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Pharmacoeconomic Analysis of Type 2 Diabetes Mellitus Patients with the Application of PGA (Use of Antimicrobials)

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) leads to a reduced immune response and increased susceptibility to infections, necessitating the use of antibiotics. However, inappropriate and excessive use of antimicrobials in humans, animals, and plants can contribute to increased antimicrobial resistance. **Objective:** This research aims to provide an overview of the application of Antibiotic Management (PGA) in the use of reserve antibiotics for T2DM patients concerning pharmacoeconomics at X Hospital in East Java. Method: **Method:** The study employed an observational approach with an exploratory descriptive method. Data were collected retrospectively from a cohort of patients who received reserve class antibiotics. The effectiveness of these antibiotics was assessed based on clinical outcomes, including patient survival or death, using medical records from October 2021 to September 2022 and October 2022 to September 2023. **Result:** The result indicated that the application of PGA using reserve antibiotics in T2DM patients had a positive and significant impact on pharmacoeconomics. The Incremental Cost Effectiveness Ratio (ICER) for T2DM patients with infections who received reserve antibiotics decreased after PGA implementation. **Conclusion:** The study concludes that PGA application in T2DM patients with infections yielded positive results, including a reduction in ICER, indicating improved cost-effectiveness and clinical outcomes. **Recommendation:** Proper and controlled use of reserve antibiotics through PGA can help mitigate antimicrobial resistance, a critical global health issue.

Keywords: type 2 diabetes mellitus, pharmacoeconomics, antimicrobial resistance, antimicrobial use

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is known to compromise immune function, thereby heightening patients' vulnerability to infections and often necessitating frequent antibiotic use (1). This situation has drawn increasing attention in light of recent global and national data on antimicrobial resistance, which has emerged as a critical public health concern. The World Health Organization (WHO) recognizes antimicrobial resistance as one of the top ten global health threats requiring urgent action (2). In line with the rapid advancement of modern society, the burden of antimicrobial resistance continues to grow, significantly contributing to the incidence of life-threatening infections such as pneumonia and sepsis. Alarmingly, projections indicate that by 2030, Indonesia may rank among the top five countries most affected by antimicrobial resistance. In 2019 alone, WHO estimated that more than 4.9 million deaths across 204 countries were linked—either directly or indirectly—to infections caused by antimicrobial-resistant bacteria (3).

Incorrect and excessive use of antimicrobials in humans, animals, and plants leads to increased antimicrobial resistance (2). This resistance results in higher mortality, morbidity, and treatment costs. Globally, it is estimated that by 2050, the economic losses due to antimicrobial resistance could reach around $100 trillion. Although antimicrobial resistance is a natural phenomenon that cannot be entirely eliminated, it can be mitigated by the prudent use of antibiotics. Preventing microbial resistance involves avoiding the emergence of resistant microbes through careful antibiotic use and controlling their spread. Adhering to these principles also enhances compliance with precautionary measures (4-5).

Coronary Heart Disease (CHD) is the most common complication and leading cause of death in Type 2 Diabetes Mellitus (DM2). The incidence of CHD as a cause of death in DM2 patients is 4-5 times higher compared to non-DM individuals. CHD in DM2 is influenced by various risk factors, including those assessed by the Framingham Score (6).

The X Hospital in East Java, as a level A referral health facility, has established an Antimicrobial Resistance Control Committee (KPRA) since 2016, in line with the implementation of Minister of Health Regulation No. 8 of 2015. In 2022, the Antimicrobial Stewardship Team (PGA) at X Hospital in East Java implemented pre-authorization for the prescription of Reserve category antibiotics. Given this background, research is needed to evaluate the implementation of antimicrobial resistance control program policies, particularly before and after the introduction of pre-authorization for Reserve category antibiotics by the PGA team at RSUD Sidoarjo, in terms of usage profiles and cost-effectiveness. X Hospital in East Java was chosen for this study because it has been running an Antibiotic Stewardship Program (PPRA), has a microbiology laboratory, and has implemented pre-authorization for Reserve category antibiotics.

METHODS

Design

This study employed the observational study with an exploratory descriptive approach. The study population comprised all medical records (MR) of patients who were administered reserve antibiotics during their stay in the inpatient ward

Sample, sample sie & sampling technique

The study utilized all medical records of hospitalized patients who were administered Reserve group antibiotics during their inpatient stay at Sidoarjo District General Hospital. The medical record data from October 2021 to September 2022 and from October 2022 to September 2023 were used to describe the overview of the application of Antibiotic Management (PGA) in the use of reserve antibiotics for T2DM patients concerning pharmacoeconomics.

Data Collection process

Data collection was conducted using a retrospective cohort approach on a population of patients who received Reserve group antibiotics. The effectiveness was assessed based on clinical outcomes, specifically patient survival or mortality, as documented in the medical records (MR) during the study period.

Patient data were retrieved from the Pharmacy Information System (SIM Apotek) to identify individuals who received Reserve

category antibiotics while being treated in the inpatient wards of Sidoarjo District General Hospital during the fourth quarters of 2021 and 2022. Patient medical records and hospitalization cost data were extracted from the Hospital Management Information System (LPD). The collected variables included patient demographics (identity, date of birth or age, and sex), dates of admission and discharge (length of stay), medical history, details of Reserve antibiotic administration (dosage, frequency, and duration), clinical outcomes post-antibiotic treatment (survival or mortality), and the total cost incurred during hospitalization.

All collected data were organized into a master dataset and subjected to descriptive analysis within a retrospective cohort framework. Metrics included the Defined Daily Dose (DDD) per 100 patient-days and clinical effectiveness of Meropenem, as reflected by patient outcomes (survival or mortality). Additionally, a pharmacoeconomic evaluation was performed using Cost-Effectiveness Analysis (CEA) for the respective periods of October 2021 to September 2022 and October 2022 to September 2023

Data analysis

The deskriptive statistic was used to describe the data demographic of patients. The paired t-test was employed to compare the cost effectiveness ratio of t2dm patients with infections who received reserve antibiotics before and after the implementation of pga. All data was tested for normal distribution with significantly p-value <.05**.**

Ethical consideration

This study has been approved from institutional review board universitas esa unggul. All respondents are required to sign the informed consent before participating in this study

RESULT

Data demographic

Data analysis shows that before and after the implementation of the Antimicrobial Stewardship Program (PGA), Type 2 Diabetes Mellitus (T2DM) patients who received reserve antibiotics were predominantly men (65% after PGA), aged 40-70 years, and primarily used meropenem as a reserve antibiotic (90% after PGA). Although cultures were not performed for the majority of patients (73.58% before PGA), the use of blood cultures increased (30% after PGA). The length of stay (LOS) was mostly in the range of 5-10 days (40% after PGA), and unfortunately, the majority of T2DM patients died both before and after the implementation of PGA (60% after PGA).

Table 1. Data demographic

Gender	Before PGA		After PGA	
	N	%	N	%
Gender Male Female	23 30	43.3 56.6	13 7	65 35
Type of reserve Meropenem Cefepime	53 0	100	18 2	90 10
Type of culture Fluid Blood Blood and sputum Not cultural sputum	2 11 1 39 0	3.77 20.75 1.89 73.58 0	0 6 2 10 2	0 30 10 50 10
Los <5 5-10 11-20 21-30	14 19 13 7	26.42 35.85 24.53 13.21	6 8 5 1	30 40 25 5
Patient conditions Life Dead	26 27	49. 06 50.94	8 12	40 60

Cost-Effectiveness ratio of T2DM patients with infections who received reserve antibiotics before and after the implementation of PGA

The average Cost-Effectiveness Ratio for T2DM patients with infections who received reserve antibiotics before the implementation of PGA is shown in Table 4.3 above. The highest average Cost-Effectiveness Ratio is IDR 4,679,734, while the lowest is IDR 268,898. The Cost-Effectiveness Ratios were averaged across 53 patients, resulting in a total cost of IDR 34,303,526.

Table 2. Cost-Effectiveness Ratio (ICER) Before and After Implementing PGA

	Before PGA	After PGA
Total cost	1,059,200,785	364,651,475
Effectiveness	573	168
ACER	118,902,471	34,303,526.70
ICER		84.598.944

Table 2 shows that the total cost of treating T2DM patients who received reserve antibiotics was higher before PGA (IDR 1,059,200,785) compared to after PGA (IDR 364,651,475). This indicates that PGA has succeeded in reducing maintenance costs.

Effectiveness (E): Effectiveness is measured by the number of patients successfully treated. Before PGA, 537 patients were successfully treated, whereas after PGA, only 168 patients were successfully treated. This suggests that PGA may have led to a decrease in the number of patients successfully treated.

Average Cost-Effectiveness Ratio (ACER): ACER represents the average cost per unit of effectiveness. Before PGA, the ACER was IDR 118,902,471 per patient, while after PGA it decreased to IDR 34,303,526.70 per patient. This indicates that PGA has improved cost-effectiveness, as the cost per successfully treated patient is lower.

Cost-Effectiveness Ratio (ICER): ICER is the ratio of incremental costs per unit of incremental effectiveness. The ICER in this table is IDR 84,598,944. This means that for each additional patient successfully treated after PGA, an extra cost of IDR 84,598,944 is incurred.

DISCUSSION

The research results describing the number of T2DM patients based on gender who experienced infections and received reserve antibiotics before and after the application of PGA showed that the majority of T2DM patients, both before and after the application of PGA, were male.

The prevalence of Type 2 Diabetes Mellitus (T2DM) varies by gender, with more males affected before puberty and more females affected after menopause (7). Women are also more susceptible to impaired glucose tolerance after eating, which can lead to an underestimation of T2DM prevalence if relying only on fasting blood glucose measurements (8). Although women are at greater risk of developing T2DM, the effectiveness of diabetes therapies such as SGLT-2 inhibitors and GLP-1 receptor agonists may differ by gender. This difference may be related to physiological and lifestyle variations between men and women (9).

Research shows that the prevalence of Type 2 Diabetes Mellitus (T2DM) is higher in women than in men (10). Contributing factors include unhealthy eating patterns, low physical activity, and hormonal changes (11). Women tend to have more visceral adipose tissue, which increases insulin resistance and the risk of T2DM. However, age did not show a significant relationship with the incidence of T2DM at Karsa Husada Hospital in Batu City (12). It is important to note that T2DM can develop at any age, including in children, due to the rising prevalence of unhealthy lifestyles.

Research also shows a significant relationship between age and the incidence of T2DM (13). This is caused by a decrease in physical strength and the body's defense mechanisms, which makes the body more susceptible to unhealthy lifestyles and disease manifestations such as T2DM (Sharma, 2015). Although T2DM generally occurs in middle or old age, trends show an increase in cases at younger ages due to unhealthy lifestyles (14)

Regarding the T2DM patients based on the type of reserve antibiotic who experienced infections and received reserve antibiotics before and after the implementation of PGA show that the majority of T2DM patients, both before and after the implementation of PGA, were treated with the reserve antibiotic meropenem.

In line with a study reported an increase in the use of ciprofloxacin, gentamicin, and amikacin, while the use of ampicillin, ampicillin-sulbactam, ceftazidime, and meropenem decreased (15). This trend aligns with the WHO report, which highlights high levels of quinolone use in Southeast Asia. Ciprofloxacin is the most frequently used antibiotic, and fluoroquinolone use is associated with the prevalence of pneumonia (16).

However, restrictions on ciprofloxacin use

in Europe (17-18) are due to potential side effects (19- 20). Differences in antibiotic use trends between hospitals and countries may be influenced by factors such as patient characteristics, type of infection, and antibiotic use policies (18). This study also observed a decrease in the use of ampicillin, ampicillin-sulbactam, ceftazidime, and meropenem, which are important antibiotics.

Length of Stay (LOS) who experienced infections and received reserve antibiotics before and after the implementation of PGA show that the majority of T2DM patients, both before and after the implementation of PGA, had a LOS of 5 to 10 days.

Length of stay (LOS) is an important indicator for assessing the quality of hospital services, with a shorter LOS suggesting more efficient and effective service (21).

Research at RSIA Trisna Medika Tulungagung from October to December 2021 analyzed the effectiveness of Cefazoline and Ceftriaxone as antibiotics for prophylaxis in cesarean sections and the factors influencing LOS (22). The results showed that LOS for cesarean section patients ranged from 3 to 7 days, with factors such as complications, type of surgery, and type of disease affecting the duration of treatment (23). This study involved 214 cesarean section patients divided into two groups: Cefazoline and Ceftriaxone (50:50). Data were analyzed using the Mann-Whitney U Test due to non-normal and non-homogeneous data distribution.

The research results describing the number of T2DM patients based on their condition who experienced infections and received reserve antibiotics before and after the implementation of PGA indicate that the majority of T2DM patients, both before and after the implementation of PGA, died.

Previous research indicates that doctors tend to prescribe broad-spectrum antibiotics like ceftriaxone, especially in patients with good general condition and without signs of sepsis (24). Culture tests are typically performed only in patients with debilitated conditions, sepsis, or prolonged LOS. Physicians at Sleman Regional Hospital are familiar with local germ patterns and use this data as a basis for administering empirical antibiotics. The availability of antibiotics in hospitals does not significantly influence the prescription of antibiotics for diabetic ulcer patients.

The analysis results show that PGA has succeeded in reducing the costs of treating T2DM patients. Although the number of successfully treated patients decreased after PGA, the cost per successfully treated patient was lower. This indicates that PGA has improved cost-effectiveness. However, additional costs are required for each additional patient successfully treated after PGA.

Cost-effectiveness analysis (CEA) is a method used to compare and select the most effective and efficient health or treatment program from several options with the same goal (25). CEA is typically calculated using the Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER), which show the costs required for each improvement in treatment outcome (25). CEA has the advantage of providing a monetary value for each unit of effectiveness but also has drawbacks, such as the need for compared treatments to have the same or related results (26). Culture plays a crucial role in infection treatment by helping clinicians select appropriate and rational antimicrobials. The Rational Antibiotic Movement (PGA) program promotes the use of culture to reduce empirical antibiotics and improve microbiologically targeted therapy. Research by Garg et al. (2021) demonstrated that the percentage of cultures conducted increased from 47.3% in the first quarter to 77.6% in the fourth quarter of the same year after implementing PGA. This underscores the importance of PGA in reducing the use of empirical antibiotics and enhancing therapy based on microbiological targets (27).

CONCLUSION

Based on the analysis results, the implementation of the reserve antibiotic program through the Pharmacy and Therapeutics Group (PGA) in patients with Type 2 Diabetes Mellitus (T2DM) has a positive and significant impact on pharmacoeconomics. T2DM patients are prone to infections and frequently require antibiotics, so adhering to PGA guidelines helps improve the effectiveness

of patient management. The role of the Pharmacy and Therapeutics Review and Assessment (PPRA) is also essential in overseeing the antibiotic prescribing process.

The implementation of PGA has shown a positive and significant impact on the use of reserve antibiotics. This program supports the principles of antibiotic stewardship, emphasizing accurate diagnosis and careful selection of the antibiotic type, dosage, interval, route, and duration to prevent antibiotic resistance. In addition, PGA influences the length of stay (LOS) of T2DM patients using reserve antibiotics. After the program was implemented, the use of meropenem decreased by 90%, while LOS increased by 30% from the initial rate of 62.4%.

From a cost-effectiveness analysis (CEA) perspective, PGA also demonstrated positive results. Before the program was implemented, the Average Cost-Effectiveness Ratio (ACER) ranged from IDR 195,263 to IDR 6,522,619, with a total cost of IDR 118,902,471 for 53 patients. After PGA implementation, the Incremental Cost-Effectiveness Ratio (ICER) dropped significantly from IDR 118,902,471 to IDR 34,303,526.70.

Implication

The positive impact of PGA implementation suggests that structured antibiotic stewardship programs should be an integral part of clinical pathways for managing T2DM patients. Healthcare providers, especially in tertiary hospitals, need to adopt PGA protocols to ensure rational antibiotic use, minimize the risk of antimicrobial resistance, and improve patient outcomes.

The significant reduction in the use of reserve antibiotics, such as meropenem, indicates that adherence to PGA can lead to more judicious prescribing behavior. This reinforces the need to expand antibiotic stewardship teams and provide regular education to prescribers on diagnostic precision and appropriate antibiotic selection.

Given the significant pharmacoeconomic impact, the Ministry of Health and hospital accreditation bodies could consider mandating the adoption of similar antibiotic stewardship models (like PGA) in national health regulations and hospital performance evaluations

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