Analysis Of Potential Drug Interactions In Prescribing Type 2 Diabetes Mellitus Patients At A Pharmacy In Medan City

Kiki Rawitri[1*], Sri Wahyuni[2], Syilvi Rinda Sari[3]

[1,2,3]Faculty of Pharmacy, Universitas Muslim Nusantara Al Washliyah
Medan, North Sumatera 20147, Indonesia
* Corresponding author:
Email: kikirawitri@umnaw.ac.id

Abstract.
Multiple drugs or polypharmacy received by patients with diabetes mellitus (DM) during therapy can trigger drug-related problems, one of which is drug interactions. The occurrence of drug interactions causes uncontrolled blood sugar levels which can affect the patient's morbidity, mortality, and quality of life. This study aims to look at the description of potential drug interactions in prescribing type 2 DM patients at a Pharmacy in Medan City for the period January-April 2022. This study is a descriptive study and data were taken retrospectively on 126 prescription sheets for type 2 DM patients who met the inclusion criteria. Identification of potential drug interactions using online literature such as Medscape Drug Interaction Checker, Drugs.com, and Drug Interaction Fact 2009 e-book. Data analysis was carried out univariately to describe the percentage of drug interactions. The results showed that from 126 prescription sheets for type 2 DM patients there were 108 patients (85.71%) who had the incidence potential drug interactions with a total of 238 potential drug interactions. The number of potential drug interactions based on the mechanism of action, namely pharmacodynamic interactions were 117 events (49.15%), pharmacokinetic interactions were 22 events (9.24%), and unknown were 99 events (41.61%) with The severity level was severe (major) with 1 event (0.42%), moderate (moderate) with 223 events (93.69%) and mild (minor) with 14 events (5.89%). Based on the results of the study, it was concluded that an analysis of 126 patients with type 2 diabetes mellitus, there were found 108 (85.71%) prescriptions to potential antidiabetic interactions.

Keywords: *Type 2 Diabetes Mellitus, Potential Drug Interactions, Antidiabetic Drugs, Prescription*

I. INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by an increase in blood glucose levels (hyperglycemia) resulting from a lack of insulin secretion, insulin action, or both [1]. The number of people with type 2 DM has increased significantly every year, this is evidenced by the incidence of type 2 DM in the world. Based on data published by the International Diabetes Federation (IDF) in 2019, type 2 DM sufferers in the world reached 463 million people and it is estimated that this will increase in 2030 to 578 million people. In Indonesia, based on Basic Health Research data, DM sufferers increased from 6.9% in 2013 to 10.9% in 2018 and according to the International Diabetes Federation (IDF), Indonesia is the seventh highest ranking in the world. The world that has DM sufferers with a total of 10.7 million people in 2019 [2,3].Blood glucose levels that are not controlled properly cause complications that interfere with health and cause death. Therefore, various treatments often occur for each symptom that appears, causing the administration of more than one drug and tends to encourage irrational treatment patterns by using more than one kind of drug that is not necessary, resulting in overprescribing or polypharmacy [4,5]. Treatment with several drugs at once (polypharmacy) can facilitate drug interactions [6].Polypharmacy is defined as the concurrent use of large amounts of drugs in 1 prescription by a patient but not according to the condition of the patient or the clinical effect indicated [7].

The risk of drug interactions and drug-induced problems increases with the use of multiple drugs [8]. In some clinical conditions, interactions between drugs can be beneficial to the patient, for example, antidotes are injected in cases of overdose), poor interactions (potentially harmful interactions that must be identified early), and unfavorable interactions (interactions that have a little clinical impact). and have a low risk) [9].The results of research conducted by Ariani and Prihandawati (2021) at a pharmacy in Banjarmasin showed that the number of drug combinations that had potential interactions based on the mechanism of action was 149 (39.52%), including pharmacodynamic interactions with as many as 74 events (48.05%), pharmacokinetic interactions were 33 events (21.43%), and unknown were 47 events (30.52%). Based on the severity level, the serious category was 1 event (0.65%), moderate was 121 (78.57%), and minor was 32 events (20.78%) [10]. The potential for drug interactions in type 2 DM patients at pharmacies still shows a

high category. Therefore, this study aims to determine the incidence of potential drug interactions that may occur, the mechanism of interaction, drugs that have the potential to interact, and the severity of their interactions in prescribing type 2 DM patients at a Pharmacy in Medan City.

II. METHODS

This research is a descriptive type of research with retrospective data collection on the prescription of type 2 DM patients in January-April 2022 at one of the Pharmacies in Medan City.The study population was all prescriptions containing antidiabetic drugs. The number of samples was obtained using the Slovin formula [11]. The minimum number of samples taken in this study was 124 prescription sheets and met the inclusion criteria. Inclusion criteria included: type 2 DM patient prescription sheets (both general prescriptions and National Health Insurance prescriptions) for the period January-April 2022 containing antidiabetic drugs, prescriptions containing 2 drugs, and containing at least one antidiabetic drug. Exclusion criteria included: prescription sheets for general patients and National Health Insurance patients outside the January – April 2022 period, prescription sheets that did not contain antidiabetic drugs, and illegible or unclear prescription sheets.Potential drug interactions were identified using online literature such as Medscape Drug Interaction Checker, Drugs.com, and Drug Interaction Fact 2009 e-book [12,13,14].

The drugs entered in the online literature are all drugs prescribed to patients, both drugs antidiabetic and non-antidiabetic. The data taken after the drugs were identified using the online literature Medscape Drug Interaction Checker and Drugs.com are details of the drugs that cause interactions, the severity, the mechanism of drug interactions, and the management of each interaction that occurs. Drug interactions that are taken focus on interactions between drugs and drugs.Data analysis was carried out by univariate analysis using descriptive analysis to see a brief description of the patient's characteristic data. The data used in the descriptive analysis are patient characteristics which include age, gender, comorbidities, and number of drugs prescribed. The results of the identification of potential drug interactions include a description of the incidence of potential drug interactions based on the mechanism of action and the severity that occurs. The results of univariate analysis are presented in terms of number and frequency (percentage).

III. RESULT AND DISCUSSION

1. Characteristics of Type 2 Diabetes Mellitus Patients

The number of prescription sheets for type 2 diabetes mellitus patients, both general patients and National Health Insurance patients at one of the Pharmacies in Medan City for the January-April 2022 period, was 126 sheets and met the inclusion criteria. Characteristics of type 2 DM patients based on prescription sheets can be seen in Table 1.

Table 1. Characteristics of Type 2 DM Patients Based on Prescription Sheets

Characteristic	Category	Number of Prescription Sheets for Type 2 DM Patients (n=126)	Percentage (%)
Gender	Male	56	44.44
	Female	70	55.56
Age	< 45 years	6	4.76
	45-65 years	101	80.15
	> 65 years	19	15.09
Number of drugs (R/)	< 5 drugs	44	34.92
	≥ 5 drugs	82	65.08
Comorbidity	Present	113	89.68
	Absent	13	10.32

Based on **Table 1**, it can be seen that the majority of patients with type 2 DM are 70 women (55.56%) while 56 people (44.44%) are male. Physically, women are more at risk of developing type 2 DM because they have a greater chance of increasing body mass index, due to premenstrual and postmenopausal syndromes, which make the distribution of body fat easy to accumulate due to hormonal processes. Therefore, the prevalence of DM in women is higher than in men [15].Menstrual disorders are important indicators that indicate impaired reproductive system function that can be associated with an increased risk

of various metabolic diseases, one of which is type 2 diabetes. This is because there are hormones that have antagonistic effects on blood glucose levels, namely estrogen hormone receptors on pancreatic cells which cause the release of insulin which plays an important role in glucose homeostasis in the blood [16].Based on the age category, it was found that the highest number of patients with Type 2 DM were at the age of 45-65 years, as many as 101 people (80.15%). The American Diabetes Association (ADA) states that people over the age of 45 have a higher risk factor for the development of the disease [17]. Based on the Basic Health Research, the prevalence of DM shows an increase with increasing age of the patient, which reaches its peak at the age of 55 to 64 years and decreases after passing this age range [3]. Someone who has reached the age of > 45 years has an increased risk of DM disease due to degenerative factors, namely decreased body functions [1].

Age over 40 years is an age at risk for Type 2 DM due to glucose intolerance and the aging process that causes a lack of pancreatic beta cells to produce insulin [18].The results showed that the majority of patients who received more than 5 drugs were 82 people (65.08%), followed by patients who received less than 5 drugs as many as 44 people (34.92%). Polypharmacy and combinations of several drugs in patients with type 2 DM may be unavoidable because apart from being used to control blood sugar levels, these drugs are also used to control several complications that arise in patients with type 2 DM [19]. Based on the research by Handayani et al (2019) on type 2 DM patients at the outpatient pharmacy at X Hospital, Central Jakarta, it was stated that the average number of drugs affected the incidence of potential drug interactions. The results showed that patients who received more than 5 drugs had 10.278 times higher risk of experiencing potential drug interactions. Increasing the number of drugs used can increase the risk of potential drug interactions [20].Based on the comorbidities suffered by type 2 DM patients, the results showed that the majority of type 2 DM patients had comorbidities as many as 113 people (89.68%), and 13 people without comorbidities (10.32%). These results are in line with research conducted by Fitriani et al. (2022) related to the analysis of potential antidiabetic drug interactions in inpatients with type 2 DM at PKU Muhammadiyah Gamping Hospital, Yogyakarta that as many as 88.30% of patients have comorbidities. The presence of comorbidities in type 2 DM patients will significantly affect the number of drugs prescribed [21]. Potential drug interactions based on the number of prescription sheets for type 2 DM patients can be seen in Table 2.

Table 2. Potential drug interactions based on the number of prescription sheets for type 2 DM patients

Incident of Interaction	Number of Prescription Sheets	Percentage (%)
With potential drug interaction	108	85.71
Without potential drug interaction	18	14.29

Based on **Table 2**, it was found that as many as 108 prescription sheets for type 2 DM patients (85.71%) had the potential for drug interactions to occur and as many as 18 prescription sheets (14.29%) did not have the potential for drug interactions. This is in line with the number of comorbidities in the prescription suffered by the patient according to the prescription. So that it can be seen that the number of prescriptions with possible interactions is higher than the number of prescriptions without drug interactions. Polypharmacy or administration of drugs >5 drugs in one prescription often occurs in elderly patients who require therapy for patients with chronic diseases such as diabetes and hypertension. Most drug interactions can be avoided and minimized with proper knowledge of pharmacodynamic and pharmacokinetic interactions because cardiovascular drugs should not be discontinued simply because of the potential for interactions. Steps that are often taken to treat drug interactions effectively are dose adjustment, monitoring of high-risk patients, or continuation of treatment if the drug effect is in optimal doses or there are no clinically relevant interactions [22].

2. Antidiabetic Drugs Use Profile

Antidiabetic drugs contained in the prescription of type 2 DM patients can be seen in **Table 3**.

Table 3. Antidiabetic drugs use profile

Type of Therapy	Drug Class/ Drug Type	Amount	Percentage (%)
Monotherapy	Insulin		
	- Glulisine/glargine/aspart/aspart protamine/detemir	41	32.53
	Sulfonylurea:		
	- Glimepiride	13	10.31
	Biguanide:		
	- Metformin	8	6.34
Total of monotherapy		**62**	**49.18**
Combination of 2 drugs	Sulfonylurea + Biguanide		
	- Glimepiride + Metformin	49	38.95
	- Glipizide + Metformin	4	3.17
	Sulfonylurea + Thiazolidinedion		
	- Glimepiride + Pioglitazone	1	0.79
	Sulfonylurea + Inhibitor alpha glucosidase		
	- Glimepiride + Acarbose	4	3.17
	Insulin + Sulfonylurea		
	- Insulin aspart protamine + Glimepiride	1	0.79
	Insulin + Biguanide		
	- Insulin aspart + Metformin	2	1.58
	DPP-4 inhibitor + Biguanide		
	- Sitagliptin + Metformin	1	0.79
Total Combination of 2 drugs		**62**	**49.18**
Combination of 3 drugs	Sulfonylurea + Biguanide + inhibitor alpha glucosidase		
	- Glimepiride + Metformin + Acarbose	2	1.58
Total Combination of 3 drugs		**2**	**1.58**
Total (all)		**126**	**100**

Based on **Table 3**, the most widely used type of oral antidiabetic therapy was a combination of a sulfonylurea group (glimepiride/glipizide) and a biguanide (metformin) in as many as 53 people (42.12%). Based on the ADA guidelines (2020), metformin is the first-line therapy for type 2 diabetes. Metformin belongs to the biguanide group with the mechanism of action of triggering peripheral tissue glucose uptake which increases insulin sensitivity, then suppresses glucose production in the liver, reduces free fatty acid oxidation, and reduces insulin resistance. increase the use of glucose in the intestine through a non-oxidative process [5]. In addition, the effectiveness of metformin to reduce glycemic levels is quite good (a decrease in HbA1c 1.0-2.0%), a low risk of hypoglycemia, and a lower cost [23]. The sulfonylurea group is known to be more effective in lowering blood sugar levels in patients whose pancreatic cell function produces insulin. The combination of these two drugs based on the mechanism of action can lower blood glucose more quickly than the use of a single oral antidiabetic. This is supported by research from The United Kingdom Prospective Diabetes Study in 2017 which states that the mechanism of action of this drug combination lowers blood glucose more quickly so that the combination of metformin with sulfonylurea can be recommended from the beginning of diabetes management [24]. A study conducted by Gumantara and Rasmi (2017) stated that a sulfonylurea-metformin combination was more effective in controlling hyperglycemia compared to monotherapy in patients with uncontrolled blood glucose. Combination therapy resulted in a greater reduction in HbA1c than monotherapy [25].

3. Potential Drug Interactions Based on Antidiabetic Drugs Used

Potential drug interactions based on antidiabetic drugs used can be seen in **Table 4**.

Table 4. Potential Drug Interactions Based on Antidiabetic Drugs Used

Drug Class	Total number of antidiabetic drugs (n= 289)	
	Interact (%)	Not Interacting (%)

Insulin:		
- Glulisine	14 (4,84)	4 (1,38)
- Glargine	38 (13,15)	5 (1,73)
- Aspart	34 (11,77)	2 (0,69)
- Aspart Protamine	9 (3,11)	2 (0,69)
- Detemir	5 (1,73)	1 (0,35)
Total	**100 (34,60)**	**14 (4,84)**
Sulfonilurea:		
- Glimepiride	77 (26,64)	4 (1,38)
- Glipizide	3 (1,04)	3 (1,04)
Total	**80 (27,68)**	**7 (2,42)**
Biguanide:		
- Metformin	56 (19,38)	25 (8,65)
Total	**56 (19,38)**	**25 (8,65)**
Thiazolidinedion		
- Pioglitazone	1 (0,35)	0 (0,00)
Total	**1 (0,35)**	**0 (0,00)**
Inhibitor alpha glucosidase		
- Acarbose	1 (0,35)	5 (1,73)
Total	**1 (0,35)**	**5 (1,73)**
Total (all)	**238 (82,35)**	**51 (17,65)**

The number of drugs used is the total number of drugs prescribed in type 2 DM patients. Based on the table, from a total of 126 prescription sheets, there are 289 antidiabetic drugs prescribed. Of the 289 antidiabetic drugs in all prescriptions, 238 antidiabetic drugs (82.35%) had the potential for drug interactions and 51 antidiabetic drugs (17.65%) had no potential for drug interactions.The potential drug interactions analyzed were the use of antidiabetic drugs with antidiabetic and non-antidiabetic drugs. The results showed that the most potential drug interactions occurred with the use of insulin-type antidiabetics with 100 events (34.60%), then the sulfonylurea group (glimepiride/glipizide) with 80 events (27.68%), followed by the biguanides (metformin) as many as 56 events (19.38%), and the thiazolidinedione group (pioglitazone) and alpha-glucosidase inhibitors (acarbose) each with 1 event (0.35%). Of the antidiabetic groups used, insulin is the majority of antidiabetics with potential drug interactions.

4. The Results of The Analysis of Potential Drug Interactions Based on the Mechanism and Severity

The results of the analysis of potential drug interactions based on the mechanism and severity can be seen **Table 5**.

Table 5. The Results of the Analysis of Potential Drug Interactions Based on the Mechanism and Severity

Drug Interaction Mechanism	Drug A	Drug B	Severity	Number of Incidence	Percentage (%)
Pharmaco-dynamic	Glimepiride	Bisoprolol	Moderate	7	2.94
		Hydrocortisone	Minor	1	0.42
		Levofloxacin	Mayor	1	0.42
		Metformin	Moderate	38	15.97
		Methylprednisolone	Moderate	1	0.42
		Ramipril	Moderate	3	1.26
	Glipizide	Bisoprolol	Moderate	1	0.42
		Metformin	Moderate	2	0.84
	Insulin aspart	Aspirin	Moderate	2	0.84
		Bisoprolol	Moderate	4	1.68
		Metformin	Moderate	1	0.42
	Insulin aspart protamine	Aspirin	Moderate	1	0.42
		Bisoprolol	Moderate	1	0.42
		Metformin	Moderate	1	0.42
	Insulin detemir	Aspirin	Moderate	1	0.42
		Bisoprolol	Moderate	1	0.42

	Insulin glargine	Aspirin	Moderate	1	0.42
		Bisoprolol	Moderate	4	1.68
		Fenofibrate	Moderate	3	1.26
		Furosemide	Moderate	2	0.84
	Insulin glulisine	Aspirin	Moderate	1	0.42
		Bisoprolol	Moderate	2	0.84
		Furosemide	Moderate	1	0.42
	Metformin	Amlodipine	Moderate	34	14.28
		Levofloxacin	Moderate	1	0.42
		Methylprednisolone	Moderate	1	0.42
		Nifedipine	Moderate	4	1.68
		Spironolactone	Moderate	2	0.84
	Pioglitazone	Simvastatin	Moderate	1	0.42
Pharmaco-kinetic	Glimepiride	Fenofibrate	Moderate	3	1.26
		Gemfibrozil	Moderate	2	0.84
		Omeprazole	Minor	6	2.52
		Ranitidine	Moderate	4	1.68
	Metformin	Acarbose	Minor	1	0.42
		Nifedipine	Minor	4	1.68
		Ranitidine	Moderate	2	0.84
Unknown	Acarbose	Sucralfate	Moderate	1	0.42
	Glimepiride	Furosemid	Moderate	2	0,84
		Meloxicam	Moderate	1	0,42
		Natrium diklofenak	Moderate	6	2,52
		Sucralfate	Moderate	2	0.84
	Insulin aspart	Candesartan	Moderate	18	7.56
		Fenofibrate	Moderate	3	1.26
		Furosemide	Moderate	2	084
		Gemfibrozil	Moderate	1	0.42
		Levothyroxine	Moderate	1	0.42
		Sucralfate	Moderate	2	0.84
	Insulin aspart protamine	Candesartan	Moderate	5	2.10
		Clozapine	Moderate	1	0.42
	Insulin detemir	Candesartan	Moderate	3	1.26
	Insulin glargine	Candesartan	Moderate	24	1009
		Gemfibrozil	Moderate	1	0.42
		Levothyroxine	Moderate	1	0.42
		Sucralfate	Moderate	2	0.42
	Insulin glulisine	Candesartan	Moderate	10	4.20
	Metformin	Folic acid	Minor	2	0.84
		Meloxicam	Moderate	1	0.42
		Ramipril	Moderate	1	0.42
		Sucralfate	Moderate	3	1.26
Total				**238**	**100**

Based on the **Table 5**, it is known that the potential for antidiabetic drug interactions occurs with the antihypertensive drug class, given that hypertension is the most common comorbidity in type 2 DM patients [26]. The most potential drug interactions that occur are between Injection of Insulin (Aspart/Aspart protamine/Glargine/Glulisine)-Candesartan as many as 52 events (21.85%), potential drug interactions Glimepiride-Metformin as many as 38 events, and Metformin-Amlodipine as many as 34 events (14.28%). These results are not different from the research conducted by Utami (2013) which showed that the types of antidiabetics, especially oral antidiabetics that often interacted were glimepiride and metformin. The sulfonylureas and biguanides affect insulin receptor sensitivity, so the combination of the two has a mutually supportive effect, where the sulfonylureas will start by stimulating pancreatic secretion which provides the opportunity for biguanides to work effectively, experience shows that the combination of these two groups can be effective in many diabetics who have diabetes previously not useful when used alone [27,28]. Types of drug interaction mechanisms and severity can be seen **Table 6**.

Table 6. Types of Drug Interaction Mechanisms and Severity

Drug Interactions Mechanism		
Type	**Number of Incidence**	**Percentage (%)**
Pharmacodynamic	117	49.15
Pharmacokinetic	22	9.24
Unknown	99	41.61
Total	**238**	**100**
Severity		
Type	**Number of Incidence**	**Percentage (%)**
Minor	14	5.89
Moderate	223	93.69
Mayor	1	0.42
Total	**238**	**100**

Based on the **Table 6**, it is found that the most common drug interaction mechanism is pharmacodynamics with 117 events (49.15%), followed by unknown interaction mechanisms with 99 events (41.61%) and pharmacokinetics with 22 events (9.24%). In pharmacodynamic interactions, the type of potential drug interaction with the highest number of occurrences was Glimepiride-Metformin with 38 events (15.97%), followed by Metformin-Amlodipine drug interactions with 34 events (14.28%). In interactions with an unknown mechanism, the most common type of potential drug interaction was Insulin-Candesartan injection with 52 events (21.85%), followed by Glimepiride-Diclofenac sodium with 6 events (2.52%). In the pharmacokinetic interactions, the most common type of potential drug interaction was Glimepiride-Omeprazole with 6 events (2.52%). The results of this study are not different from the research conducted by Ariani and Prihandiwati (2021) regarding the evaluation of the potential interactions of oral antidiabetic drugs at the Pioneer Pharmacy Kuripan Banjarmasin that there were 70.42% of patients who experienced drug interactions from 142 prescriptions with 47 pharmacodynamic interactions, 95%, unknown at 31.50% and pharmacokinetic interactions by 20.55% [10].In this study, there were 117 (49.15%) types of pharmacodynamic interactions, 22 (9.24%) types of pharmacokinetic interactions, and unknown interaction mechanisms 99 (41.61%) types of 238 identified potential drug interactions. It can be seen that the type of pharmacodynamic interaction is the most common interaction found in this study. Pharmacodynamic interactions constitute the majority of clinically important drug interactions. This indicates that the potential for interactions occurs more at the level of the receptor system, physiological system, or the same workplace, resulting in additive, synergistic, or antagonistic effects.

The occurrence of pharmacodynamic interactions can be predicted so that it can be avoided beforehand if the mechanism of action of the drug is known [28]. In contrast to pharmacokinetic interactions, pharmacodynamic interactions can be extrapolated to other drugs belonging to the same class as the interacting drug, because the classification of drugs is based on similarities in their pharmacodynamic effects. These interactions can usually be predicted from knowledge of the pharmacology of the interacting drugs [29].Based on **Table 6**, it was obtained that the severity of drug interactions that occurred the most was the moderate category with 223 events (93.23%). While the severity level is mild (minor) as many as 14 events (5.89%) and severe category (major) as many as 1 event (0.42%). The severity of the interaction can also provide insight into patient monitoring priorities. Based on the results of the study, it was found that the potential for drug interactions was dominated in the moderate category, so this was a concern for health workers, especially pharmacists and doctors. If the effects of drug interactions that occur can cause a decrease in the patient's clinical status, additional treatment, extension of treatment, discontinuation, or even a change of medication and hospitalization may be necessary. Interactions with moderate severity are usually drug combinations to be avoided, it is better to use the combination only in special circumstances. The severity of the severe category major has a major effect that can endanger lives or result in permanent damage. Moderate severity results in changes in the patient's clinical status. Minor severity has a less irritating effect and does not require additional therapy. So by knowing the severity of a drug interaction can prevent things that are not desired by the patient. The potential for moderate drug interactions is more common in some drugs (polypharmacy) than minor drug interactions.

In order to improve the quality of treatment for patients, it is better to avoid the use of concurrent drugs that cause the possibility of severe and moderate interactions, because the risk of interaction may be higher than the benefits obtained and it is also necessary to minimize the occurrence of unwanted drug interactions so that the goal treatment can be achieved [30].The incidence of potential drug interactions with moderate pharmacodynamic severity category is Glimepiride-Metformin. This potential interaction causes a hypoglycemic effect, where management for this potential interaction is that low doses of glimepiride are required when given concomitantly with metformin. Blood glucose should be monitored regularly and the patient should be educated regarding signs of hypoglycaemia such as dizziness, headache, drowsiness, nervousness, confusion, tremor, hunger, weakness, palpitations and tachycardia.In pharmacokinetics, one of the potential drug interactions found in this study is between Metformin-Ranitidine. Concomitant use of metformin and ranitidine has the potential to enhance the effects of metformin by reducing renal clearance by inhibiting renal tubular secretion of metformin. Ranitidine decreased metformin renal clearance by 27% and increased AUC by 50%, thereby increasing metformin plasma levels and pharmacological effects. Therefore, it is advisable to change therapy. Ranitidine decreased metformin renal clearance by 27% and increased AUC by 50%. Taking metformin with ranitidine has the potential to cause a life-threatening condition called lactic acidosis. This causes weakness, increased drowsiness, slow heart rate, slow heart rate, muscle pain, shortness of breath, stomach pain, dizziness and fainting [14,31].The potential for drug interactions with the highest severity of mild category is Glimepiride-Omeprazole with pharmacokinetic mechanism of drug interaction. It is known that glimepiride is a substrate of the CYP2C9 enzyme, meaning that glimepiride is metabolized by the CYP2C9 enzyme.

Omeprazole is one of the inhibitory agents of the CYP2C9 enzyme, so when given together with glimepiride, omeprazole can inhibit glimepiride metabolism. This causes an increase in the serum concentration of glimepiride which results in an increase in the hypoglycemic effect. Patients receiving this combination are advised to regularly monitor blood sugar levels, provide education on how to recognize and treat hypoglycemia (eg, headache, dizziness, drowsiness, nausea, tremors, hunger, weakness, or palpitations), inform the doctor if this occurs. occurs, and a dose reduction of glimepiride is required [32].The most mayor category interactions were Glimepiride – Levofloxacin. Levofloxacin may interfere with the therapeutic effect of insulin and other antidiabetic agents. The use of quinolones has been associated with impaired blood glucose homeostasis stemming from effects on the ATP-sensitive potassium channels of pancreatic beta cells that regulate insulin secretion. Both hyperglycemia and hypoglycemia have been reported, usually in diabetic patients receiving concomitant treatment with oral hypoglycemic agents or insulin. Although hyperglycemia is significantly more common and infection itself may be an underlying risk factor, hypoglycemia can lead to greater morbidity and mortality. Management of this potential interaction i.e. blood sugar levels should be monitored appropriately, especially in patients who are elderly, have renal impairment, or are seriously ill. Patients should be advised if there is an increased risk of dysglycemia which has the potential for headache, dizziness, drowsiness, nervousness, unconsciousness, tremor, hunger, fatigue, dyspnea, palpitations and tachycardia. Avoid quinolone antibiotics in patients receiving sulfonylurea therapy, and alternative antibiotics are needed [14].

IV. CONCLUSION

Based on the results of the study, an analysis of 126 patients with type 2 diabetes mellitus found 108 (85.71%) prescriptions suspected to be antidiabetic interactions at a Pharmacy in Medan City.

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