## **BUKTI KORESPONDENSI**

## Jurnal Nasional Terakreditasi Peringkat 3 dan 4

Judul Artikel : Evaluation of Anti-diabetic Drugs using ATC/DDD and DU90%

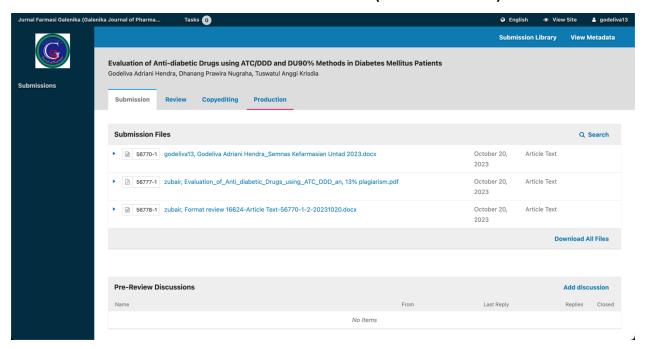
Methods in Diabetes Mellitus Patients

Jurnal : Galenika Journal of Pharmacy Vol. 10, No. 1, Maret 2024.

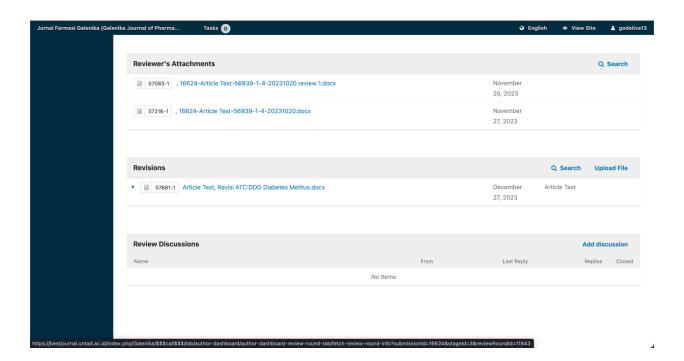
Penulis :

No.	Perihal	Tanggal
1.	Bukti konfirmasi submit artikel	20 Oktober 2023
2.	Pemberitahuan revisi pertama	20 November 2023
3.	Submit revisi	27 Desember 2023
4.	Pemberitahuan revisi kedua	5 Januari 2024
5.	Submit revisi	31 Januari 2024
6.	Pemberitahuan revisi ketiga	9 Februari 2024
7.	Submit revisi	15 Februari 2024
8.	Accept Submission	23 Februari 2024
9.	Copyediting	2 Maret 2024
10.	Publish artikel	4 Maret 2024

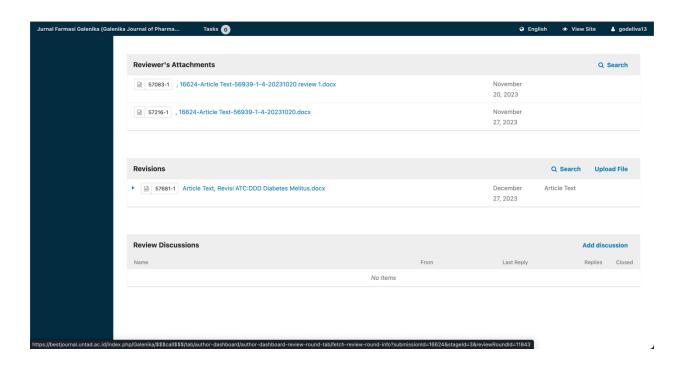
## **Bukti Konfirmasi Submit Artikel (20 Oktober 2023)**



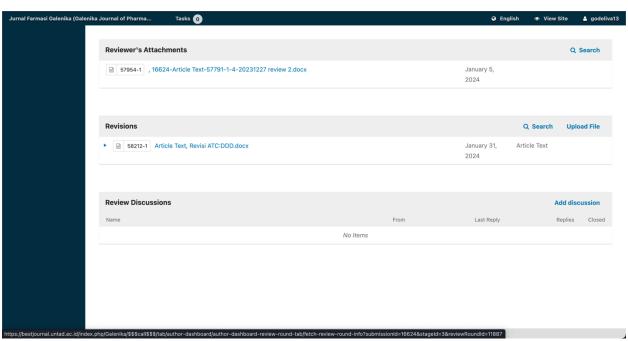
## Pemberitahuan Revisi Pertama (20 November 2023)



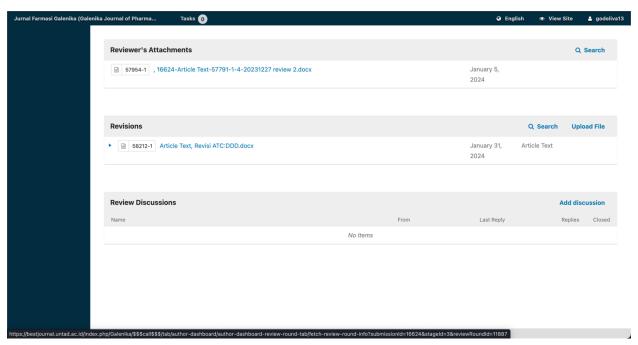
## Submit Revisi (27 Desember 2023)



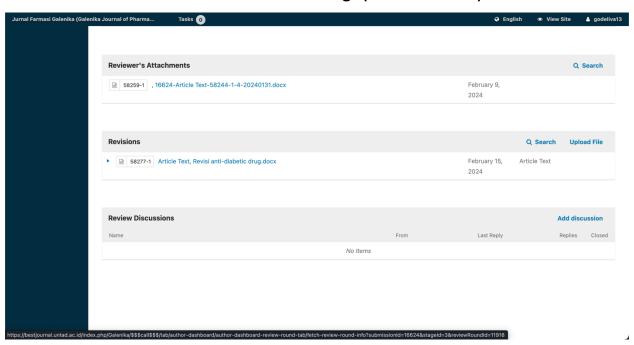
## Pemberitahuan Revisi Kedua (5 Januari 2024)



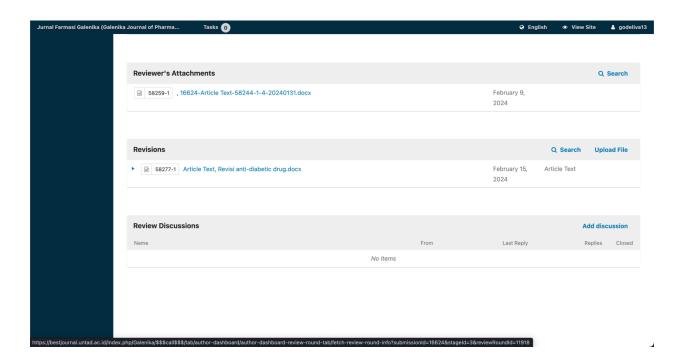
## Submit Revisi (31 Januari 2024)



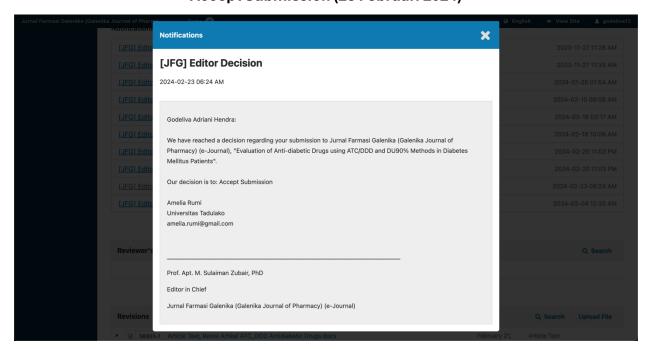
## Pemberitahuan Revisi Ketiga (9 Februari 2024)



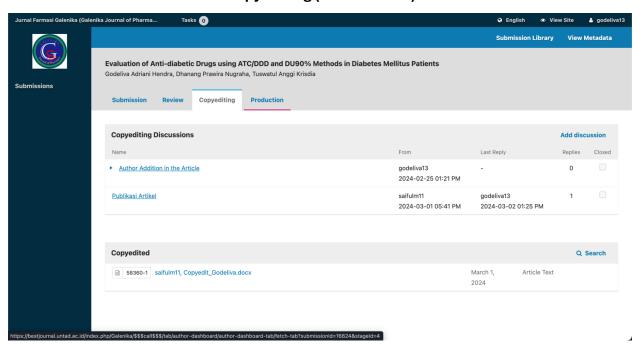
## Submit Revisi (15 Februari 2024)



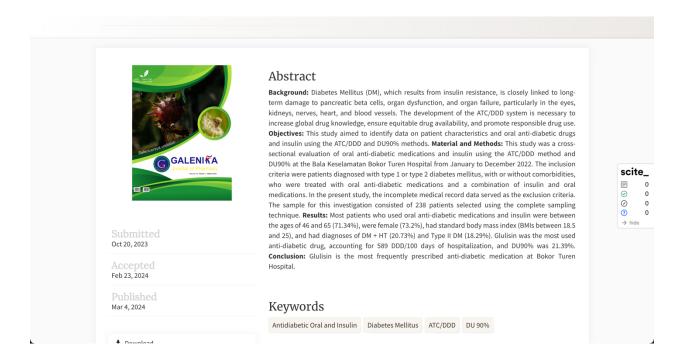
## Accept Submission (23 Februari 2024)



### Copyediting (2 Maret 2024)



## Publish artikel (4 Maret 2024)





### Jurusan Farmasi Fakultas Matematika dan Ilmu Pengetahuan Alam Universitas Tadulako

Jurnal Farmasi Galenika (Galenika Journal of Pharmacy) (e-Journal)

ISSN 2442-7284 (print) || ISSN 2442-8744 (online)

Jl. Soekarno Hatta km. 9, Palu, Sulawesi Tengah, Indonesia. Telp/Fax : (0451) 422611 Homepage Journal: https://bestjournal.untad.ac.id/index.php/Galenika/

## **SURAT KETERANGAN**

Nomor: 6/JFG/III/2024

Kepada Yth.

Godeliva Adriani Hendra, Dhanang Prawira Nugraha, Tuswatul Anggi Krisdia

Program Studi Farmasi, Fakultas Ilmu Kesehatan, Universitas Ma Chung, Malang, Indonesia.

Berdasarkan proses penelaahan artikel yang telah dilakukan oleh tim Reviewer, maka artikel saudara yang berjudul:

## Evaluation of Anti-diabetic Drugs using ATC/DDD and DU90% Methods in Diabetes Mellitus Patients

dinyatakan diterima (accepted) untuk diterbitkan dalam Jurnal Farmasi Galenika (Galenika Journal of Pharmacy) (e-Journal) Volume 10, Nomor 1, Maret 2024

Demikian pengumuman ini dibuat, atas perhatiannya diucapkan terima kasih.

Palu, 1 Maret 2024 Pimpinan Redaksi,



Prof. apt. Muhammad Sulaiman Zubair, M.Si., Ph.D.



## Jurusan Farmasi Fakultas Matematika dan Ilmu Pengetahuan Alam Universitas Tadulako

Jurnal Farmasi Galenika (Galenika Journal of Pharmacy) (e-Journal)

ISSN 2442-7284 (print) || ISSN 2442-8744 (online)

Jl. Soekarno Hatta km. 9, Palu, Sulawesi Tengah, Indonesia. Telp/Fax: (0451) 422611

Homepage Journal: https://bestjournal.untad.ac.id/index.php/Galenika/

## Lampiran:

Untuk proses berikutnya, kami memohon kerjasamanya untuk melengkapi beberapa hal di bawah ini:

- Kesediaan untuk merevisi artikel, jika ada catatan dari Reviewer artikel (keterlambatan mengirimkan revisi berakibat keterlambatan pada publikasi). Penulis dimungkinkan juga, apabila ingin memperbaiki atau menambahkan kekurangan bagian artikel yang mungkin luput dari penelaahan editor maupun reviewer, dapat mengirimkan naskah perbaikannya ke email: jurnalgalenika.farmasiuntad@gmail.com.
- Kesediaan untuk memberi biaya kontribusi sebesar Rp. 500.000,- (lima ratus ribu rupiah). Semua biaya dikirim ke rekening **BNI 0155360681 a.n M. Sulaiman Zubair**. Bukti transfer dikirim melalui email: <u>jurnalgalenika.farmasiuntad@gmail.com</u> dengan cara membalas (*reply*) dari email LoA yang dikirimkan.

## Evaluation of Anti-diabetic Drugs using ATC/DDD and DU90% Methods in Diabetes Mellitus Patients

3 4 5

1

2

#### **ABSTRACT**

6 7 8

9

10 11

12

13 14

15

16

17

18

19

20 21 Background: Diabetes Mellitus (DM), which results from insulin resistance, is closely linked to long-term damage to pancreatic beta cells, organ dysfunction, and organ failure, particularly in the eyes, kidneys, nerves, heart, and blood vessels. The development of the ATC/DDD system is necessary to increase global drug knowledge, ensure equitable drug availability, and promote responsible drug use. Objectives: This study aimed to identify data on patient characteristics and oral anti-diabetic drugs and insulin using the ATC/DDD and DU90% methods. Material and Methods: This study is a cross-sectional evaluation of oral anti-diabetic medications and insulin using the ATC/DDD method and DU90% at the Bala Keselamatan Bokor Turen Hospital from January to December 2022. The inclusion criteria were individuals diagnosed with type 1 or type 2 diabetes mellitus, with or without comorbidities, who were treated with oral anti-diabetic medications and a combination of insulin and oral medications. In the present study, the incomplete medical record data served as the exclusion criteria. The sample for this investigation consisted of 238 patients selected using the complete sampling technique. Results: The majority of patients who used oral anti-diabetic medications and insulin were between the ages of 46 and 65 (71.34%), were female (73.2%), had standard body mass indices (BMIs between 18.5 and 25), and had diagnoses of DM + HT (20.73%) and Type II DM (18.29%). Glulisin was the most commonly used anti-diabetic drug, accounting for 589 DDD/100 days of hospitalization, and DU90% was 21.39%. Conclusion: Glulisin is the most frequently prescribed anti-diabetic medication at Bokor Turen Hospital.

Keywords: Antidiabetic Oral and Insulin; Diabetes Mellitus; ATC/DDD; DU 90%

26 27

#### **ABSTRAK**

28 29 30

31

32

33 34

35

36

37 38

39

40

41

42

43

Latar Belakang: Resistensi insulin yang berkembang menjadi Diabetes Melitus (DM) erat hubungannya dengan terjadinya kerusakan sel beta pankreas dalam jangka panjang, disfungsi organ, dan kegagalan organ terutama pada mata, ginjal, saraf, jantung, dan pembuluh darah. Pengembangan sistem ATC/DDD diperlukan untuk meningkatkan pengetahuan tentang penggunaan obat di seluruh dunia, memastikan ketersediaan obat secara merata, dan mendorong penggunaan obat yang bijak. Tujuan penelitian ini adalah mengidentifikasi data karakteristik pasien serta obat anti-diabetes oral dan insulin menggunakan metode ATC/DDD dan DU90%. Bahan dan Metode: Rancangan penelitian ini menggunakan cross-sectional study yang mengevaluasi obat antidiabetes oral dan insulin dengan metode ATC/DDD dan DU90% di RS Bala Keselamatan Bokor Turen bulan Januari hingga Desember 2022. Kriteria inklusi terdiri dari pasien DM tipe 1 dan tipe 2 dengan dan atau tanpa komorbid, menggunakan obat anti-diabetes oral dan insulin/kombinasi keduanya. Sedangkan, kriteria eksklusinya berupa data rekam medis tidak lengkap. Populasi penelitian ini sebanyak 238 pasien menggunakan teknik total sampling. Hasil: Data karakteristik pasien pengguna obat anti-diabetes oral dan insulin terbanyak berusia 46 hingga 65 tahun (71,34%); jenis kelamin perempuan (73,2%); Indeks Masa Tubuh normal sebesar 53,66% (IMT= 18,5-25); diagnose DM+HT (20,73%) dan DM Tipe II (18,29%). Penggunaan obat anti-diabetes tertinggi adalah obat glulisin sebesar 589 DDD/100 hari rawat inap dan DU90% sebesar 21,39%. Kesimpulan: Obat anti-diiabetes yang paling banyak digunakan di RS Bokor Turen adalah glulisin.

44 45 46

Kata kunci: Obat Anti-diabetes Oral dan Insulin; Diabetes Melitus; DDD; DU 90%

47 48

#### INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder. The presence of risk factors, damage to insulin secretion and sensitivity leads to an increase in blood glucose and changes in fat and protein metabolism (DiPiro, 2020). The lack of insulin function contributes to the development of

Comment [MOU1]: Past tenses

Comment [MOU2]: Index?

microvascular, macrovascular, and neuropathy as a chronic consequence of DM (Almasdy *et al.*, 2015).

The World Health Organization (WHO) in 2023 states that in 2014, 8.5% of adults aged 18 years and over have diabetes. In 2019, diabetes was the direct cause of 1.5 million deaths, and 48% of all deaths from diabetes occurred before the age of 70. Furthermore, 460,000 deaths from kidney disease are caused by diabetes, and elevated blood glucose causes about 20% of deaths from cardiovascular disease (WHO, 2023). DM is more common in low- and moderate-income countries and countries undergoing major economic and demographic transformations. DM is a significant global health problem and requires proper prevention and management measures. DM in Indonesia is currently a serious problem. Most DM sufferers are type 2 DM groups. Therefore, it is essential to evaluate the use of the drug as a basis for selection to ensure that the drug is used appropriately, safely, and efficiently (Pitasari, Andayani and Wijayanti, 2022).

There is a need to develop ATC/DDD systems to acquire knowledge about drug use worldwide to achieve equitable drug availability and prudent drug use, especially in developing countries. The primary purpose of the ATC/DDD system is to facilitate research on drug use and improve the overall quality of drug use (Tahar *et al.*, 2020). A retrospective study using a *cross-sectional study*, which evaluated drug use patterns and costs associated with Type 2 DM in Saudi Arabia, showed that biguanide (metformin) was most widely prescribed as a monotherapy drug followed by a *fixed-dose combination*. The effectiveness of monotherapy drugs decreases with the duration of treatment; in these cases, combination drugs are prescribed. The most commonly prescribed combination drug is a biguanide with sulfonylurea/biguanide with thiazolidinedione, according to guidelines by the *American Diabetes Association* (ADA). The combination of sitagliptin and metformin is most widely preferred and widely prescribed in *fixed-dose combination therapy*, followed by vildagliptin and metformin (Ali *et al.*, 2022). Combination drugs are used when a single pill cannot achieve the desired blood glucose level in diabetic patients (Okoro, Nmeka and Erah, 2018).

Evaluation of the use of anti-diabetic drugs with ATC/DDD and DU90% methods can provide insight into the dominant drug use patterns and the extent to which these drugs follow existing treatment recommendations and guidelines. Therefore, this study evaluated oral anti-diabetic drugs and insulin using ATC/DDD and DU90% in DM patients with and without comorbidities at the Bokor Turen

84 Safety Army Hospital.

#### MATERIAL AND METHODS

**Comment [MOU3]:** Please explain about the hospital, namely its level of accreditation, etc

The study design used a cross-sectional study with retrospective data collection through patient

medical records. Quantitative evaluation of the use of anti-diabetic drugs using ATC / DDD and DU

86

87

88

**Research Methods** 

#### 89 90% techniques. This research has gone through the health research ethics committee with no E.5.a/145/KEPKUMM/V/2023. 90 91 92 **Population and Sample** 93 This population is in the form of patients hospitalized with a diagnosis of DM and or without Comment [MOU4]: Past tenses 94 comorbidities at the Bokor Turen Salvation Army Hospital. The study sample included patients 95 hospitalized with a diagnosis of DM and without comorbidities from January to December 2022 and 96 who met the inclusion and exclusion criteria. Inclusion criteria include patients aged $\geq 17$ years with a 97 diagnosis of DM and without comorbidities. Exclusion criteria are patients whose medical record data Comment [MOU5]: 98 is incomplete. 99 100 Sampling Techniques 101 The sampling technique is total sampling, where the number of samples is equal to a population of 164 Comment [MOU6]: 102 patients and meets the criteria for inclusion and exclusion of the study. 103 **Data Analysis** 104 105 The calculation in evaluating the use of ATC / DDD method anti-diabetic drugs in the hospitalization 106 of the Bokor Turen Salvation Army Hospital uses the formula: Comment [MOU7]: Do not use a $\frac{\textit{DDD}}{\textit{100}} \textit{ hari rawat inap} = \frac{\textit{Jumlah antidiabetik (gram)}}{\textit{Standar DDD WHO (gram)}} \ \textit{x} \ \frac{\textit{100}}{\textit{LOS}}$ 107 108 DU 90% is used to identify the amount of drug used as much as 90% of the total use of prescribed medicines and compare it with the amount of residual drug use (RI, 2017). The efficiency of drug use 109 110 must be observed if the amount of drug use in 10% is more. The DU value of 90% is known after 111 calculating DDD / 100 days of hospitalization per year. DU 90% is obtained by arranging the use of 112 antibiotics from highest to lowest, then determining the cumulative percentage up to 90%. Comment [MOU8]: ??? 113 114 RESULTS 115 a. Demographic Characteristics of Diabetes Mellitus Patients Comment [MOU9]: Is this the 116 The demographic characteristics of Diabetes Mellitus patients at the Bokor Turen Salvation Army number population in 1 year that meet Hospital from January to December 2022 were 164 patients in age, gender, BMI, diagnosis, the criteria? What is the total population 117

in 1 year?is it only 164?

comorbidities, drug names, administration intervals, and duration of administration. Judging from the most significant number, in the age characteristics of 117 patients aged 46-65, as many as 120 were female, and as many as 88 patients had a regular Body Mass Index (BMI) of 18.5-25 (Table 1).

118

119120

121

122123

124

125126

127128

Table 1. Data on the characteristics of diabetes mellitus patients

Karakteristik		Bulan (Tahun 2022)											Jumlah pasien (n=164)	%
	Jan	Feb	Mar	Apr	Mei	Jun	Jul	Agust	Sept	Okt	Nov	Des		
	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022		
Usia														
17- 45 thn	1	0	1	1	0	2	3	3	0	0	1	0	12	7,32
46 – 65 thn	11	6	13	12	7	12	13	8	8	14	8	5	117	71,34
66 – 95 thn	5	5	1	8	1	5	0	2	1	4	1	2	35	21,34
Mean $\pm$ SD	59,71	63,54	57,46	62,28	57,62	57,57	52,68	58,46	58,11	61,38	56,3	60,29	58,78	
	$\pm 9,18$	±	±	±	±	±	±	±	±	±	±	±	$\pm 2,52$	
		7,09	8,46	10,95	6,47	13,38	7,88	11,68	4,93	5,89	6,97	7,29	_	
Total	17	11	15	21	8	19	16	13	9	18	10	7	164	100
Jenis kelamin														
Perempuan	12	9	11	14	5	16	13	8	7	10	10	5	120	73,2
Laki-laki	5	2	4	7	3	3	3	5	2	8	0	2	44	26,8
Total	17	11	15	21	8	19	16	13	9	18	10	7	164	100
IMT														
Kurus < 18,4	1	1	1	2	0	0	0	0	1	0	0	0	6	3,66
Normal 18,5 –	11	4	5	11	4	12	10	11	4	6	7	3	88	53,66
Gemuk > 25	5	6	9	8	4	7	6	2	4	12	3	4	70	42,68
Mean ± SD	23,07	24,89	25,94	24,44	24,85	24 ±	24,15	23,26	25,48	26,37	23,71	25,40	24,63	
	$\pm 3,07$	±	±	±	±	4,16	±	$\pm 2,33$	±	±	±	±	$\pm 1,08$	
		4,93	4,12	4,94	2,39	-	3,52		5,98	3,92	3,82	3,06		
Total	17	11	15	21	8	19	16	13	9	18	10	7	164	100

The description of DM and or without comorbidities at the Bokor Turen Salvation Army Hospital showed that the most patients with a diagnosis of DM and Hypertension (HT) were 34 patients (20.73%), followed by patients with a diagnosis of Type 2 DM as many as 28 patients (18.29%). At the same time, DM patients with other comorbidities have fewer than ten patients (Table 2).

Table 2. Description of Patients with Diabetes Mellitus and or Without Comorbidities

**Comment [MOU10]:** Use the table format, not a images

Please present in English and the numbers of patient in 1 years, not every month

Diagnosis dengan Komorbid	Jumlah (n = 164)	%
DM (HT)	34	20,73
DM T2	28	18,29
DM (HT, CAD)	6	3,66
DM (Anemia)	5	3,05
DM (CAD)	5	3,05
DM (CKD)	5	3,05
DM (CVA)	5	3,05
DM (COPD)	5	3,05
DM (CVA, HT)	4	2,44
DM (Anemia, Thalasemia)	3	1,83
DM (Dispepsia)	3	1,83
DM (GERD, HT)	3	1,83
DM (HT, Anemia)	3	1,83
DM (Asma)	2	1,22
DM (DKD)	2	1,22
DM (DKD, HT)	2	1,22
DM (HT, CKD)	2	1,22
DM (HT, HF)	2	1,22
DM (HT, Vertigo)	2	1,22
DM (STEMI)	2	1,22
DM (Vertigo)	2	1,22
DM (GERD)	1	0,61
DM (Anemia, PAD)	1	0,61
DM (AKI)	1	0,61
DM (Anemia, CKD)	1	0,61
DM (Anemia, Dispepsia)	1	0,61
DM (Angina, Thalasemia)	1	0,61
DM (CAD, COPD)	1	0,61
DM (CAD, CVA, HT)	1	0,61
DM (CAD, HT)	1	0,61
DM (CAD, STEMI)	1	0,61
DM (CAD, TB)	1	0,61

**Comment [MOU11]:** Use the table format, not a images

Please present in English

129

130

131

Table 2. Description of Patients with Diabetes Mellitus and Without Comorbidities

(Continued)

**Comment [MOU12]:** Use the table format, not a images

Please present in English

Diagnosis dengan Komorbid	Jumlah (n = 164)	%
DM (CKD, HT, TB)	1	0,61
DM (CKD, STEMI)	1	0,61
DM (CKD, Thallasemia)	1	0,61
DM (COPD, Dispepsia)	1	0,61
DM (COPD, HT)	1	0,61
DM (CVA, susp covid)	1	0,61
DM (Gastritis)	1	0,61
DM (GERD, HF)	1	0,61
DM (Hepatitis)	1	0,61
DM (HF)	1	0,61
DM (HF, CAD, COPD)	1	0,61
DM (HF, Hepatitis)	1	0,61
DM (HT, HF, dispepsia)	1	0,61
DM (HT, CA infark)	1	0,61
DM (HT, CAD, Gerd)	1	0,61
DM (HT, CAD, Parkinson)	1	0,61
DM (HT, COPD, CVA)	1	0,61
DM (HT, COPD, Dispepsia)	1	0,61
DM (HT, Dispepsia)	1	0,61
DM (HT, HF, CAD)	1	0,61
DM (HT, STEMI)	1	0,61
DM (Myalgia)	1	0,61
DM (PAD)	1	0,61
DM (PAD, Vertigo)	1	0,61
DM T1 (HT)	1	0,61
Total	164	100

Based on the DM treatment profile seen in the 12 months of 2022, it shows that the use of anti-diabetic drugs is the most in the use of glargine drugs with a dose strength of 100U/ml in as many as 71 patients. Followed by glulisine drugs with a dose strength of 100U/ml for as many as 57 patients. The third highest use was aspart 100U/ml, as many as 54 patients. Concerning the administration interval of most anti-diabetic drugs given every 24 hours a day with the duration of most drug administration for 4-6 days (Table 3).

Table 3. Profile of Anti-diabetic Drug Use

Bulan (Tahun 2022) Karakteristik Total Jan Okt % Feb Mar Apr Mei Jun Jul Agust Sept Nov Des (n=293)Nama obat Acarbos 50 mg 1,7 Glulisin 100U/ml 19,5 Glargine 100U/ml 24,2 Glibenklamid 5 mg 1,0 Glikuidon 30 mg 6.1 Glimepirid 2 mg Glimepirid 4 mg 6,1 Glimepirid 3 mg Lispro 100U/ml 2,4 Detemir 100U/ml 13,0 Metformin 500 mg 6,8 Aspart 100U/ml 18,4 Pioglitazon 30 mg 0,3 Degludec-Aspart 100U/ml 0,3 Interval pemberian 53,6 24 jam 12 jam 7,2 38,9 8 jam 6 jam 0,3 Total

Karakteristik	Bulan (Tahun 2022)											Total (n=293)	%	
	Jan 2022	Feb 2022	Mar 2022	Apr 2022	Mei 2022	Jun 2022	Jul 2022	Agust 2022	Sept 2022	Okt 2022	Nov 2022	Des 2022		
Durasi														
1–3 Hari	7	15	12	10	5	20	14	13	9	15	4	3	127	43,3
4 – 6 Hari	22	6	14	26	12	17	15	9	9	17	11	8	166	56,7
Total	29	21	26	36	17	37	29	22	18	32	15	11	293	100

#### b. Evaluation of the Use of Anti-diabetic Drugs with ATC/DDD and DU 90% Methods

The results of the evaluation of the use of anti-diabetic drugs using the ATC / DDD method showed that the use of antidiabetics that are often used is glulisine drugs with a dose strength of  $100 \, \text{U}$  / ml of  $589.02 \, \text{DDD}$  /  $100 \, \text{days}$  of hospitalization, which means that during  $100 \, \text{days}$  of treatment in the hospital around  $589 \, \text{diabetic}$  patients received glulisine amounting to  $40 \, \text{IU}$  every day. The total number of patients hospitalized and using anti-diabetic drugs from January to December  $2022 \, \text{was} \, 568 \, \text{days}$ . The second most significant use of anti-diabetic medications is aspart with a dose strength of  $100 \, \text{U}$  / ml of  $519.72 \, \text{DDD}$  /  $100 \, \text{days}$  of hospitalization, which means that during  $100 \, \text{days}$  of hospitalization in the hospital around  $520 \, \text{DM}$  patients received aspart drugs of  $40 \, \text{IU}$  (Table 4).

Table 4. Analysis of the Use of Anti-diabetic Drugs using the ATC / DDD Method

Please present in English

No.	Kode ATC	Nama Obat	DDD (WHO)	LOS (Hari)	DDD/100 Hari rawat inap
1	A10AB06	Glulisin 100 U/ml	40 UI		589,02
2	A10AB05	Aspart 100 U/ ml	40 UI	-	519,72
3	A10BB12	Glimepirid 2 mg, 3 mg, 4 mg	2 mg	_	474,28
4	A10AE04	Glargine 100 U/ml	40 UI	_	426,85
5	A10AE05	Detemir 100 U/ml	40 UI	_	221,38
6	A10BA02	Metformin 500 mg	2 g	568	198,80
7	A10BB08	Glikuidon 30 mg	60 mg	Hari	129,22
8	A10AB04	Lispro 100 U/ ml	40 UI	-	85,20
9	A10BF01	Acarbos 50 mg	0,3 g		43,55
10	A10BB01	Glibenklamid 5 mg	10 mg	_	31,24
11	A10BG03	Pioglitazon 30 mg	30 mg	_	22,72
12	A10AD06	Degludec- Aspart 100 U/ ml	40 UI		11,36

The 90% DU in this study was used to evaluate the use of anti-diabetic drugs in the top 90% of services in the population. There were 12 anti-diabetic assessed drugs in 90% DU and showed that glulycin, aspart, glimepiride 2 mg, glimepiride 3 mg, glimepiride 4 mg, glargine 100U/ml, detemir 100U/ml, and metformin 500 mg were anti-diabetic drugs that accounted for 90% of the highest anti-diabetic drug use in the DM patient population at the Bokor Turen Salvation Army Hospital (Table 5).

Table 5. Profile of Anti-diabetic Drug Use with DU Method 90%

Kode ATC	Nama Obat	DDD/100 Hari rawat inap	Persentase	Persentase Kumulatif	Segmen	
A10AB06	Glulisin 100 U/ml	589,02	21,39%	21,39%	D 000/	
A10AB05	Aspart 100 U/ ml	519,72	18,88%	40,27%	Du 90%	

Table 5. Profile of Anti-diabetic Drug Use with DU Method 90% (Continued)

**Comment [MOU14]:** Use the table format, not a images

Please present in English

166167168

165

170171

172

169

173174

175176

	Glimepirid 2 mg				
A10BB12	Glimepirid 3 mg	474,28	17,23%	57,49%	
	Glimepirid 4 mg				_
A10AE04	Glargine 100 U/ml	426,85	15,50%	73,00%	_
A10AE05	Detemir 100 U/ml	221,38	8,04%	81,04%	_
A10BA02	Metformin 500 mg	198,80	7,22%	88,26%	
A10BB08	Glikuidon 30 mg	129,22	4,69%	92,95%	
A10AB04	Lispro 100 U/ ml	85,20	3,09%	96,05%	
A10BF01	Acarbos 50 mg	43,55	1,58%	97,63%	
A10BB01	Glibenklamid 5 mg	31,24	1,13%	98,76%	Du 10%
A10BG03	Pioglitazon 30 mg	22,72	0,83%	99,59%	_
A10AD06	Degludec- Aspart 100 U/ ml	11,36	0,41%	100,00%	
		2753,33	99,99		

#### **DISCUSSION**

Insulin glulisine (Apidra) in this study occurred in patients with Type 2 diabetes with comorbidities, such as hypertension, coronary artery disease (CAD), and chronic kidney disease (CKD). On average, DM patients who get apidra drugs are given every 8 hours, and this drug is widely presented to 76% of female patients with an age range of 58-61 years. This insulin is widely recommended at the Bokor Turen Salvation Army Hospital because it can lower blood sugar levels quickly and has a more negligible risk of hypoglycemia. Following the 2021 PERKENI guidelines, Apidra is insulin rapidacting, generally used with food. Apidra is designed to decrease glucose levels in the blood after a meal rapidly or when blood glucose levels are high. Apidra is commonly combined with basal insulins such as Lantus (insulin glargine) and Levemir (insulin detemir) (Soelistijo et al., 2021). A study examining the clinical effects of Type 2 DM patients with cardiovascular comorbidities where patients used insulin rapid-acting showed that it could have beneficial effects from insulin glulisine administration associated with death and stroke. Still, there was no difference in coronary heart disease (CHD) or cardiovascular disease (CVD) (Svensson et al., 2017).

Insulin aspart (novorapid) is given to patients with type 2 diabetes with comorbid HT accompanied by CAD, ST-Elevation Myocardial Infarction (STEMI), and Heart Failure (HF). The interval of insulin

administration averaged every 8 hours per day and was used by 66% of female patients with an average of 58-61 years. Like glulisine insulin, this insulin can also quickly lower blood sugar levels and has a low risk of hypoglycemia. This insulin is also rapid-acting, which provides therapeutic effectiveness after 15 minutes, with the peak of therapeutic efficacy occurring within 1-2 hours and can last up to 4-6 hours. In the case of the population in Japan, administering insulin aspart to type 2 DM patients can significantly reduce cardiovascular complications within 5 to 10 years, resulting in improved quality of life and lower costs compared to *human insulin* (Pollock et al., 2011).

The third most significant use of anti-diabetic drugs is glimepiride doses of 2mg, 3 mg, and 4 mg. This drug is given to patients with type 2 diabetes with cardiovascular comorbidities and an interval of 24 hours per day and primarily female patients (83%) with an average age of 58 years. Regular glimepiride is combined with insulin or another oral medication such as metformin. In the case study of type 2 DM patients with CVD, the average patient suffering from DM was around 5.7 ± 4.8 years. CVD suffered by type 2 DM patients in the form of hypertension (68.5% of patients); dyslipidemia (47.9% of patients); CAD (25.4% of patients); Transient Ischemic Attack (TIA) in 3.6% of patients; peripheral artery disease (PAD) accounted for 4.8% of patients and heart failure in 2.9% of patients. Type 2 DM patients with various comorbidities receive the drug glimepiride/metformin Fixed Dose Combination (FDC) as a first-line therapy. As many as 68.2% of FDC patients achieved blood pressure within optimal limits. Most of the other patients experienced an increase in glycemic parameters and a change in body weight of about 18.4%. 59.2% of patients experienced weight loss (Ray et al., 2022). Glimepiride is a sulfonylurea class drug that has pharmacological effects to increase insulin production by pancreatic beta cells. The most common side effects are hypoglycemia and weight gain.

The limitation of this study is that data were taken only retrospectively from patient medical record data and did not make direct observations on DM patients.

#### CONCLUSION

Based on the analysis of demographic data and treatment profiles of DM patients, DM patients are dominated by the age group of 46-65 years, with women who use anti-diabetic drugs more. Patients with comorbidities use more anti-diabetic medications than patients with non-comorbid DM. Evaluation of anti-diabetic drugs ATC / DDD method shows that insulin glulisine (Apidra) is most used in DM patients with and without comorbidities. Through the DU method, 90% of glulisine, aspart, glargine, glimepiride, determir, and metformin drugs were most widely used in DM patients.

**Comment [MOU15]:** Why is inslin glusine more often choice than aspart?

**Comment [MOU16]:** Why is metformin not among the top three most widely used antidiabetic drug? Wasn't it the first choice?

**Comment [MOU17]:** Please compare the result of this research with the previous reasearch

**Comment [MOU18]:** Please explain benefit and follow up from the result of research for the hospital or science?

230	
231	CONFLICT OF INTEREST
232	All authors declare no conflict of interest.
233	REFERENCES
234 235 236 237	Ali, M.D. <i>et al.</i> (2022) 'Evaluation of drug utilization pattern and cost associated with diabetes mellitusType two management in Saudi Arabia', <i>Brazilian Journal of Pharmaceutical Sciences</i> , 58, p. E20681. Available at: https://doi.org/10.1590/s2175-97902022e20681.
238 239 240 241	Almasdy, D. <i>et al.</i> (2015) 'Evaluation of the Use of Anti-diabetic Drugs in Type-2 Diabetes Mellitus Patients in a Government Hospital of Padang City — West Sumatra', <i>Journal of Pharmaceutical &amp; Clinical Science</i> , 2(1), p. 104. Available at: https://doi.org/10.29208/jsfk.2015.2.1.58.
242 243	DiPiro, J.T. (ed.) (2020) <i>Pharmacotherapy: a pathophysiologic approach</i> . Eleventh edition. New York: McGraw Hill Medical.
244 245 246	Okoro, R.N., Nmeka, C. and Erah, P.O. (2018) 'Utilization study of antidiabetes medicines at a tertiary care hospital in Nigeria', <i>Future Journal of Pharmaceutical Sciences</i> , 4(2), pp. 109–115. Available at: https://doi.org/10.1016/j.fjps.2017.11.004.
247 248 249 250	Pitasari, N.W.N., Andayani, T.M. and Wijayanti, T. (2022) 'Evaluation of the Use of Antidiabetic Drugs in Patients of Back-Referral Program at the Demak District Pharmacy', <i>Journal of Management and Pharmacy Practice</i> , 12(2), p. 125. Available at: https://doi.org/10.22146/jmpf.73841.
<ul><li>251</li><li>252</li><li>253</li><li>254</li></ul>	Pollock, R.F. <i>et al.</i> (2011) 'The cost effectiveness of rapid-acting insulin aspart compared with human insulin in type 2 diabetes patients: an analysis from the Japanese third-party payer perspective', <i>Journal of Medical Economics</i> , 14(1), pp. 36–46. Available at: https://doi.org/10.3111/13696998.2010.541045.
255 256 257	Ray, S. et al. (2022) 'Usage Pattern of Glimepiride/Metformin Fixed-dose Combination in Type 2 Diabetes Patients with CVD or at Risk of CVD: An Experience in Indian Setting', Asian Journal of Diabetology, 23(2), pp. 13–19.
258	RI, K. (2017) 'Technical Guidelines for Evaluation of Drug Use in Health Facilities'.
259 260	Soelistijo, S.A. dkk. (2021) 'Guidelines for the management and prevention of adult type 2 diabetes mellitus in INDONESIA - 2021', <i>PB. PERKENI</i> , p. 119.
261 262 263 264	Svensson, AM. <i>et al.</i> (2017) 'Clinical effects, cardiovascular and renal outcomes associated with rapid-acting insulin analogs among individuals with type 2 diabetes: a nation-wide observational cohort study', <i>Clinical Diabetes and Endocrinology</i> , 3(1), p. 5. Available at: https://doi.org/10.1186/s40842-017-0043-2.

265	Tahar, N.dkk. (2020) 'EVALUATION OF THE USE OF ORAL ANTI-DIABETIC DRUGS IN TYPE
266	2 DIABETES MELLITUS PATIENTS USING ATC/DDD AND DU 90% METHODS', The
267	2nd Alauddin Pharmaceutical Conference and Expo (ALPHA-C) 2020 [Preprint]. Available
268	at: https://doi.org/10.24252/kesehatan.v1i1.18380.
269 270	WHO (2023) <i>Diabetes</i> . Available at: https://www.who.int/news-room/fact-sheets/detail/diabetes (Accessed: September 21, 2023).

## Evaluation of Anti-diabetic Drugs using ATC/DDD and DU90% Methods in Diabetes Mellitus Patients

### ABSTRACT

**Comment [AR1]:** English to poor, please check proofreading and grammar

Background: Diabetes Mellitus (DM), which results from insulin resistance, is closely linked to long-term damage to pancreatic beta cells, organ dysfunction, and organ failure, particularly in the eyes, kidneys, nerves, heart, and blood vessels. The development of the ATC/DDD system is necessary to increase global drug knowledge, ensure equitable drug availability, and promote responsible drug use. Objectives: This study aimed to identify data on patient characteristics and oral anti-diabetic drugs and insulin using the ATC/DDD and DU90% methods. Material and Methods: This study is a cross-sectional evaluation of oral anti-diabetic medications and insulin using the ATC/DDD method and DU90% at the Bala Keselamatan Bokor Turen Hospital from January to December 2022. The inclusion criteria were individuals diagnosed with type 1 or type 2 diabetes mellitus, with or without comorbidities, who were treated with oral anti-diabetic medications and a combination of insulin and oral medications. In the present study, the incomplete medical record data served as the exclusion criteria. The sample for this investigation consisted of 238 patients selected using the complete sampling technique. Results: The majority of patients who used oral anti-diabetic medications and insulin were between the ages of 46 and 65 (71.34%), were female (73.2%), had standard body mass indices (BMIs between 18.5 and 25), and had diagnoses of DM + HT (20.73%) and Type II DM (18.29%). Glulisin was the most commonly used anti-diabetic drug, accounting for 589 DDD/100 days of hospitalization, and DU90% was 21.39%. Conclusion: Glulisin is the most frequently prescribed anti-diabetic medication at Bokor Turen Hospital.

Keywords: Antidiabetic Oral and Insulin; Diabetes Mellitus; ATC/DDD; DU 90%

#### **ABSTRAK**

Latar Belakang: Resistensi insulin yang berkembang menjadi Diabetes Melitus (DM) erat hubungannya dengan terjadinya kerusakan sel beta pankreas dalam jangka panjang, disfungsi organ, dan kegagalan organ terutama pada mata, ginjal, saraf, jantung, dan pembuluh darah. Pengembangan sistem ATC/DDD diperlukan untuk meningkatkan pengetahuan tentang penggunaan obat di seluruh dunia, memastikan ketersediaan obat secara merata, dan mendorong penggunaan obat yang bijak. Tujuan penelitian ini adalah mengidentifikasi data karakteristik pasien serta obat anti-diabetes oral dan insulin menggunakan metode ATC/DDD dan DU90%. Bahan dan Metode: Rancangan penelitian ini menggunakan cross-sectional study yang mengevaluasi obat antidiabetes oral dan insulin dengan metode ATC/DDD dan DU90% di RS Bala Keselamatan Bokor Turen bulan Januari hingga Desember 2022. Kriteria inklusi terdiri dari pasien DM tipe 1 dan tipe 2 dengan dan atau tanpa komorbid, menggunakan obat anti-diabetes oral dan insulin/kombinasi keduanya. Sedangkan, kriteria eksklusinya berupa data rekam medis tidak lengkap. Populasi penelitian ini sebanyak 238 pasien menggunakan teknik total sampling. Hasil: Data karakteristik pasien pengguna obat anti-diabetes oral dan insulin terbanyak berusia 46 hingga 65 tahun (71,34%); jenis kelamin perempuan (73,2%); Indeks Masa Tubuh normal sebesar 53,66% (IMT= 18,5-25); diagnose DM+HT (20,73%) dan DM Tipe II (18,29%). Penggunaan obat anti-diabetes tertinggi adalah obat glulisin sebesar 589 DDD/100 hari rawat inap dan DU90% sebesar 21,39%. Kesimpulan: Obat anti-diiabetes yang paling banyak digunakan di RS Bokor Turen adalah glulisin.

Kata kunci: Obat Anti-diabetes Oral dan Insulin; Diabetes Melitus; DDD; DU 90%

#### INTRODUCTION

1

6 7

8

9

10

11

12

13 14

15

16

17

18

19

20 21

22

23

24 25

26 27

28 29

30

31

32 33

34

35

36

37

38 39

40

41

42

43

44

45 46

47 48

49 50

51

Diabetes Mellitus (DM) is a chronic metabolic disorder. The presence of risk factors, damage to insulin secretion and sensitivity leads to an increase in blood glucose and changes in fat and protein metabolism (DiPiro, 2020). The lack of insulin function contributes to the development of

Comment [AR2]: not fit for purpose

microvascular, macrovascular, and neuropathy as a chronic consequence of DM (Almasdy *et al.*, 2015).

The World Health Organization (WHO) in 2023 states that in 2014, 8.5% of adults aged 18 years and over have diabetes. In 2019, diabetes was the direct cause of 1.5 million deaths, and 48% of all deaths from diabetes occurred before the age of 70. Furthermore, 460,000 deaths from kidney disease are caused by diabetes, and elevated blood glucose causes about 20% of deaths from cardiovascular disease (WHO, 2023). DM is more common in low- and moderate-income countries and countries undergoing major economic and demographic transformations. DM is a significant global health problem and requires proper prevention and management measures. DM in Indonesia is currently a serious problem. Most DM sufferers are type 2 DM groups. Therefore, it is essential to evaluate the use of the drug as a basis for selection to ensure that the drug is used appropriately, safely, and efficiently (Pitasari, Andayani and Wijayanti, 2022).

There is a need to develop ATC/DDD systems to acquire knowledge about drug use worldwide to achieve equitable drug availability and prudent drug use, especially in developing countries. The primary purpose of the ATC/DDD system is to facilitate research on drug use and improve the overall quality of drug use (Tahar *et al.*, 2020). A retrospective study using a *cross-sectional study*, which evaluated drug use patterns and costs associated with Type 2 DM in Saudi Arabia, showed that biguanide (metformin) was most widely prescribed as a monotherapy drug followed by a *fixed-dose combination*. The effectiveness of monotherapy drugs decreases with the duration of treatment; in these cases, combination drugs are prescribed. The most commonly prescribed combination drug is a biguanide with sulfonylurea/biguanide with thiazolidinedione, according to guidelines by the *American Diabetes Association* (ADA). The combination of sitagliptin and metformin is most widely preferred and widely prescribed in *fixed-dose combination therapy*, followed by vildagliptin and metformin (Ali *et al.*, 2022). Combination drugs are used when a single pill cannot achieve the desired blood glucose level in diabetic patients (Okoro, Nmeka and Erah, 2018).

Evaluation of the use of anti-diabetic drugs with ATC/DDD and DU90% methods can provide insight into the dominant drug use patterns and the extent to which these drugs follow existing treatment recommendations and guidelines. Therefore, this study evaluated oral anti-diabetic drugs and insulin using ATC/DDD and DU90% in DM patients with and without comorbidities at the Bokor Turen Safety Army Hospital.

#### MATERIAL AND METHODS

#### 86 **Research Methods**

- 87 The study design used a cross-sectional study with retrospective data collection through patient
- 88 medical records. Quantitative evaluation of the use of anti-diabetic drugs using ATC / DDD and DU
- 89 90% techniques. This research has gone through the health research ethics committee with no
- E.5.a/145/KEPKUMM/V/2023. 90

91

#### 92 **Population and Sample**

- 93 This population is in the form of patients hospitalized with a diagnosis of DM and or without
- 94 comorbidities at the Bokor Turen Salvation Army Hospital. The study sample included patients
- 95 hospitalized with a diagnosis of DM and without comorbidities from January to December 2022 and
- 96 who met the inclusion and exclusion criteria. Inclusion criteria include patients aged  $\geq 17$  years with a
- 97 diagnosis of DM and without comorbidities. Exclusion criteria are patients whose medical record data
- 98 is incomplete.

99

100

#### **Sampling Techniques**

- 101 The sampling technique is total sampling, where the number of samples is equal to a population of 164
- 102 patients and meets the criteria for inclusion and exclusion of the study.

103

#### **Data Analysis** 104

- 105 The calculation in evaluating the use of ATC / DDD method anti-diabetic drugs in the hospitalization
- 106 of the Bokor Turen Salvation Army Hospital uses the formula:

$$\frac{\textit{DDD}}{\textit{100}} \textit{hari rawat inap} = \frac{\textit{Jumlah antidiabetik (gram)}}{\textit{Standar DDD WHO (gram)}} \ \textit{x} \ \frac{\textit{100}}{\textit{LOS}}$$

107

- 108 DU 90% is used to identify the amount of drug used as much as 90% of the total use of prescribed medicines and compare it with the amount of residual drug use (RI, 2017). The efficiency of drug use
- 109
- 110 must be observed if the amount of drug use in 10% is more. The DU value of 90% is known after
- 111 calculating DDD / 100 days of hospitalization per year. DU 90% is obtained by arranging the use of
- 112 antibiotics from highest to lowest, then determining the cumulative percentage up to 90%.

113

114

115

#### RESULTS

#### a. Demographic Characteristics of Diabetes Mellitus Patients

- 116 The demographic characteristics of Diabetes Mellitus patients at the Bokor Turen Salvation Army
- 117 Hospital from January to December 2022 were 164 patients in age, gender, BMI, diagnosis,

Comment [AR3]: With english

Comment [AR4]: All table and picture with full english

comorbidities, drug names, administration intervals, and duration of administration. Judging from the most significant number, in the age characteristics of 117 patients aged 46-65, as many as 120 were female, and as many as 88 patients had a regular Body Mass Index (BMI) of 18.5-25 (Table 1).

Table 1. Data on the characteristics of diabetes mellitus patients

Karakteristik		Bulan (Tahun 2022)											Jumlah pasien (n=164)	%
	Jan	Feb	Mar	Apr	Mei	Jun	Jul	Agust	Sept	Okt	Nov	Des		
	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022		
Usia														
17- 45 thn	1	0	1	1	0	2	3	3	0	0	1	0	12	7,32
46 - 65  thn	11	6	13	12	7	12	13	8	8	14	8	5	117	71,34
66 – 95 thn	5	5	1	8	1	5	0	2	1	4	1	2	35	21,34
Mean $\pm$ SD	59,71	63,54	57,46	62,28	57,62	57,57	52,68	58,46	58,11	61,38	56,3	60,29	58,78	
	$\pm 9,18$	±	±	±	±	±	±	±	±	±	±	±	$\pm 2,52$	
		7,09	8,46	10,95	6,47	13,38	7,88	11,68	4,93	5,89	6,97	7,29		
Total	17	11	15	21	8	19	16	13	9	18	10	7	164	100
Jenis kelamin														
Perempuan	12	9	11	14	5	16	13	8	7	10	10	5	120	73,2
Laki-laki	5	2	4	7	3	3	3	5	2	8	0	2	44	26,8
Total	17	11	15	21	8	19	16	13	9	18	10	7	164	100
IMT														
Kurus < 18,4	1	1	1	2	0	0	0	0	1	0	0	0	6	3,66
Normal 18,5 –	11	4	5	11	4	12	10	11	4	6	7	3	88	53,66
25														
Gemuk > 25	5	6	9	8	4	7	6	2	4	12	3	4	70	42,68
Mean ± SD	23,07	24,89	25,94	24,44	24,85	24 ±	24,15	23,26	25,48	26,37	23,71	25,40	24,63	
	$\pm 3,07$	±	±	±	±	4,16	±	$\pm 2,33$	±	±	±	±	$\pm 1,08$	
		4,93	4,12	4,94	2,39	-	3,52	-	5,98	3,92	3,82	3,06		
Total	17	11	15	21	8	19	16	13	9	18	10	7	164	100

The description of DM and or without comorbidities at the Bokor Turen Salvation Army Hospital showed that the most patients with a diagnosis of DM and Hypertension (HT) were 34 patients (20.73%), followed by patients with a diagnosis of Type 2 DM as many as 28 patients (18.29%). At the same time, DM patients with other comorbidities have fewer than ten patients (Table 2).

Table 2. Description of Patients with Diabetes Mellitus and or Without Comorbidities

DM (HT)         34         20,73           DM T2         28         18,29           DM (HT, CAD)         6         3,66           DM (Anemia)         5         3,05           DM (CAD)         5         3,05           DM (CKD)         5         3,05           DM (CVA)         5         3,05           DM (CVA, T)         4         2,44           DM (Anemia, Thalasemia)         3         1,83           DM (GERD, HT)         3         1,83           DM (GERD, HT)         3         1,83           DM (MKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Thalasemia)         1         0,61           DM (Anemia, Thalasemia)	Diagnosis dengan Komorbid	Jumlah (n = 164)	%
DM (HT, CAD)         6         3,66           DM (Anemia)         5         3,05           DM (CAD)         5         3,05           DM (CKD)         5         3,05           DM (CVA)         5         3,05           DM (CVPD)         5         3,05           DM (CVA, HT)         4         2,44           DM (Anemia, Thalasemia)         3         1,83           DM (Dispepsia)         3         1,83           DM (DERD, HT)         3         1,83           DM (Asma)         2         1,22           DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, FKD)         2         1,22           DM (HT, HF)         2         1,22           DM (HT, FTerigo)         2         1,22           DM (STEMI)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Anemia, Dispepsia) <t< th=""><th>DM (HT)</th><th>34</th><th>20,73</th></t<>	DM (HT)	34	20,73
DM (Anemia)         5         3,05           DM (CAD)         5         3,05           DM (CKD)         5         3,05           DM (CVA)         5         3,05           DM (CVA)         5         3,05           DM (CVA)         4         2,44           DM (CVA, HT)         4         2,44           DM (Anemia, Thalasemia)         3         1,83           DM (Dispepsia)         3         1,83           DM (GERD, HT)         3         1,83           DM (Asma)         2         1,22           DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, HF)         2         1,22           DM (HT, HF)         2         1,22           DM (STEMI)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD, CVA, HT)         1 </td <td>DM T2</td> <td>28</td> <td>18,29</td>	DM T2	28	18,29
DM (CAD)         5         3,05           DM (CKD)         5         3,05           DM (CVA)         5         3,05           DM (CVA)         5         3,05           DM (COPD)         5         3,05           DM (COPD)         5         3,05           DM (COPD)         5         3,05           DM (CVA, HT)         4         2,44           DM (Asmai, Thalasemia)         3         1,83           DM (DERD, HT)         3         1,83           DM (HT, Anemia)         3         1,83           DM (Asma)         2         1,22           DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (CERD)         1         0,61           DM (Acmia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1	DM (HT, CAD)	6	3,66
DM (CKD)         5         3,05           DM (CVA)         5         3,05           DM (COPD)         5         3,05           DM (CVA, HT)         4         2,44           DM (Dispepsia)         3         1,83           DM (Dispepsia)         3         1,83           DM (DERD, HT)         3         1,83           DM (HT, Anemia)         3         1,83           DM (Asma)         2         1,22           DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, GKD)         2         1,22           DM (HT, HF)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, CVA, HT) <td>DM (Anemia)</td> <td>5</td> <td>3,05</td>	DM (Anemia)	5	3,05
DM (CVA)         5         3,05           DM (COPD)         5         3,05           DM (CVA, HT)         4         2,44           DM (Anemia, Thalasemia)         3         1,83           DM (Dispepsia)         3         1,83           DM (GERD, HT)         3         1,83           DM (HT, Anemia)         3         1,83           DM (Asma)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (STEMI)         2         1,22           DM (Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (STEMI)         2         1,22           DM (Vertigo)         2         1,22           DM (Aremia, PAD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD,	DM (CAD)	5	3,05
DM (COPD)         5         3,05           DM (CVA, HT)         4         2,44           DM (CVA, HT)         4         2,44           DM (Anemia, Thalasemia)         3         1,83           DM (Dispepsia)         3         1,83           DM (HT, Anemia)         3         1,83           DM (HT, Anemia)         2         1,22           DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, Wertigo)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (CKD)		3,05
DM (CVA, HT)         4         2,44           DM (Anemia, Thalasemia)         3         1,83           DM (Dispepsia)         3         1,83           DM (GERD, HT)         3         1,83           DM (Asma)         2         1,22           DM (Asma)         2         1,22           DM (DKD)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, HF)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (CVA)	5	3,05
DM (Anemia, Thalasemia)         3         1,83           DM (Dispepsia)         3         1,83           DM (GERD, HT)         3         1,83           DM (GERD, HT)         3         1,83           DM (HT, Anemia)         3         1,83           DM (DKD, DM)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, Wertigo)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (COPD)	5	3,05
DM (Dispepsia)         3         1,83           DM (GERD, HT)         3         1,83           DM (HT, Anemia)         3         1,83           DM (HT, Anemia)         2         1,22           DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, Wertigo)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (CVA, HT)	4	2,44
DM (GERD, HT)         3         1,83           DM (HT, Anemia)         3         1,83           DM (Asma)         2         1,22           DM (DKD)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, FIF)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (Anemia, Thalasemia)	3	1,83
DM (HT, Anemia)         3         1,83           DM (Asma)         2         1,22           DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, Wertigo)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (Vertigo)         2         1,22           DM (Vertigo)         2         1,22           DM (Vertigo)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (ARI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (Dispepsia)	3	1,83
DM (Asma)         2         1,22           DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, Wertigo)         2         1,22           DM (STEMI)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (GERD, HT)	3	1,83
DM (DKD)         2         1,22           DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, GKD)         2         1,22           DM (HT, HF)         2         1,22           DM (STEMI)         2         1,22           DM (Vertigo)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (AKI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (HT, Anemia)	3	1,83
DM (DKD, HT)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, CKD)         2         1,22           DM (HT, HF)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (Vertigo)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (AKI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (Asma)		1,22
DM (HT, CKD)         2         1,22           DM (HT, HF)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (ARI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (DKD)	2	1,22
DM (HT, HF)         2         1,22           DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (Vertigo)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (AKI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (DKD, HT)		1,22
DM (HT, Vertigo)         2         1,22           DM (STEMI)         2         1,22           DM (Vertigo)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (AKI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (HT, CKD)		1,22
DM (STEMI)         2         1,22           DM (Vertigo)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (HT, HF)		1,22
DM (Vertigo)         2         1,22           DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (AKI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (HT, Vertigo)		1,22
DM (GERD)         1         0,61           DM (Anemia, PAD)         1         0,61           DM (AKI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (STEMI)	2	1,22
DM (Anemia, PAD)         1         0,61           DM (AKI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (Vertigo)	2	1,22
DM (AKI)         1         0,61           DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, TEMI)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (GERD)	1	0,61
DM (Anemia, CKD)         1         0,61           DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (Anemia, PAD)	1	0,61
DM (Anemia, Dispepsia)         1         0,61           DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (AKI)	1	0,61
DM (Angina, Thalasemia)         1         0,61           DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, TT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (Anemia, CKD)	1	0,61
DM (CAD, COPD)         1         0,61           DM (CAD, CVA, HT)         1         0,61           DM (CAD, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (Anemia, Dispepsia)	1	0,61
DM (CAD, CVA, HT)         1         0,61           DM (CAD, HT)         1         0,61           DM (CAD, STEMI)         1         0,61	DM (Angina, Thalasemia)	1	0,61
DM (CAD, HT) 1 0,61 DM (CAD, STEMI) 1 0,61	DM (CAD, COPD)	1	0,61
DM (CAD, STEMI) 1 0,61		1	0,61
	DM (CAD, HT)		0,61
DM (CAD, TB) 1 0.61			0,61
	DM (CAD, TB)	1	0,61

 $\textbf{Table 2.} \ \ \textbf{Description of Patients with Diabetes Mellitus and Without Comorbidities}$ 

131 (Continued)

129

130

Comment [AR5]: Add abbreviations

Diagnosis dengan Komorbid	Jumlah (n = 164)	%
DM (CKD, HT, TB)	1	0,61
DM (CKD, STEMI)	1	0,61
DM (CKD, Thallasemia)	1	0,61
DM (COPD, Dispepsia)	1	0,61
DM (COPD, HT)	1	0,61
DM (CVA, susp covid)	1	0,61
DM (Gastritis)	1	0,61
DM (GERD, HF)	1	0,61
DM (Hepatitis)	1	0,61
DM (HF)	1	0,61
DM (HF, CAD, COPD)	1	0,61
DM (HF, Hepatitis)	1	0,61
DM (HT, HF, dispepsia)	1	0,61
DM (HT, CA infark)	1	0,61
DM (HT, CAD, Gerd)	1	0,61
DM (HT, CAD, Parkinson)	1	0,61
DM (HT, COPD, CVA)	1	0,61
DM (HT, COPD, Dispepsia)	1	0,61
DM (HT, Dispepsia)	1	0,61
DM (HT, HF, CAD)	1	0,61
DM (HT, STEMI)	1	0,61
DM (Myalgia)	1	0,61
DM (PAD)	1	0,61
DM (PAD, Vertigo)	1	0,61
DM T1 (HT)	1	0,61
Total	164	100

Based on the DM treatment profile seen in the 12 months of 2022, it shows that the use of anti-diabetic drugs is the most in the use of glargine drugs with a dose strength of 100U/ml in as many as 71 patients. Followed by glulisine drugs with a dose strength of 100U/ml for as many as 57 patients. The third highest use was aspart 100U/ml, as many as 54 patients. Concerning the administration interval of most anti-diabetic drugs given every 24 hours a day with the duration of most drug administration for 4-6 days (Table 3).

Table 3. Profile of Anti-diabetic Drug Use

Karakteristik					Bu	lan (Ta	ahun 20	)22)					Total	
Karakteristik	Jan	Feb	Mar	Apr	Mei	Jun	Jul	Agust	Sept	Okt	Nov	Des	(n=293)	%
Nama obat	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022	2022	(n-293)	
Acarbos 50 mg	1	0	0	0	0	1	2	0	0	0	0	1	5	1,7
Glulisin 100U/ml	4	7	8	10	5	7	2	3	1	5	3	2	57	19,5
Glargine 100U/ml	8	9	8	8	4	9	4	4	5	7	3	2	71	24,2
Glibenklamid 5 mg	1	0	0	0	0	0	1	1	0	0	0	0	3	1,0
Glikuidon 30 mg	2	0	4	1	0	1	1	1	1	4	2	1	18	6,1
Glimepirid 2 mg	2	0	0	3	2	3	3	3	2	0	0	0		
Glimepirid 4 mg	0	0	0	1	0	1	1	0	2	0	0	0	18	6,1
Glimepirid 3 mg	0	0	0	0	1	0	0	0	0	0	0	0		
Lispro 100U/ml	1	0	0	0	0	1	2	0	1	0	0	2	7	2,4
Detemir 100U/ml	2	0	3	6	3	5	4	2	2	7	2	2	38	13,0
Metformin 500 mg	2	1	0	4	1	2	3	3	1	1	1	1	20	6,8
Aspart 100U/ml	6	3	3	4	2	8	7	4	5	8	4	0	54	18,4
Pioglitazon 30 mg	0	0	0	0	0	0	0	1	0	0	0	0	1	0,3
Degludec-Aspart 100U/ml	0	1	0	0	0	0	0	0	0	0	0	0	1	0,3
Total	29	21	26	36	17	37	29	22	18	32	15	11	293	100
Interval pemberian														
24 jam	15	10	16	20	9	18	14	11	9	20	9	6	157	53,6
12 jam	2	1	0	3	1	3	3	2	3	2	1	0	21	7,2
8 jam	12	10	10	13	7	16	12	9	6	10	4	5	114	38,9
6 jam	0	0	0	0	0	0	0	0	0	0	1	0	1	0,3
Total	29	21	26	36	17	37	29	22	18	32	15	11	293	100

Karakteristik	Bulan (Tahun 2022)								Total (n=293)	%				
	Jan 2022	Feb 2022	Mar 2022	Apr 2022	Mei 2022	Jun 2022	Jul 2022	Agust 2022	Sept 2022	Okt 2022	Nov 2022	Des 2022		
Durasi														
1–3 Hari	7	15	12	10	5	20	14	13	9	15	4	3	127	43,3
4 – 6 Hari	22	6	14	26	12	17	15	9	9	17	11	8	166	56,7
Total	29	21	26	36	17	37	29	22	18	32	15	11	293	100

#### b. Evaluation of the Use of Anti-diabetic Drugs with ATC/DDD and DU 90% Methods

The results of the evaluation of the use of anti-diabetic drugs using the ATC / DDD method showed that the use of antidiabetics that are often used is glulisine drugs with a dose strength of  $100 \, \text{U}$  / ml of  $589.02 \, \text{DDD}$  /  $100 \, \text{days}$  of hospitalization, which means that during  $100 \, \text{days}$  of treatment in the hospital around  $589 \, \text{diabetic}$  patients received glulisine amounting to  $40 \, \text{IU}$  every day. The total number of patients hospitalized and using anti-diabetic drugs from January to December  $2022 \, \text{was} \, 568 \, \text{days}$ . The second most significant use of anti-diabetic medications is aspart with a dose strength of  $100 \, \text{U}$  / ml of  $519.72 \, \text{DDD}$  /  $100 \, \text{days}$  of hospitalization, which means that during  $100 \, \text{days}$  of hospitalization in the hospital around  $520 \, \text{DM}$  patients received aspart drugs of  $40 \, \text{IU}$  (Table 4).

Table 4. Analysis of the Use of Anti-diabetic Drugs using the ATC / DDD Method

No.	Kode ATC	Nama Obat	DDD (WHO)	LOS (Hari)	DDD/100 Hari rawat inap
1	A10AB06	Glulisin 100 U/ml	40 UI		589,02
2	A10AB05	Aspart 100 U/ ml	40 UI		519,72
3	A10BB12	Glimepirid 2 mg, 3 mg, 4 mg	2 mg	_	474,28
4	A10AE04	Glargine 100 U/ml	40 UI		426,85
5	A10AE05	Detemir 100 U/ml	40 111		221,38
6	A10BA02	Metformin 500 mg	2 g	568 Hari	198,80
7	A10BB08	Glikuidon 30 mg	60 mg		129,22
8	A10AB04	Lispro 100 U/ ml	40 UI		85,20
9	A10BF01	Acarbos 50 mg	0,3 g		43,55
10	A10BB01	Glibenklamid 5 mg	10 mg	_	31,24
11	A10BG03	Pioglitazon 30 mg		22,72	
12	A10AD06	Degludec- Aspart 100 U/ ml	40 UI	_	11,36

The 90% DU in this study was used to evaluate the use of anti-diabetic drugs in the top 90% of services in the population. There were 12 anti-diabetic assessed drugs in 90% DU and showed that glulycin, aspart, glimepiride 2 mg, glimepiride 3 mg, glimepiride 4 mg, glargine 100U/ml, detemir 100U/ml, and metformin 500 mg were anti-diabetic drugs that accounted for 90% of the highest anti-diabetic drug use in the DM patient population at the Bokor Turen Salvation Army Hospital (Table 5).

**Table 5.** Profile of Anti-diabetic Drug Use with DU Method 90%

Kode ATC	Nama Obat	DDD/100 Hari rawat inap	Persentase	Persentase Kumulatif	Segmen
A10AB06	Glulisin 100 U/ml	589,02	21,39%	21,39%	Du 90%
A10AB05	Aspart 100 U/ ml	519,72	18,88%	40,27%	Du 90%

Table 5. Profile of Anti-diabetic Drug Use with DU Method 90% (Continued)

	Glimepirid 2 mg				
A10BB12	Glimepirid 3 mg	474,28	17,23%	57,49%	
	Glimepirid 4 mg				_
A10AE04	Glargine 100 U/ml	426,85	15,50%	73,00%	_
A10AE05	Detemir 100 U/ml	221,38	8,04%	81,04%	_
A10BA02	Metformin 500 mg	198,80	7,22%	88,26%	
A10BB08	Glikuidon 30 mg	129,22	4,69%	92,95%	
A10AB04	Lispro 100 U/ ml	85,20	3,09%	96,05%	
A10BF01	Acarbos 50 mg	43,55	1,58%	97,63%	
A10BB01	Glibenklamid 5 mg	31,24	1,13%	98,76%	Du 10%
A10BG03	Pioglitazon 30 mg	22,72	0,83%	99,59%	_
A10AD06	Degludec- Aspart 100 U/ ml	11,36	0,41%	100,00%	
		2753,33	99,99		

#### **DISCUSSION**

Insulin glulisine (Apidra) in this study occurred in patients with Type 2 diabetes with comorbidities, such as hypertension, coronary artery disease (CAD), and chronic kidney disease (CKD). On average, DM patients who get apidra drugs are given every 8 hours, and this drug is widely presented to 76% of female patients with an age range of 58-61 years. This insulin is widely recommended at the Bokor Turen Salvation Army Hospital because it can lower blood sugar levels quickly and has a more negligible risk of hypoglycemia. Following the 2021 PERKENI guidelines, Apidra is insulin rapidacting, generally used with food. Apidra is designed to decrease glucose levels in the blood after a meal rapidly or when blood glucose levels are high. Apidra is commonly combined with basal insulins such as Lantus (insulin glargine) and Levemir (insulin detemir) (Soelistijo et al., 2021). A study examining the clinical effects of Type 2 DM patients with cardiovascular comorbidities where patients used insulin rapid-acting showed that it could have beneficial effects from insulin glulisine administration associated with death and stroke. Still, there was no difference in coronary heart disease (CHD) or cardiovascular disease (CVD) (Svensson et al., 2017).

Insulin aspart (novorapid) is given to patients with type 2 diabetes with comorbid HT accompanied by CAD, ST-Elevation Myocardial Infarction (STEMI), and Heart Failure (HF). The interval of insulin

administration averaged every 8 hours per day and was used by 66% of female patients with an average of 58-61 years. Like glulisine insulin, this insulin can also quickly lower blood sugar levels and has a low risk of hypoglycemia. This insulin is also rapid-acting, which provides therapeutic effectiveness after 15 minutes, with the peak of therapeutic efficacy occurring within 1-2 hours and can last up to 4-6 hours. In the case of the population in Japan, administering insulin aspart to type 2 DM patients can significantly reduce cardiovascular complications within 5 to 10 years, resulting in improved quality of life and lower costs compared to *human insulin* (Pollock et al., 2011).

The third most significant use of anti-diabetic drugs is glimepiride doses of 2mg, 3 mg, and 4 mg. This drug is given to patients with type 2 diabetes with cardiovascular comorbidities and an interval of 24 hours per day and primarily female patients (83%) with an average age of 58 years. Regular glimepiride is combined with insulin or another oral medication such as metformin. In the case study of type 2 DM patients with CVD, the average patient suffering from DM was around 5.7 ± 4.8 years. CVD suffered by type 2 DM patients in the form of hypertension (68.5% of patients); dyslipidemia (47.9% of patients); CAD (25.4% of patients); Transient Ischemic Attack (TIA) in 3.6% of patients; peripheral artery disease (PAD) accounted for 4.8% of patients and heart failure in 2.9% of patients. Type 2 DM patients with various comorbidities receive the drug glimepiride/metformin Fixed Dose Combination (FDC) as a first-line therapy. As many as 68.2% of FDC patients achieved blood pressure within optimal limits. Most of the other patients experienced an increase in glycemic parameters and a change in body weight of about 18.4%. 59.2% of patients experienced weight loss (Ray et al., 2022). Glimepiride is a sulfonylurea class drug that has pharmacological effects to increase insulin production by pancreatic beta cells. The most common side effects are hypoglycemia and weight gain.

The limitation of this study is that data were taken only retrospectively from patient medical record data and did not make direct observations on DM patients.

#### CONCLUSION

Based on the analysis of demographic data and treatment profiles of DM patients, DM patients are dominated by the age group of 46-65 years, with women who use anti-diabetic drugs more. Patients with comorbidities use more anti-diabetic medications than patients with non-comorbid DM. Evaluation of anti-diabetic drugs ATC / DDD method shows that insulin glulisine (Apidra) is most used in DM patients with and without comorbidities. Through the DU method, 90% of glulisine, aspart, glargine, glimepiride, detemir, and metformin drugs were most widely used in DM patients.

230	
231	CONFLICT OF INTEREST
232	All authors declare no conflict of interest.
233 234 235 236 237	Ali, M.D. <i>et al.</i> (2022) 'Evaluation of drug utilization pattern and cost associated with diabetes mellitusType two management in Saudi Arabia', <i>Brazilian Journal of Pharmaceutical Sciences</i> , 58, p. E20681. Available at: https://doi.org/10.1590/s2175-97902022e20681.
238 239 240 241	Almasdy, D. <i>et al.</i> (2015) 'Evaluation of the Use of Anti-diabetic Drugs in Type-2 Diabetes Mellitus Patients in a Government Hospital of Padang City – West Sumatra', <i>Journal of Pharmaceutical &amp; Clinical Science</i> , 2(1), p. 104. Available at: https://doi.org/10.29208/jsfk.2015.2.1.58.
242 243	DiPiro, J.T. (ed.) (2020) <i>Pharmacotherapy: a pathophysiologic approach</i> . Eleventh edition. New York: McGraw Hill Medical.
244 245 246	Okoro, R.N., Nmeka, C. and Erah, P.O. (2018) 'Utilization study of antidiabetes medicines at a tertiary care hospital in Nigeria', <i>Future Journal of Pharmaceutical Sciences</i> , 4(2), pp. 109–115. Available at: https://doi.org/10.1016/j.fjps.2017.11.004.
247 248 249 250	Pitasari, N.W.N., Andayani, T.M. and Wijayanti, T. (2022) 'Evaluation of the Use of Antidiabetic Drugs in Patients of Back-Referral Program at the Demak District Pharmacy', <i>Journal of Management and Pharmacy Practice</i> , 12(2), p. 125. Available at: https://doi.org/10.22146/jmpf.73841.
251 252 253 254	Pollock, R.F. <i>et al.</i> (2011) 'The cost effectiveness of rapid-acting insulin aspart compared with human insulin in type 2 diabetes patients: an analysis from the Japanese third-party payer perspective', <i>Journal of Medical Economics</i> , 14(1), pp. 36–46. Available at: https://doi.org/10.3111/13696998.2010.541045.
255 256 257	Ray, S. <i>et al.</i> (2022) 'Usage Pattern of Glimepiride/Metformin Fixed-dose Combination in Type 2 Diabetes Patients with CVD or at Risk of CVD: An Experience in Indian Setting', <i>Asian Journal of Diabetology</i> , 23(2), pp. 13–19.
258	RI, K. (2017) 'Technical Guidelines for Evaluation of Drug Use in Health Facilities'.
259 260	Soelistijo, S.A. dkk. (2021) 'Guidelines for the management and prevention of adult type 2 diabetes mellitus in INDONESIA - 2021', <i>PB. PERKENI</i> , p. 119.
261 262 263	Svensson, AM. <i>et al.</i> (2017) 'Clinical effects, cardiovascular and renal outcomes associated with rapid-acting insulin analogs among individuals with type 2 diabetes: a nation-wide observational cohort study', <i>Clinical Diabetes and Endocrinology</i> , 3(1), p. 5. Available at:

**Comment [AR6]:** All English and all authors in references must be written in full

https://doi.org/10.1186/s40842-017-0043-2.

264

265	Tahar, N.dkk. (2020) 'EVALUATION OF THE USE OF ORAL ANTI-DIABETIC DRUGS IN TYPE
266	2 DIABETES MELLITUS PATIENTS USING ATC/DDD AND DU 90% METHODS', The
267	2nd Alauddin Pharmaceutical Conference and Expo (ALPHA-C) 2020 [Preprint]. Available
268	at: https://doi.org/10.24252/kesehatan.v1i1.18380.
269 270	WHO (2023) <i>Diabetes</i> . Available at: https://www.who.int/news-room/fact-sheets/detail/diabetes (Accessed: September 21, 2023).