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Cost-Effectiveness Analysis of Monotherapy Oral Antidiabetic Metformin and Glimepiride in Diabetes Mellitus at Bahteramas Hospital

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Abstract
Healthcare expenditures associated with diabetes mellitus in Indonesia are relatively high, with medication costs representing the largest component. Drug expenses account for the greatest proportion of overall healthcare costs in diabetes management. Therefore, the efficiency and cost-effectiveness of medication use are critical considerations. This study aimed to evaluate the cost-effectiveness of oral antidiabetic therapy in patients with type 2 diabetes mellitus at Bahteramas Hospital, Southeast Sulawesi. A descriptive study design with quantitative analysis was employed, using patient's' medical record data from 2023. Samples were selected through purposive sampling based on the following inclusion criteria: (1) patients aged 17–70 years, (2) patients receiving monotherapy with either metformin or glimepiride, and (3) patients with complete medical records. A total of 61 patients met these criteria. The results indicated that glimepiride had a lower Average Cost-Effectiveness Ratio (ACER) (IDR 18,389) compared to metformin (IDR 25,405), suggesting greater cost-efficiency. However, based on the Incremental Cost-Effectiveness Ratio (ICER), metformin had an ICER of IDR 50,070. Overall, based on ACER, glimepiride was found to be more cost-effective than metformin and may be recommended as a single oral antidiabetic therapy at Bahteramas Hospital.

Keywords: Bahteramas Hospital, cost, diabetes mellitus, effectiveness

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Analisis Efektivitas Biaya Monoterapi Antidiabetes Oral pada Pasien Diebetes Melitus di Rumah Sakit Bahteramas

Abstrak
Pengeluaran layanan kesehatan yang terkait dengan diabetes melitus di Indonesia relatif tinggi, dengan biaya obat sebagai komponen terbesar. Biaya obat menyumbang proporsi terbesar dari total biaya layanan kesehatan dalam pengelolaan diabetes. Oleh karena itu, efisiensi dan efektivitas biaya penggunaan obat menjadi pertimbangan yang sangat penting. Penelitian ini bertujuan untuk mengevaluasi efektivitas biaya terapi antidiabetik oral pada pasien diabetes melitus tipe 2 di Rumah Sakit Bahteramas, Sulawesi Tenggara. Penelitian ini menggunakan desain deskriptif dengan analisis kuantitatif, berdasarkan data rekam medis pasien tahun 2023. Sampel dipilih menggunakan teknik purposive sampling dengan kriteria inklusi sebagai berikut: (1) pasien berusia 17–70 tahun, (2) pasien yang menerima monoterapi baik metformin maupun glimepirid, dan (3) pasien dengan rekam medis lengkap. Sebanyak 61 pasien memenuhi kriteria tersebut. Hasil penelitian menunjukkan bahwa glimepirid memiliki nilai *Average Cost-Effectiveness Ratio* (ACER) yang lebih rendah (Rp18.389) dibandingkan metformin (Rp25.405), yanghal tersebut menunjukkan adanya efisiensi biaya yang lebih baik. Namun, berdasarkan *Incremental Cost-Effectiveness Ratio* (ICER), metformin memiliki nilai ICER sebesar Rp50.070. Secara keseluruhan, berdasarkan ACER, glimepirid ditemukan lebih cost-effective dibandingkan metformin dan dapat direkomendasikan sebagai terapi antidiabetik oral tunggal di Rumah Sakit Bahteramas.

Kata Kunci: biaya, diabetes melitus, efektivitas, Rumah Sakit Bahteramas

1. Introduction

Hyperglycemia is a defining feature of diabetes mellitus (DM), a disease brought on by uncontrolled metabolic processes in the body.[1] It is currently one of the diseases that threatens global health. According to the Basic Health Research (Riskesdas) statistics and information center of the Republic of Indonesia's Ministry of Health, 1.5% of the population had diabetes mellitus in 2013, while 2% of Indonesia's 15-year-old population had the disease in 2018. This suggests that from 2013 to 2018, the prevalence of DM disease increased by 0.5% in the 15-year-old population.[2]

A report from the International Diabetes Federation (IDF) in 2021 shows that the number of people with diabetes mellitus worldwide continues to increase. Indonesia is the fifth country with the largest number of people with diabetes mellitus in the world in 2021, with an estimated population of 19.5 million.[3]

Health expenditure due to diabetes mellitus (aged 20-79 years) in Indonesia is US$ 143 per person. This cost increased to US$ 171.1 for each person in 2015 and to US$ 365.2 for each person in 2019.[3,4]

The largest expenditure on health costs is drug purchases. Drug costs in Indonesia represent 40-50% of health operational costs and continue to increase every year. Research by Andayani showed that in Dr. Sardjito Hospital, Yogyakarta, the largest percentage of direct medical costs was the cost of antidiabetics (59.5%), followed by costs to overcome complications (31%). The burden of health costs in Diabetes Mellitus treatment includes drug costs. Therefore, the efficiency and cost-effectiveness of drug use are very important to be considered.[5]

One of the pharmacoeconomics methods that can easily be used is cost-effectiveness analysis (CEA) or cost-utility analysis (CUA). This method can provide an assessment of the cost-effectiveness of a treatment, thereby obtaining recommendations for the best and most cost-effective therapy for the treatment of diabetes mellitus.[6] The final results of CEA are described by the Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER) values to obtain the best cost-effective treatment alternatives.[7]

Patients with type 2 diabetes mellitus will require lifelong diabetes mellitus therapy to manage the disease and prevent complications. Variations in the utilization of therapies will lead to differences in treatment costs.[8,9] The Indonesian Ministry of Health issued a guidebook on pharmaceutical services in patients with diabetes mellitus that recommends using single antidiabetics and various combination antidiabetics. Bahteramas Hospital uses two types of single drugs, namely metformin and glimepiride. Still, the cost-effective analysis of the treatment of outpatient type 2 diabetes mellitus patients is not yet known for certain.[10]

Based on the information described previously, this study analyzed the cost-effective use of oral diabetic drugs in outpatient type 2 diabetes mellitus patients at Bahteramas Hospital, Kendari City.

2. Materials and Method

This study was an observational descriptive study with a cross-sectional research design. Data were collected retrospectively using secondary data, medical records, and outpatient treatment costs with type 2 diabetes mellitus in January-December 2023. Data collection was carried out in the medical record room of Bahteramas Hospital. The sampling technique used was purposive sampling. This study was approved by Mandala Waluya University ethical committee with approval number 117/KEP.UMW/V/2024.

2.1. Tools

This study used Microsoft Excel to process data. The data collected included patient demographics, drug use profiles, treatment cost profiles, and drug use effectiveness.

The Incremental Cost-Effectiveness Ratio (ICER) is used to determine the additional cost and Incremental effectiveness of an alternative therapy compared to a better

2.2. Data Collection

Data were collected using observational methods and a retrospective data collection flow. The inclusion criteria in this study were (1) Patients with a diagnosis of type 2 diabetes mellitus, (2) Patients who used a single oral antidiabetic therapy metformin or glimepiride, (3) Type 2 diabetes mellitus patients with complete medical record data including patient name, diagnosis, previous treatment history, patient medical history, oral diabetes medication prescribed by a doctor, and patient lab data (random blood sugar),, (4) type 2 diabetes mellitus patients aged 17-70 years, (5) outpatient type 2 diabetes mellitus patients at Bahteramas Hospital 2023.

Exclusion criteria in this study were (1) Inpatients diagnosed with type 2 diabetes mellitus at Bahteramas in 2023, (2) Patients with incomplete medical records (patient name, disease diagnosis, medications prescribed by the doctor, blood glucose data) (3)

patients with incomplete details of medication costs, (3) Type 2 diabetes mellitus patients using insulin therapy and oral antidiabetic combinations.

Based on the inclusion criteria in this study, a sample of 61 patients was obtained.

2.3. Data Analysis

The data obtained were analyzed and calculated on average using the 'Average Cost Effectiveness Ratio' (ACER) method, which is the average of the direct treatment costs of each drug therapy divided by the effectiveness of the therapy, which is the objective examination using the formula, namely:

$$\text{ACER} = \frac{Average\ cost\ of\ drug\ type\ (IDR)}{effectiveness\ (\%)}$$

The Incremental Cost-Effectiveness Ratio (ICER) is used to determine the additional cost and Incremental effectiveness of an alternative therapy compared to a better therapy. This ratio describes the additional cost required to achieve an additional effect by changing intervention A to intervention B. The formula ICER, namely :

$$\text{ICER} = \frac{Drug\ cost\ A - Drug\ cost\ B\ (IDR)}{Effectiveness\ of\ Drug\ A - Effectiveness\ of\ Drug\ B}$$

3. Result

In this study, 61 patients with type 2 diabetes mellitus who underwent outpatient therapy at Bahteramas Regional General Hospital from January to December 2023 were included according to the inclusion and exclusion criteria. Table 1 shows data on the characteristics of type 2 diabetes mellitus patients in the Bahteramas hospital outpatient department in 2023, based on gender, age, and comorbid conditions.

Table 2 presents random blood glucose levels before and after the administration of single oral antidiabetic therapy. Laboratory data on blood glucose measurements were obtained from medical records. Pre-test values were taken from the first recorded random blood glucose test documented in the records, while post-test values were obtained from the most recent recorded random blood glucose test. All data were collected from patients' medical records.

Therapeutic effectiveness of the use of oral antidiabetic drugs based on intermittent blood glucose (GDS) in patients with type 2 diabetes mellitus for glimepiride 15 patients (65.21%), and metformin (89.5%), at Bahteramas hospital in 2023 (Table 3).

Table 4 shows that the total average cost includes oral antidiabetic drug costs, other medicine costs, and laboratory scost. The average fee for glimepiride therapy (IDR 1.279.154) was lower than metformin therapy (IDR 2,273,054).

4. Discussion

The study results in Table 1 show that the percentage of patients with type 2 diabetes mellitus is greater in women than men because women experience hormonal imbalances that can lead to irregular menstrual cycles or what is commonly referred to

Table 1. Type 2 diabetes mellitus patient profile data (number of patients, n= 61)

Demographics data	Glimepiride	Metformin	p-value
Gender			
Male	6 (26.1%)	8 (21.1%)	0.410
Female	17 (73.9%)	30 (78.9%)	
Age (Years)			
28-45	1 (4.3%)	9 (23.68%)	
46-65	22 (95.7%)	26 (68.42%)	0.449
66-75	0%	3 (7.9%)	
Comorbid			
Hypertention	5 (21.75%)	7 (18.42%)	
Hyperuricemia	8 (34.78%)	11(28.9%)	
Diabetic Nephropathy	2 (8.69%)	4 (10.56%)	0.435
Cardiovasculer	4 (17.39%)	2 (5.28%)	
Hyperlipidemia	4 (17.39%)	12 (31.58%)	
Neuropathy	0 (0%)	2 (5.28%)	

* Analysis using the Mann-Whitney test

Table 2. Intermittent blood glucose before and after single oral antidiabetic administration

Intermittent blood Glucose value	Glimepiride		Metformin	
	Pre	Post	Pre	Post
71-199	0 (0%)	15(65.21%)	0 (0%)	34 (89.5%)
>200	23 (100%)	8(34.79%)	23 (100%)	4 (10.5%)

Blood glucose test results were obtained from the patient's laboratory data recorded during their first and last hospital visits

as polycystic ovary syndrome.[11,12] Women who have experienced gestational DM (DMG) during pregnancy can also increase the risk of type 2 DM by 3-5% in the future.[13,14] Women with a history of gestational diabetes mellitus (GDM) have an increased risk of developing type 2 diabetes mellitus later in life, which is closely associated with complex and persistent pathophysiological mechanisms.

During pregnancy, levels of diabetogenic hormones such as human placental lactogen, progesterone, and cortisol increase, leading to insulin resistance. In women with GDM, this insulin resistance does not fully resolve after delivery, thereby contributing to chronic hyperglycemia. In addition, GDM is characterized by pancreatic beta-cell dysfunction, specifically the inability of beta cells to compensate for the increased insulin demand during pregnancy; this dysfunction may persist postpartum and lead to a progressive decline in insulin secretion.[15]

Furthermore, exposure to hyperglycemia during pregnancy can result in glucotoxicity, while elevated levels of free fatty acids induce lipotoxicity, both of which contribute to pancreatic beta-cell damage. This condition is further exacerbated by chronic low-grade inflammation, characterized by increased levels of proinflammatory cytokines such as TNF-α and IL-6, which worsen insulin resistance. Additionally, dysregulation of adipokines, including decreased adiponectin and increased leptin levels, contributes to impaired glucose metabolism and reduced insulin sensitivity.[16,17] The combination of these mechanisms leads to progressive disruption of glucose homeostasis, resulting in an estimated 3–5% annual risk of progression to T2DM among women with a history of GDM.[18]

The results of this study are in line with research conducted by Permatasari (2019) at Dr. Moewardi Hospital in 2018, which found that the percentage of women affected by type 2 DM was higher (66%) than that of men (34%).[19]

According to statistical analysis (Table 1), - no significant difference in gender, age, and comorbidities (P>0.05, Mann-Whitney test).Based on the age characteristics of patients (Table 1), the results showed that type 2 DM patients aged 44-65 years had a higher percentage (95.7% of glimepiride and 68.2% of metformin) than other age groups. Based on age, in this study, patients with diabetes mellitus were higher over the age of 45 because individuals over 45 years old have a higher risk of damaging the endocrine system compared to those under 45 years of age. Other factors, due to a lack of physical activity, increased body weight, and muscle mass, will decrease with age, causing dysfunction of the pancreas, so that it increases blood sugar levels due to the absence of insulin production. Another cause is due to a decrease in the function of the body's organ systems, which causes uncontrolled blood glucose levels, resulting in diabetes mellitus.[20]

Another study showed that patients over 45 years of age will experience aging in a transitional stage called the clinical stage, which includes a decline in all body system functions, including the immune, metabolic, endocrine, sexual and reproductive, cardiovascular, gastrointestinal, muscle, and nervous systems. Physical strength and defense mechanisms tend to decline with age, and the body is no longer able to cope with unhealthy lifestyle choices, leading to diabetes. By 2030, across the world, it is estimated that the largest number of individuals with diabetes mellitus will be between the ages of 45-64 Years.[21]

Table 3. Overview of Average Direct Medical Cost

Type of Cost	Cost Average	
	Glimepiride	Metformin
Patients	23	38
Oral Antidiabetes drug cost	IDR 18.320	IDR 33.798
Cost of other drugs	IDR 19.143	IDR 45.364
Laboratory Costs*	IDR 3.800.000	IDR 6.740.000
Total Cost Average	IDR 1.279.154	IDR 2.273.054

Source: Data on Laboratory Fee Details based on Regional Regulations and Data Bahteramas Hospital, Southeast Sulawesi in 2023
* This examination fee is based on the 2023 annual examination costs of patients treated with metformin and glimepiride

Table 4. Average cost-effectiveness ratio (ACER) calculation

Treatment of antidiabetics	Number of Patients	Patients with a blood glucose level ≤ 200 mg/dl	Average Total Cost	Effectiveness	ACER
Glimepiride	23 (37.70%)	16	IDR 1.279.154	69.56%	IDR 18,389
Metformin	38 (62.30%)	34	IDR 2.273.054	89.47%	IDR 25,405

Source: Data were obtained from the medical records of patients diagnosed with diabetes mellitus in 2023.

The most common comorbidity found in patients with DM taking glimepiride was hyperuricemia (34.78%), while patients with DM taking metformin had dyslipidemia (31.58%). Dyslipidemia is a condition that shows an increase in blood fat levels (Triglycerides >250 mg/dl). There is an association between elevated plasma insulin and low HDL (< 35 mg/dl), which is often found in diabetic patients.[22]

Hyperuricemia or overproduction of uric acid can lead to elevated uric acid levels, especially since the normal limit is less than 7 mg/dL in men and 6 mg/dL in women. In patients with type 2 diabetes, hyperuricemia is associated with insulin resistance and increased proinflammatory cytokine activity. [23]

Based on Table 2, type 2 diabetes mellitus patients were mostly prescribed metformin (62.30%) compared to glimepiride (37.70%). The results of this study are in line with research by Indarto et al. (2023) showing that metformin is a drug that lowers blood glucose levels, works by reducing the amount of glucose produced by the liver, and increases the body's response to insulin so that it helps the body to regulate blood glucose levels.[24,25]

Based on Table 3, the average cost of metformin therapy is 2,273,054, which is greater than that of metformin therapy of 1,279,154. Direct medical costs are costs that are directly related to the process of treatment, detection, and prevention of a disease. In this study, direct medical fees consisted of antidiabetic fees, other drug fees, and laboratory fees. Antidiabetic costs are costs used to pay for oral antidiabetic drugs, namely glimepiride and metformin.

The cost is calculated based on the unit price of the antidiabetics used by the patient. Other drug costs are costs used to treat the patient's comorbidities, which are calculated based on the unit price of the comorbidity drug. Laboratory costs are the costs of examinations that can help determine the diagnosis of the disease, calculated based on the price of one examination.

Cost-effectiveness analysis aims to compare health outcomes and costs and is used to evaluate alternative treatments in terms of a hospital's perspective. The cost-effectiveness analysis was calculated using the average cost-effectiveness ratio (ACER) formula and the Incremental Cost Effectiveness Ratio (ICER) calculation based on the current blood sugar (GDS). The parameter used to measure the effectiveness of therapy in this study was the level of Blood Glucose (GDS), 80 - 200 mg/dl, at the next patient visit at the outpatient clinic. The effectiveness of therapy was measured by the percentage of patients who had achieved the GDS target divided by the total number of patients who were treated with the same antidiabetic group.

Based on Table 4, the highest ACER value was shown in metformin therapy of IDR 25,450 compared to glimepiride therapy of IDR 18,389. The results of this study are in line with Meliawati's (2023) research, which shows that metformin is the most cost-effective (with a lower ACER value) compared to glimepiride. A drug therapy is declared the most cost-effective if it has a lower or smaller ACER value compared to the ACER value in other drug therapy groups.[26] Since metformin therapy is more costly and effective than glimepiride in this study, the ICER must be determined. ICER value is determined by calculating the average total cost of glimepiride minus the average total cost of metformin divided by the effectiveness of glimepiride minus the effectiveness of metformin.

Table 5 shows that the ICER value of glimepiride therapy can save costs, which is worth IDR 50.070. Glimepiride belongs to the sulfonylurea group, which inhibits the increase in blood sugar through the mechanism of increasing insulin secretion. Based

Table 5. Calculation of Incremental Cost-Effectiveness Ratio (ICER)

Treatment of antidiabetics	Cost	Effectiveness	ICER
Glimepiride	IDR -996,900	19,91	IDR -- 50.070
Metformin			

Source: Data on Bahteramas Hospital in South East Sulawesi in 2023

on the ICER value, glimepiride is the best alternative therapy because it can reduce treatment costs. If the ICER value shows a negative value, it shows that the drug is more effective. The results of this study are in line with Widya's research (2021). [27]

The ICER calculation can be done if an intervention costs more but its effectiveness is high, or the cost of an intervention is lower but its effectiveness is low. The ICER value is used to determine the increase in therapy costs with the addition or replacement of treatment that may increase costs, but provide a better drug effect, used to determine the additional cost for each unit of effectiveness of a therapy.[28]

5. Conclusion

The results of the research conducted can be concluded as follows: the most effective single oral antidiabetic therapy, with an effectiveness of 89.47%, is declared more cost-effective based on the highest Average Cost Effectiveness Ratio (ACER) value, which is shown by metformin therapy at around IDR 25,450. The most economical oral antidiabetic treatment is glimepiride therapy with an Incremental Cost-Effectiveness Ratio (ICER) value of Rp-49,919, which can save costs by increasing the effectiveness of therapy.

Conflict of Interest

None to declare.

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