Analysis of Antidiabetic Drug Utilization at Cilacap Regional General Hospital in 2022 Using ATC/DDD and DU90% Methods

Irma Nur Oktavina[1],[*], Sunarti[2], Galih Samodra[3]

Pharmacy Study Program, Faculty of Health Sciences, Universitas Harapan Bangsa, Purwokerto
[1]vinairma03@gmail.com, [2]sunarti@uhb.ac.id, [3]galihsamodra@uhb.ac.id

ABSTRACT

Diabetes mellitus is a chronic disease caused by metabolic disorders characterized by elevated blood glucose levels or hyperglycemia. The aim of diabetes mellitus treatment is to control blood glucose levels within the normal range, eliminate accompanying clinical symptoms, and reduce the risk of acute complications. To achieve therapeutic goals, pharmacological therapy can be administered using antidiabetic drugs. This research is an observational study involving retrospective data collection of outpatients with type 2 diabetes mellitus who used antidiabetic drugs. The prescribed antidiabetic drugs were then analyzed using the Anatomical Therapeutic Chemical (ATC) and Defined Daily Dose (DDD) methods. Data on antidiabetic drugs were collected and entered into the Microsoft Excel program to calculate the DDD/1000 KPRJ value and the 90% Du segment. The results showed that there were 7 antidiabetic drugs used, namely glimepiride, gliquidone, gliclazide, metformin, acarbose, vildagliptin, and pioglitazone, with glimepiride having the highest DDD value of 445.92 DDD/1000 KPRJ and gliquidone having the lowest DDD value of 128.70 DDD/1000 KPRJ. Meanwhile, glimepiride and metformin were the antidiabetic drugs included in the 90% Du segment.

Keywords: Antidiabetics, Outpatients, Type 2 Diabetes Mellitus, ATC/DDD and DU 90%

1. INTRODUCTION

Diabetes mellitus is a chronic condition caused by metabolic abnormalities characterized by high blood glucose levels or hyperglycemia (Ford et al., 2021). Increased blood glucose levels or hyperglycemia can cause damage to various body systems, particularly leading to disorders of the heart, vision, skin, kidneys, and causing wounds that are difficult to heal (Alfiani et al., 2017). If blood sugar levels continue to rise without proper treatment, it can lead to complications. Chronic complications frequently experienced by individuals with diabetes mellitus include microvascular and macrovascular complications (Isnaini & Ratnasari, 2018).

In 2021, the number of individuals diagnosed with diabetes mellitus reached 537 million people and is expected to continue to increase to 643 million by 2030 and 783 million by 2045 (Ford et al., 2021). Indonesia ranks 5th out of 10 countries with the highest number of diabetics, with 19.5 million people (Ford et al., 2021). With the increasing cases, diabetes mellitus management is needed. Individuals with type 2 diabetes mellitus are treated using oral hypoglycemic drugs and lifestyle changes (Patil et al., 2017). To achieve therapeutic targets, pharmacological therapy using

Irma Nur Oktavina.
Tel.: 0895384049481
Email: vinairma03@gmail.com

antidiabetic drugs is intended to control diabetes mellitus management with the aim of achieving appropriate blood glucose levels, with an HbA1c level of less than 7%.

The use of antidiabetic drugs plays an important role in achieving successful therapy in patients. Analysis of drug use is carried out using the WHO ATC and DDD Assignment Guidelines for 2018, where the Anatomical Therapeutic Chemical (ATC) codes are classified. Information on ATC classification can be accessed through the website http://www.whocc.no/atc_ddd_index/. The analysis is performed quantitatively using the ATC/DDD method. The ATC/DDD system aims as a research tool to evaluate drug use by identifying whether drugs are being used excessively or not, so as to improve the quality of drug use (Siahaan, 2018).

Previous research conducted by Nurshalati Tahar et al. (2020) on "Evaluation of oral antidiabetic use in patients with type 2 diabetes mellitus using the ATC/DDD and DU 90% methods" at Hikmah Hospital Makassar found that the most widely used oral antidiabetic was metformin, with a total of 1020 units and a dose per unit of 500 mg, with total use reaching 601,000 mg or 99.56% of the total. Gliclazide was used in 48 units with a dose per unit of 60 mg, total dose reaching 2520 mg or 0.41%. Meanwhile, glimepiride was used in 41 units with a dose per unit of 2 mg, with total use of 82 mg or 0.01%. Of the three types of oral antidiabetics, metformin and its use reached the DU 90% segment, in accordance with the WHO DDD standard which sets the minimum use of oral antidiabetic metformin at 2000 mg/day.

The application of the ATC/DDD method can be combined with the concept of DU 90% (drug utilization) to identify the most dominant drug use segment in the analysis of drug use in a population group (Patel et al., 2016). The purpose of DU 90% is to categorize information about drug use to allow for an assessment of the quality of drug use. Data from DU 90% can be expressed in quantitative or qualitative formats.

Based on this background, the researchers are interested in conducting a study on the analysis of antidiabetic drug use in patients with type 2 diabetes who underwent treatment at Cilacap Regional Public Hospital in 2022 by applying the ATC/DDD and DU 90% methods.

This study is intended to provide an understanding of the patterns of antidiabetic drug use in the management of type 2 diabetes mellitus based on the ATC/DDD and DU 90% method approaches.

2. RESEARCH METHODOLOGY

2.1 Research Type and Design
This study used a cross-sectional method with retrospective data collection.

2.2 Research Location and Time
The location of this research coincides with Cilacap Regional Public Hospital which was carried out according to the research schedule, namely August 2023. The Ethics Committee of Universitas Harapan Bangsa approved this investigation with the number B.LPPM-UHB/2246/08/2023.

2.3 Population and Sample
The population in this study was taken from the number of patients with type 2 DM who reside in the working area of Cilacap Regional Public Hospital, totaling 125 patients using the total sampling technique. The sample in this study were patients who used antidiabetic drugs that met the inclusion criteria.

2.4 Research Instruments
The instrument used in this study was medical records, which are documents that include information about the patient's identity, diagnosis, and medical history (Wati & Nuraini, 2019). Patient medical records were obtained based on the specified time period. Medical records were adjusted according to the inclusion and exclusion criteria determined for observation at Cilacap Regional Public Hospital.

2.5 Data Collection Techniques
The data collection technique used was retrospective. Data on antidiabetic use were collected from outpatient medical records at the Pharmacy unit of Cilacap Regional Public Hospital by taking information on the number of outpatient visits during 2022. Furthermore, patient data were recorded including the type of antidiabetic, name of antidiabetic, amount of antidiabetic, dose, dosage form, and dosage strength.

84

2.6 Data Analysis

The data analysis process involved editing the data to verify its suitability for research needs. The collected antidiabetic drug data were then analyzed using the Anatomical Therapeutic Chemical (ATC) and Defined Daily Dose (DDD) methods. The drug data were then entered into the Microsoft Excel program to calculate the DDD/1000 KPRJ value using the formula:

$$\text{DDD/1000 KPRJ} = \frac{Total\ DDD\ (1\ tahun)}{Total\ KPRJ} \times 1000$$

The next step was to arrange the drug use data in DDD units from the most to the least used. In addition, calculations were performed to determine the drugs included in the DU 90% segment.

3. RESULTS AND DISCUSSION

Characteristics of Patients Based on Gender

Tabel 1. Number of Patients Based on Gender at Cilacap Regional Public Hospital 2022

Gender	Number	Percentage Results%
Laki-Laki	53	42.4
Perempuan	72	57.6

Based on table 1, there were 125 patients who received antidiabetic drugs, with 53 male patients (42.4%) and 72 female patients (57.6%), indicating that the most patients receiving antidiabetic drugs were female. This is in line with the research by Arania et al. (2021) which showed that the prevalence of diabetes was higher in women than in men (27.8%). The majority of respondents who suffered from diabetes mellitus were elderly (47.6%). This study is in accordance with previous research which showed that most patients with type 2 diabetes in the working area of the Mulyorejo Health Center, Surabaya City were women, reaching 56.0% (Nurayati & Adriani, 2017). This study is also in line with the research by Tresnowati et al. (2022). The study showed that out of a total of 30 people with type 2 diabetes, 18 people (60%) were women, while only 12 people (40%) were men.

Based on the analysis in table 1, it shows that women received the most antidiabetic therapy, namely 72 people (57.6%), because women have a higher tendency due to the hormones estrogen and progesterone which can increase the body's insulin response.

Characteristics of Patients Based on Age

Table 2. Number of Patients Based on Age at Cilacap Regional Public Hospita 2022

Age Range	Number	Percentage Results %
25-44 years	12	9.6
45-64 years	88	70.4
>65 years	25	20

Based on table 2, the age group that received the most antidiabetic therapy at Cilacap Regional General Hospital in 2022 was those aged between 45 and 64 years. Above the age of 40, the risk of developing type 2 diabetes increases with age, especially in individuals over 40 who have a less physically active lifestyle, lose muscle mass, and gain weight. This is in line with the research by Arania et al. (2021). Most of the respondents who suffered from diabetes mellitus were elderly (47.6%). This study is also in line with the research by Tresnowati et al. (2022) which showed that 21 respondents, or as many as 70%, experienced diabetes mellitus between the ages of 30 and 59 years. However, the majority of people with type 2 diabetes are over 40 years old. From the results obtained, patients over the age of 40 are at risk of suffering from diabetes mellitus because at that age there is an aging process and glucose intolerance which can lead to a decrease in pancreatic beta cells that produce insulin.

Profile of Antidiabetic Drug Use Based on ATC/DDD Classification

Table 3. Types of Antidiabetic Groups Used

85

Antidiabetic Group	DDD Code	Drug
Sulfonylureas	A10BB12	Glimepiride
	A10BB08	Gliquidone
	A10BB09	Gliclazide
Biguanides	A10BA02	Metformin
Alpha glucosidase	A10BF01	Acarbose
DPP-4	A10BH02	Vildagliptin
Thiazolidines	A10BG04	Pioglitazone

The results showed that there were five groups of antidiabetic drugs used at Cilacap Regional Public Hospital in 2022, namely sulfonylureas, biguanides, alpha-glucosidase inhibitors, DPP-4, and thiazolidinediones. The obtained data were then processed to calculate the total quantity of use according to the guidelines set by WHO. Antidiabetic drugs are classified based on their respective ATC codes and groups. The grouping of antidiabetic drugs is sourced from WHO which can be accessed through the website http://www.whocc.no/atc_ddd_index/. All the antidiabetic drugs used in this study have ATC codes indicating that the prescribed antidiabetic drugs are registered in the ATC system and are in accordance with the guidelines from the WHO Collaborating Centre.

Quantity of Antidiabetic Drug Use in DDD Units

Table 4. Quantity of Antidiabetic Drug Use in Outpatients in DDD/1000 KPRJ

Drug Code	Drug	Usage (gram)	DDD WHO (gram)	Total DDD	DDD /1000 KPRJ
A10BB12	Glimepiride	0.107	2	92.75	445.92
A10BB08	Gliquidone	0.121	0.006	26.77	128.70
A10BB09	Gliclazide	124	2	92.75	445.91
A10BA02	Metformin	0.3	0.006	29.25	140.61
A10BF01	Acarbose	7.65	0.3	90.00	432.69
A10BH02	Vildagliptin	0.95	0.1	88.25	424.27
A10BG04	Pioglitazone	0.12	0.5	56.62	202.22

From the results of DDD calculations based on the formula:

$$\text{DDD/1000 KPRJ} = \frac{DDD\ Total\ (1\ year)}{KPRJ\ Total} \times 1000$$

KPRJ: Outpatient Visits

For the use of antidiabetic drugs with the highest DDD/1000 KPRJ value, namely glimepiride with a value of 445.92 DDD/1000 KPRJ, then followed by the second highest use, namely metformin with 445.91 DDD/1000 KPRJ. And for the least use, namely gliquidone at 128.70 DDD/1000 KPRJ.

The highest use of antidiabetic DDD/1000 KPRJ was glimepiride with a total use of 445.92 DDD/1000 KPRJ. Glimepiride is a type of sulfonylurea drug that has a very strong antihyperglycemic effect. Its maximum daily dose is 8 mg/day and can cause a decrease in HbA1c levels by 15-40%. Glimepiride works by stimulating insulin release through ATP-dependent potassium channels (KATP) in pancreatic beta cells (Madania et al., 2022). This sulfonylurea interacts with the 65-kD protein on beta cells, and can increase insulin secretion in the early and late phases. The mechanism of action of the sulfonylurea group is to stimulate pancreatic beta cells to increase insulin production.

Metformin ranks second in the use of antidiabetics with the highest DDD/1000 KPRJ, which is 445.91. Metformin is a drug that belongs to the biguanide group, which functions to increase the body's sensitivity to insulin. This drug is effective in lowering blood glucose levels without causing hypoglycemia or significant weight gain, and has minimal side effects (Flory & Lipska, 2019). The strong impact of metformin in reducing glucose levels is a result of a series of complex pharmacological interactions and possibly achieving this result through a combination of drug therapy and lifestyle changes. Both of these factors are considered important in the management of type 2 diabetes. The Biguanide group has a lower rate of side effects compared to other antidiabetic groups. The main advantage of the Biguanide group is that they do not cause weight gain, so they are often recommended for individuals with diabetes who are overweight. The use of the Biguanide group, namely Metformin, can reduce cholesterol and triglycerides.

This is in accordance with the WHO DDD standard, where the minimum dose of metformin use is 2000 mg per day, and the drug is given at least 3 times a day with a dose per drug unit of 500 mg. Therefore, the maximum

86

dose that can be given to patients per day is 1500 mg, which means the dose administered to patients does not exceed the maximum dose limit specified. Thus, this can be considered in accordance with the WHO ATC/DDD standard for 2019.

The quantity of antidiabetic drug use based on the ATC/DDD method shows that the use of glimepiride and metformin had the highest DDD/1000 patient values in 2022. Proper use of drugs in patients with type 2 diabetes mellitus can prevent complications. Complications that can occur include microvascular and macrovascular complications (Isnaini, 2018). Based on the results obtained, the DDD/1000 patient value did not exceed the DDD standard according to WHO. DDD results can provide an overview of antidiabetic consumption over a certain period of time, with appropriate drug administration that can control normal glucose levels so as to reduce the risk of acute complications.

Quantity of Antidiabetic Drug Use in DDD Units and DU 90%

Tabel 2. Quantity of Antidiabetic Drug Use in DDD Units and DU 90%

Drug Code	Drug	DDD Total	DDD /1000 KPRJ	% Usage	DU Segment
A10B B12	Glimepiride	92.75	445.92	20	90%
A10B B08	Gliquidone	26.77	128.70	6	10%
A10B B09	Gliclazide	92.75	445.91	20	90%
A10B A02	Metformin	29.25	140.61	6	10%
A10BF 01	Acarbose	90.00	432.69	19	10%
A10B H02	Vildagliptin	88.25	424.27	19	10%
A10B G04	Pioglitazone	56.62	202.22	9	10%
			2220.32	100	

It is known that the drugs included in the DU 90% segment of antidiabetics, from the most used to the least used, are glimepiride, metformin, acarbose, vildagliptin, pioglitazone, gliclazide, and gliquidone. Metformin is included in the DU 90% segment, indicating that its use is in accordance with the indication, namely for patients with type 2 diabetes mellitus. The chosen drug is in accordance with the patient's condition, and has a therapeutic effect that is in accordance with the characteristics of the disease, namely type 2 DM. The dosage is also appropriate, where metformin is the main therapy in the treatment of type 2 diabetes, and the dose given (500 mg, 3 times a day) does not exceed the recommended maximum daily dose (2000 mg) according to the WHO ATC DDD therapeutic index 2019.

Information on the use of antidiabetics in the DU 90% segment can be utilized in the preparation of essential drug lists for planning purposes (Dey et al., 2016). In addition, data on the use of antidiabetics in the DU 90% segment is also utilized in the preparation of hospital formularies. Drugs that are included in the DU 90% segment should be included in the hospital formulary.

CONCLUSION

The results showed that there were seven types of antidiabetic drugs used, namely glimepiride, gliquidone, gliclazide, metformin, acarbose, vildagliptin, and pioglitazone. Glimepiride had the highest DDD value, reaching 445.92 DDD/1000 KPRJ, while the antidiabetic drugs included in the DU 90% segment were glimepiride and metformin.

SUGGESTIONS

Future researchers are expected to be able to conduct similar research in different locations to compare the quantity of antidiabetics in other regions, so as to add references in the selection of antidiabetics. In addition, qualitative studies on the rationality of antidiabetic use are needed, especially those included in the DU 90% segment.

REFERENCES

Alfiani, N., Yulifah, R., & Sutriningsih, A. (2017). Hubungan Pengetahuan Diabetes Mellitus dengan Gaya Hidup Pasien Diabetes Mellitus di Rumah Sakit tingkat II dr.Soepraoen Malang. *Nursing News*, 2(2), 390–402. doi: https://doi.org/10.33366/nn.v2i2.485

Arania, R., Triwahyuni, T., Esfandiari, F., &

Nugraha, F. R. (2021). Hubungan Antara Usia, Jenis Kelamin, Dan Tingkat Pendidikan Dengan Kejadian Diabetes Mellitus Di Klinik Mardi Waluyo Lampung Tengah. *Jurnal Medika Malahayati*, *5*(3), 146–153. https://doi.org/10.33024/jmm.v5i3.4200

Desy Natalia Siahaan, N. F. P. H. (2018). Evaluasi Penggunaan Antibiotik Secara Kualitas Dan Kuantitas Disertai Tingkat Resistensi Dan Pola Kuman Pada Pasien Anak Rawat Inap RSUP H. Adam Malik Medan Peride Oktober – Desember 2016. *Jurnal Stikna*, *02*(October), 1–6.

Dey, D., De, A., Yadav, H. R., Guin, P. S., Choudhury, A. R., Kole, N., & Biswas, B. (2016). An Oxido-Bridged Diiron(II) Complex as Functional Model of Catechol Dioxygenase. *ChemistrySelect*, *1*(9), 1910–1916. https://doi.org/10.1002/slct.201600575

Flory, J., & Lipska, K. (2019). Metformin in 2019. *JAMA - Journal of the American Medical Association*, *321*(19), 1926–1927. https://doi.org/10.1001/jama.2019.3805

Ford, C. N., Do, W. L., Weber, M. B., Narayan, K. M. V., Ranjani, H., & Anjana, R. M. (2021). Moderate-to-vigorous physical activity changes in a diabetes prevention intervention randomized trial among South Asians with prediabetes – The D-CLIP trial. *Diabetes Research and Clinical Practice*, *174*, 108727. https://doi.org/10.1016/j.diabres.2021.10 8727

Isnaini, N., & Ratnasari, R. (2018). Faktor risiko mempengaruhi kejadian Diabetes mellitus tipe dua. *Jurnal Kebidanan Dan Keperawatan Aisyiyah*, *14*(1), 59–68. https://doi.org/10.31101/jkk.550

Madania*, Nur Rasdianah, Meli Cahayani Dalu, M. P., & Jurusan. (2022). Volume 5, Nomor 1, Februari 2022. *JMTS: Jurnal Mitra Teknik Sipil*, *5*(1), i. https://doi.org/10.24912/jmts.v5i1.17649

Nurayati, L., & Adriani, M. (2017). Hubungan Aktifitas Fisik dengan Kadar Gula Darah Puasa Penderita Diabetes Melitus Tipe 2. *Amerta Nutrition*, *1*(2), 80. https://doi.org/10.20473/amnt.v1i2.6229

Patel, S., Shah, A., Shah, R., & Buch, J. (2016). Evaluation of drug utilization pattern of antimicrobials using ATC/DDD system in intensive care unit of a tertiary-care teaching hospital. *International Journal of Medical Science and Public Health*, *5*(1), 80. https://doi.org/10.5455/ijmsph.2016.0811 2015189

Patil, S. S., Mehta, M., Thakare, V., & Shende, S. (2017). Role of insulin in management of type 2 diabetes mellitus Review Article Role of insulin in management of type 2 diabetes mellitus. *International Journal of Research in Medical Sciences*, *5*(May), 2282–2292. https://doi.org/10.18203/2320-6012.ijrms20172422

Tresnowati, G. I., Kusuma, I. Y., & Sunarti. (2022). Monitoring Kepatuhan Pengobatan Pasien Diabetes Melitus Tipe 2 dengan Media Adherence Pill Box Unit Daily Dose. *Jurnal Farmasi Indonesia*, *14*(2), 97–104.

Wati, T. G., & Nuraini, N. (2019). Analisis Kejadian Missfile Berkas Rekam Medis Rawat Jalan di Puskesmas Bangsalsari. *J-REMI : Jurnal Rekam Medik Dan Informasi Kesehatan*, *1*(1), 23–30. https://doi.org/10.25047/j-remi.v1i1.1932

88