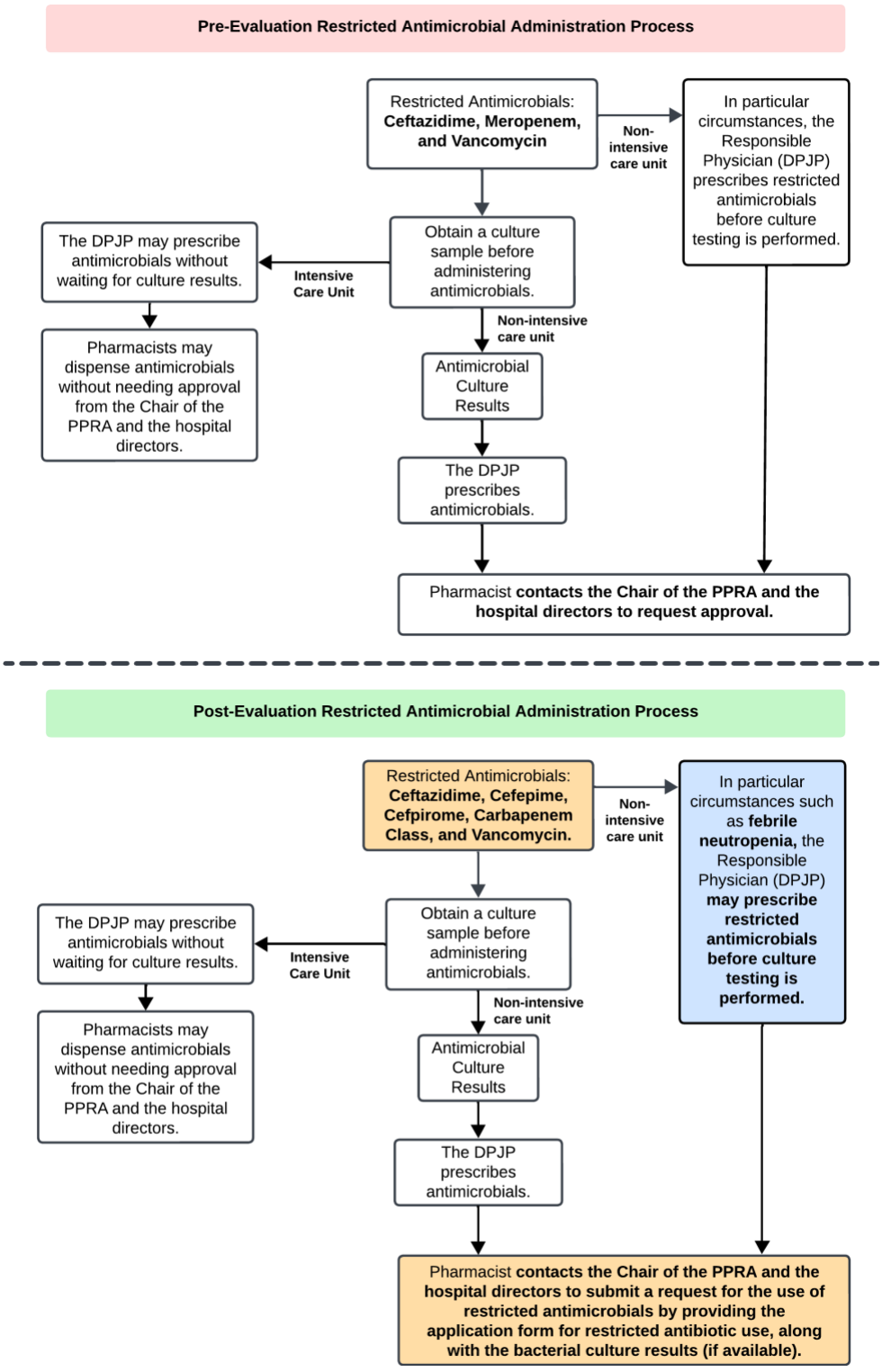
In the second flow, when the prescription and drug request form are issued by the attending physician for patients receiving treatment outside the intensive care unit, the administration of restrictive antimicrobials is only allowed after completing a blood test and culture. However, in certain urgent situations, pharmacists or pharmaceutical technicians may request special control antimicrobials by consulting with the Head of the PPRA and Hospital Director for approval before the culture examination. SOP does not clearly define the specific scenarios that may justify submitting requests for restricted antimicrobials before obtaining culture results. As stated by the Head of Pharmacy Installation in an interview: "Certain urgent situations necessitate the administration of restricted antimicrobials without waiting for culture results, specifically in post-chemotherapy patients showing symptoms of febrile neutropenia." In general, febrile neutropenia, a common side

effect of chemotherapy, is defined by a body temperature of ≥ 38°C and an absolute neutrophil count (ANC) of ≤ 500 cells/mm^3 due to the myelosuppressive effects of the treatment. This condition severely compromises the immune system, increasing susceptibility to bacteria infections, and when not addressed promptly, can delay further chemotherapy (Natawidjaja, *et al.*, 2019; Pratiwi *et al.*, 2022). Therefore, based on the evaluation of SOP-A, it is essential to incorporate specific situations that allow pharmacists or pharmaceutical technicians to administer special control antimicrobials without awaiting culture results, resulting in the creation of a new flowchart in the revised SOP-A (see Appendix 1).

After an interview with the Head of Pharmacy Installation, it was stated that "There is no special flow as pharmacists or pharmaceutical technicians contact the Head of the PPRA and Hospital Director to submit requests for restricted antimicrobials before culture examination, with the culture results to be proposed later." This indicates that there is currently no established protocol for requesting approval before submitting requests. The PPRA is managed by a specialized team responsible for formulating policies in hospitals. The primary tasks include establishing general policies and guidelines for antimicrobial use, conducting integrated case analyses regarding infectious disease management, and evaluating sensitivity to antimicrobials (Rukmini *et al.*, 2019). Therefore, SOP-A needs to establish a new protocol for pharmacists or pharmaceutical technicians to follow when contacting the Head of the PPRA and Hospital Director regarding requests for the administration of restricted antimicrobials. The revised process should include the submission of restricted antibiotic use application form, prepared by the attending physician, along with the culture results, when available, or a follow-up once the culture is in progress. Figure 1 shows differences in restricted antimicrobial administration flow before and after the evaluation, indicating the changes incorporated into the updated SOP-A (see Appendix 1).

The evaluation of SOP-A shows that the current restricted antibiotic use application form at RSUD Tabanan includes essential information such as the identities of the doctor and patient, patient diagnosis, treatment room, patient insurance, type and dosage of antimicrobial, duration of use, reason for administration, and microbial culture results. However, it lacks the patient antimicrobial use history, which is crucial for optimizing treatment outcomes. To address this gap, it is necessary to include antimicrobial usage history in restricted antibiotic use application form, as outlined in the new SOP in Appendix 1. This addition is critical because selecting appropriate antimicrobials requires considering bacteria sensitivity based on culture results, local resistance patterns, and the patient previous antimicrobial use (Adil & Kundarto, 2019).

In conclusion, all previously described evaluation results have been incorporated into the new SOP-A, as detailed in Appendix 1, enabling the implementation at RSUD Tabanan to enhance service quality and patient safety. The evaluation was conducted comprehensively, engaging informant interviews, direct observations, and comparisons with relevant literature as well as regulations to assess the suitability of SOP and implementation in practice. However, this study has limitations, as it relied on a single informant, the Head of Pharmacy Installation at RSUD Tabanan. To enhance data validity, direct observations of SOP-A implementation were also included. Future studies should adopt a similar comprehensive method to evaluate other SOP, engaging multiple informants for a broader perspective.



Description:

The process has not yet been implemented at RSUD Tabanan.

The process has been implemented at RSUD Tabanan, but it is not yet documented in SOP-A.

Figure 1. Comparison of restricted antimicrobial administration processes: pre- and post-evaluation

4. Conclusion

In conclusion, based on SOP-A evaluation, four key modifications were identified. First, the list of restricted antimicrobials must be updated to match the reserved category outlined in Indonesia Ministry of Health Regulation No. 28 of 2021. Second, a process should be introduced for administering restricted antimicrobials to patients with specific conditions without waiting for culture results. Third, an approval process requiring authorization from the Head of the PPRA and Hospital Director should be added. Finally, antimicrobial usage history should be included in restricted antibiotic use application form. These changes had been incorporated into the updated SOP-A.

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