International Journal of Global Sustainable Research (IJGSR)
Vol.1, No.3, 2023: 325-342

Problems Treatment Type II Diabetes Mellitus Patients with PCNE 9.1 and Correlation to Therapy Outcomes

Okky Intan Mawarni[1]*, Rina Herowati[2], Samuel Budi Harsono[3]
University Setia Budi
Corresponding Author: Okky Intan Mawarni okky10969@gmail.com

A R T I C L E I N F O
Keywords: T2DM, DRP'S, PCNE 9.1, Length Of Stay, Outcome Treatment

Received : 10, September
Revised : 12, October
Accepted : 15, November

A B S T R A C T
Drug-Related Problems in T2DM patients based on patient therapy patterns with or without comorbidities. DRP analysis is based on PCNE 9.1 guidelines analysing the domains causing problems in treatment, then bivariate data analysis (chi-square) to test the relationship between results and DRP type and continued with a multivariate test to see the connection between results and DRP type. The research results were three related variables related to DRPs and LOS, 15 cases of errors in drug selection, and eight instances of errors of treatment duration due to the absence of initiation of maintenance doses. Dose selection errors occurred in year 16, caused by an amount too low. It is recommended to research analysis prospectively so that the status of DRPs can be determined.

INTRODUCTION

Diabetes Mellitus (DM) is still a major health problem in the world, based on data International Diabetes Federation (IDF, 2019) DM prevalence has doubled in the last 19 years from 4.6% in 2000 to 9.5% in 2019. In 2018, the prevalence of DM in the population aged ≥ 15 years was 2% higher compared to 2013 data, namely 1.5 %, currently, there are around 463 million people worldwide suffering from diabetes and if this continues, it is estimated that as many as 700 million people aged 20-79 years will suffer from diabetes in 2045 (Saeedi et al., 2019).

Drug Related Problem (DRP) is a problem that arises from a condition in the implementation of patient therapy that causes, or has the potential to cause, not achieving optimal therapeutic results due to various factors. (Furqani et al., 2015). DM is involved in as many as 10% of deaths in patients with hypertension and other comorbidities, so there is a need for aggressive management of DM patients to prevent and inhibit disease progression and complications(Mengesha, 2007). DM therapy is a long-term treatment due to chronic hyperglycemia, impaired insulin secretion or action and functional disorders of various tissues and organs (Harreiter and Roden, 2019). DM patients with complications from other diseases, long-term medication consumption can increase side effects so that, this will affect the outcome of the therapy given. (Joddy et al., 2020).

DRPs are associated with increased health care and hospitalisation costs, reduced quality of life, and increased mortality (Naples et al., 2016; Salvi et al., 2012). Identification, resolution, and prevention of DRP are core processes of pharmaceutical care. To treat DRP, the cause must be identified, and the DRP must be appropriately classified. For this purpose, DRP classification is essential. Increased LOS in type 2 diabetes patients has been known to be caused by comorbidities such as congestive heart failure, dementia, peptic ulcers, liver disorders and kidney disorders. (Enomoto et al., 2017). Treatment of T2DM patients may increase with age (Raval et al., 2015), ICU surgery (Dungan, 2012), nosocomial infections (Dryden et al., 2015), and many therapeutic indications (Huang et al., 2015). Meanwhile, research conducted by Linkeviciute et al. (2020) states that people with Type 2 DM have a higher risk of death in women compared to men. However, it is also at stake in patients diagnosed with juvenile T2DM because they have a longer duration of diabetes and require treatment with insulin as a life-saving agent. (PERKENI, 2021).

This study aimed to analyse patterns of drug use and their influence on the therapeutic outcomes of type II diabetes mellitus patients based on length of stay. The novelty of this research is the DRP's analysis method with the latest version, namely PCNE 9.1, which was released in 2022, and there have been no other studies that have linked the results of DRP's analysis with PCNE 9.1 by testing the effect of T2DM treatment with therapeutic outcomes.

THEORETICAL REVIEW

DRPs PCNE 9.1

Drug Related Problems (DRPs) have the potential to worsen clinical outcomes in patients in critical care. Sick patients are generally more susceptible

to harm from medication-related problems due to frequent duplication of medication or polypharmacy in treatment and a complex clinical course. (Tharanon et al., 2022). PCNE is defined by Ahmed et al., (2021) as an event or circumstance involving drug therapy that actually or has the potential to interfere with desired health outcomes. The commonly used PCNE classification consists of Domain and subdomain classification, which allows each type of DRP to be coded; DRPs can be differentiated based on their style, cause, pharmacist intervention, acceptability of the intervention by the doctor, and DRP status. The DRPs of each category are clearly defined. PCNE has been validated and regularly updated and is easily translated into various languages (Koubaity et al., 2019)

PCNE, released in May 2020 at version 9.1, is essential in identifying and resolving DRPs improving the safety of complex treatments for various diseases. According to a study by Hasan et al. (2018), the factors that cause DRPs in T2DM patients are that most patients have comorbidities, so they need other drugs during treatment to overcome the disease problem. In this study, the number of patients using drugs was ≥5 types of medicines or polypharmacy. The occurrence of polypharmacy can cause drug problems in the form of adverse drug reactions and drug interactions. However, drug problems due to polypharmacy can be avoided.

H1: What are the types of DRPs in the treatment of T2DM patients through the PCNE version 9.1 study

Correlation of DRPs with Inpatient Care

Length of hospitalisation has been known to increase the cost burden of type 2 diabetes. Increased LOS in type 2 diabetes patients has been known to be caused by comorbidities. The length of stay for type 2 diabetes patients can also increase due to age (Raval et al., 2015), emergency surgery (Dungan, 2012), nosocomial infections (Dryden et al., 2015), hospital payment methods, and therapeutic efficacy (Huang et al., 2015). Research conducted by Rahmawaty (2020) states that DRPs influence the length of hospital stay on therapy outcomes.

H2: How does DRP's correlate with LOS and therapeutic outcomes in T2DM patients

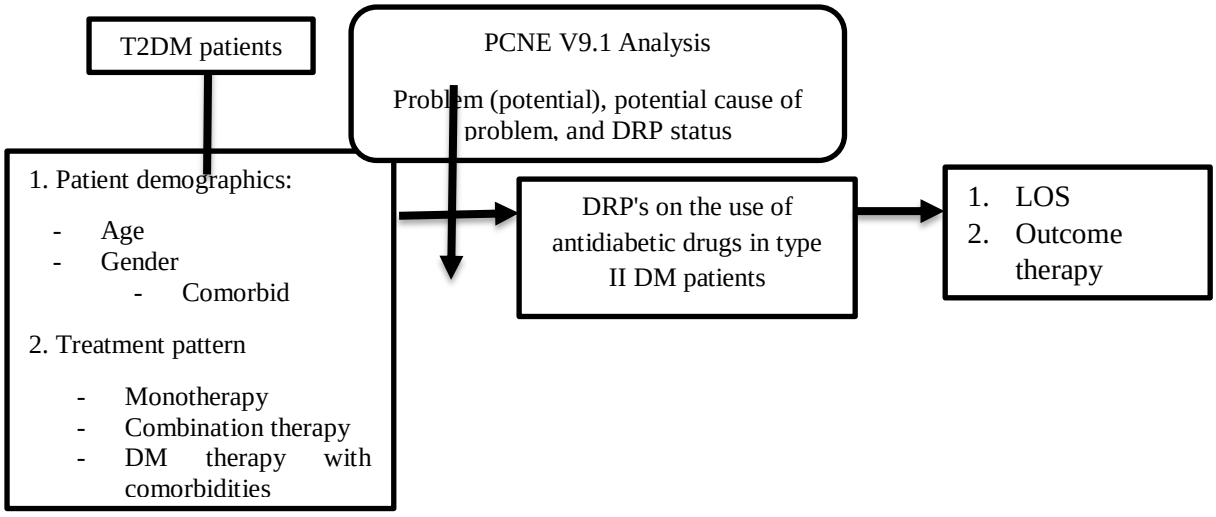

Figure 1. Conceptual Framework

METHODOLOGY

This study was a retrospective observational study with a cross-sectional data collection design aimed at analysing the use of antidiabetics and their correlation with therapeutic outcomes in Type 2 DM patients hospitalised. The data was from 01 January 2022 to 30 December 2022. The sampling technique was carried out using purposive sampling; the population was selected based on the inclusion criteria, and then the samples were analysed for DRP's status using PCNE 9.1 for correlation with therapeutic outcomes with level parameters blood sugar analysed using multivariate SPSS.

The target population in this study was Type 2 DM patients inpatients at Dr Moewardi Hospital Surakarta, Central Java, in 2022. The sample used in this study were Type 2 DM patients inpatients at Dr Moewardi Hospital Surakarta, Central Java, taken in March – July 2023. The number of samples is 95.85, rounded up to 100 pieces. Ethical Consideration in this research was opened in honest compliance Number: 390/ III / HREC / 2023 by the Health Research Ethics Commission.

RESULTS

Respondent characteristics

The frequency distribution of respondent characteristics can be seen in Table 1:

Table 1. Frequency Distribution of Respondent Characteristics

NO	Characteristics	Frequency	Percentage
1	**Age**		
	<45 y.o	13	13%
	>45 y.o	87	87%
2	**Gender**		
	Male	54	54%
	Female	46	46%
3	**Concomitant Diseases**		

NO	Characteristics	Frequency	Percentage
	Exist	97	97%
	None	3	3%
4	**LOS**		
	1-3 day	23	23%
	4-7 day	39	39%
	8-11 day	25	25%
	12-19 day	13	13%
5	**Outcome therapy**		
	Achieved	100	100%
	Not achieved	0	0%

Treatment pattern

The treatment patterns of T2DM respondents in this study were differentiated into monotherapy and combination therapy, as in Table 2 below:

Table 2. Characteristics of Treatment Patterns of T2DM Patients

NO	Characteristics	Frequency	Percentage
1	**Number of Medicine Items received**		
	<5 drugs	10	10%
	Five drugs	9	9%
	>5 drugs	81	81%
2	**Treatment Patterns**		
	Monotherapy	64	64%
	Combination Therapy	36	36%

T2DM respondents in this study received T2DM therapy as follows:

Table 3. Data on T2DM Drugs for Patients

Therapy pattern	Drugs	Amount	Percentage
Monotherapy			
Biguanide	Metformine	32	32%
Sulfonylureas	Glimepiride	1	1%
Alpha-glucosidase	Acarbose	1	1%
Insulin	Human premixed : Ryzodeg	30	30%
	Fast-acting analogue: Insulin aspart (Novorapid) Insulin glulisine (Apidra) Insulin lispo (Humalog)		
	Long-acting analogue: Insulin detemir (Levemir)		
Combination Therapy			
Oral antidiabetic	Sulfonilurea + alfaglucosidase inhibitor	7	7%

Therapy pattern	Drugs	Amount	Percentage
	+ biguanide + DPP4 inhibitor + biguanide+ SGLT2		
Oral antidiabetic+insulin	Biguanide + insulin aspart	21	21%
Insulin+insulin	Insulin aspart + insulin gargine + insulin premix + insulin detemir + insulin gluisin Insulin lispo + insulin detemir + insulin glargine	8	8%
TOTAL		**100**	**100%**

PCNE 9.1

The types of DRPs in the therapy of type 2 DM patients through the PCNE version 9.1 study can be seen in the table below:

Table 4. Potential Causes of DRPs (including possible causes for potential problems)

Code	Classification of Problem Causes	Amount	%
C1	**Selection of drugs**	16	38%
C2	The causes of DRP can be related to the choice of medication	**1**	2%
	Drug dosage form		
C3	Penyebab DRP terkait dengan sediaan obat	**16**	38%
	Pemilihan Dosis		
C4	The causes of DRP are related to drug preparation	**8**	18%
	Duration of treatment		
C6	The causes of DRP are associated with the length of treatment	**1**	2%
	Process of drug use The cause of DRP is related to the way the patient received the drug administered by a health professional or nurse, despite the proper instructions (on the label)		
	Total interactions	**42**	**100%**

Inappropriate drug combinations related to the use of antidiabetic drugs with other drugs can be seen in Table 5.

Table 5. Drug interactions for T2DM patients

Interactions	N	**Unwanted Reaction** (Claire L Preston, 2015)	**Happened/didn't happen**
Nifedipine + furosemide	4	***Calcium Channel Blockers*** can be prescribed for patients with hypertension. This drug can treat	Happened

Interactions	N	Unwanted Reaction (Claire L Preston, 2015)	Happened/didn't happen
		hypertension appropriately but can also cause peripheral oedema if given simultaneously with furosemide, which can cause hypokalemia.	
Ramipril + allopurinol	5	***Angiotensin Converting Enzyme Inhibitor*** + **Allopurinol**, the occurrence of cases of hypersensitivity if given simultaneously.	Didn't
Ranitidine + metformine	1	**Antidiabetes + Antagonis reseptor H2** Metformin and ranitidine may reduce metformin clearance and contribute to cases of metformin-associated lactic acidosis.	Happened
Antidiabetic + clonidine	1	**Antidiabetes + *clonidine*** Clonidine may be able to suppress signs and symptoms of hypoglycemia in people with diabetes. It is suspected that an interaction will occur if there is interference with diabetes control in patients given clonidine.	Didn't
Antidiabetics + methylprednisolone	3	**Antidiabetes + Kortikosteroid** Significant hyperglycemia has been seen with systemic corticosteroids and in cases with high-dose inhaled corticosteroids or high-potency topical corticosteroids.	Didn't
Glibenclamide + Co-trimoxazole	1	**Antidiabetik + Kotrimoksazol** Acute hypoglycemia has occurred in patients administered various sulfonylureas and co-trimoxazole, although pharmacokinetic studies have not demonstrated an interaction.	Happened
Antidiabetics + furosemide	17	***Loop diuretik*** Diabetes control is usually not significantly impaired by ethacrynic acid, furosemide, or torasemide, although some reports indicate that ethacrynic	Happened

Interactions	N	Unwanted Reaction (Claire L Preston, 2015)	Happened/didn't happen
		acid and furosemide may occasionally increase blood glucose levels.	
Antidiabetics + thiazide diuretics	3	**Diuretik *thiazide*** By increasing blood glucose levels, thiazides and related diuretics may reduce their antidiabetic effects and impair diabetes control. Hyponatremia has rarely been reported with chlorpropamide combined with thiazides and potassium-sparing diuretics. If this occurs, the dose can be reduced.	Didn't
Antidiabetics + glimepiride	3	**Antidiabetes + Fibrat, Sulfonylurea atau Insulin** Several reports describe hypoglycemia and increased effects of insulin and sulfonylureas in patients given fibrates. Patients should be warned that excessive hypoglycemia occurs occasionally and cannot be predicted.	Happened

Table 6. Relationship between types of DRP's and LOS

Types of DRP's	*Length Of Stay* (LOS) Occurred (day)				Didn't happen (day)				P-value	Conclusion
	1-3	**4-7**	**8-11**	**12-19**	**1-3**	**4-7**	**8-11**	**12-19**		
Drug selections	15	0	0	0	23	39	25	13	0.00	Relate
Duration treatment	8	0	0	0	15	39	13	92	0.00	Relate
Selection of preparations	1	0	0	0	22	39	25	13	0.33	Not related
Process of drug use	2	0	0	0	21	39	25	13	0.07	Not related
Dosage selection	16	0	0	0	23	39	25	13	0.00	Relate

DISCUSSION

There were more males than females, namely 54% (N: 100) in this study; this is synergistic with the global prevalence, which states that males dominate the T2DM population. Gender differences also characterise the prevalence of type 2 diabetes. Gender differences in the majority of diabetes are related to reproductive life: that is, more men have diabetes before puberty, whereas more women have diabetes after menopause and in old age (IDF, 2021). T2DM is prone to disease complications; in this study, 97% of patients with comorbidities with severe disease severity, including the majority of T2DM patients, also experience acute or chronic difficulties (PERKENI, 2021) Hyperglycemia is associated with several potentially life-threatening microvascular and macrovascular complications, including heart failure, coronary artery disease (CAD) and chronic kidney disease (CKD). Because of its difficulties, diabetes poses a risk of reduced quality of life and a high economic burden, making it a critical chronic disease to manage (Soeatmadji et al., 2023).

Treatment pattern

The number of drugs received by patients in this study was divided into three main classifications. Namely, 10% of patients received <5 drug items, 9% of 5 drug items, and 81% of >5 drug items; this was caused by a critical condition at the time the patient Admission varies greatly, geriatric conditions are also a factor in patients receiving many drugs at one time. Type 2 diabetes mellitus (T2DM) is a considerable cause of polypharmacy, explained by the need to treat microvascular and macrovascular complications but also by the presence of clusters of comorbidities. Elderly diabetes patients are at particular risk for polypharmacy for various reasons: Multimorbidity (arterial hypertension, solid or haematological malignancies, chronic heart failure, etc.), age-related pharmacokinetic variability in the setting of liver or kidney disease, lack of compliance (voluntary or involuntary— in mental disorders), and others. Additionally, elderly patients are more likely to use over-the-counter medications and herbal supplements, which can lead to drug interactions (Annani-Akollor et al., 2019; Lipska et al., 2016; Mortazavi et al., 2016; Noale et al., 2016).

The use of monotherapy in this study was 64%, and combination therapy was 36%; this condition is because T2DM is a secondary diagnosis, so blood sugar can still be controlled by administering monotherapy with metformin. Clinically, metformin is recommended as first-line glucose-lowering therapy, along with lifestyle changes. The use of monotherapy is generally considered a first-line treatment option for reasons of relatively good treatment effectiveness, minimal hypoglycemia, safe service for obese patients, improved cardio outcomes in respondents with heart comorbidities, and cost-saving drug prices.

Meanwhile, considerations for choosing combination therapy are generally related to the reasons for varying drug prices. Most respondents with combination therapy are patients with duplicate comorbid diseases or T2DM as a comorbid. Hence, the drugs used vary in type and price. According to PERKENI, it is explained that the first line used in combination therapy is low-dose metformin or thiazolidinedione, or it can also be acarbose. However,

suppose a patient receives a combination of 3 drugs simultaneously as an oral antihyperglycemic drug, and the output does not reach the therapeutic target. In that case, they can use a variety of insulin or a combination of DPP4 or SGLT2 inhibitors.

The choice of metformin monotherapy as the primary line, according to instructions (American Diabetes Association, 2022), of various pharmacological agents have been evaluated for diabetes prevention, and metformin has the most robust evidence base. First-line therapy depends on comorbidities, patient-centred treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification. Other medications (glucagon-like peptide 1 [GLP-1] receptor agonists, sodium-glucose cotransporter 2 [SGLT2] inhibitors), with or without metformin based on glycemic requirements, are appropriate initial therapy for individuals with type 2 diabetes with or at risk of high for atherosclerotic cardiovascular disease (ASCVD), HF, and chronic kidney disease (CKD). Metformin should be continued after initiating insulin therapy (unless contraindicated or not tolerated) for ongoing glycemic and metabolic benefits.

The most common combination of therapy in this study was metformin and insulin aspart, as much as 21%, where insulin aspart is an analogue of human insulin with the mechanism of inhibiting liver glycogen synthesis and encouraging blood glucose absorption, thereby normalising blood glucose levels. (Fullerton et al., 2018). However, insulin aspart has some disadvantages, such as fast elimination speed and short average residence time; metformin reduces blood glucose levels, reduces body weight, and protects heart health in T2DM patients (Zhao et al., 2022)

In research by Zhao et al. (2022), miglitol and metformin were combined with insulin aspart. Their effectiveness and reliability in the treatment of T2DM were compared. These results indicate that treatment with the combination of miglitol and insulin aspart is suitable for T2DM patients with uncontrolled blood sugar levels. In contrast, combination treatment with metformin and insulin aspart is ideal for patients who want to lower blood sugar and blood fat through weight loss and patients with cardiac and renal insufficiency. Meanwhile, research by Zhao et al. (2022) explained that metformin combined with insulin aspart to treat gestational DM and chronic hypertension can effectively control blood glucose and blood pressure levels and reduce the risk of adverse perinatal and neonatal outcomes, which has a positive effect on clinical treatment.

PCNE 9.1

1. *Problems in Selection of Dosage Forms*

DRP's errors that occurred due to dosage form errors in this study were 2%, which was caused by the patient experiencing dysphagia (difficulty swallowing) and the patient's age was 75 years; the patient's medical record said so, but the dose of the oral dosage form was not replaced with an intravenous or liquid one. Dysphagia occurs most frequently in the elderly population because the ageing process can negatively impact the swallowing process's oral, pharyngeal, and oesophagal phases. It worsens with reduced

saliva production (Fusco et al., 2015). Difficulty swallowing can lead to malnutrition, weight loss, and dehydration. At the same time, food and fluids that enter the respiratory tract can trigger respiratory infections. In patients over 65 years of age, the prevalence of dysphagia ranges from 7% to 13%,10–12 a percentage that increases with age and if the patient has had a stroke, postoperative cognitive dysfunction, or neurodegenerative diseases such as Parkinson's and dementia.a (Michelle, 2011; Setacci C et al., 2015)

2. *Drug Selection Problems*

In this study, all the drugs recorded in the medical record were indicated; however, oral use of multivitamins sometimes triggered side effects related to ADME, so it was essential to switch the route of drug administration via the vein. Still, some drugs were only available in oral form. So, this must be re-examined regarding the administration of multivitamins, which can be given intravenously to minimise the occurrence of polypharmacy, considering that the patients in this study were predominantly elderly.

3. *Drug Dosage Problems*

In this study, there are indications that the dose is too low and the dosing regimen is not frequent enough, thus requiring continuity of drug administration by therapeutic guidelines so that the interval for administering the drug is by the therapy required. No dose was too high in this study, but there were indications of giving the wrong amount for metformin therapy. The choice of amount in the survey, 38% of respondents, caused by the metformin dose being too small at 500 mg per day after seven days of treatment. Glucose effects increase with increasing metformin dose, with either immediate-release or delayed-release formulations. The maximum recommended dose of metformin is 2000 mg daily in the US. However, the maximum daily dose of metformin recommended in Europe and other regions is 3000 mg. A landmark study, the UK Prospective Diabetes Study (UKPDS), applied an average daily dose of 2550 mg/day in people with newly diagnosed T2DM (Madsen et al., 2019)

The therapeutic range for serum metformin concentrations was extrapolated from studies of diabetes-related glycemia. Based on several studies, it can range from 0.1 to 20.7 (median 4.5) µmol/L13.15–17 if kidney function is not impaired for an average drug dose of 1500 mg/day (Sutkowska et al., 2021). Research by Sutkowska et al. (2021) showed that 20 patients with a new diagnosis of pre-DM were treated with a final dose of metformin 1500/day for 15 weeks; the other 9 (for three weeks) took a higher amount: 3000 mg/day (3 × 1000 mg). However, these nine patients experienced a wash-out period with a dose reduction of up to 1500 mg/day. No patients reported significant drug side effects. Studies have shown that after a reasonably short treatment period (6 weeks after the start of treatment, four weeks from the final regimen of 1500 mg/day), patients with prediabetes reached therapeutic metformin concentrations, which are associated with glycemic effects in diabetes. Metformin in the study was taken as 1500 mg/day in regular form (three times

a day 500 mg with a time interval stated by respondents of around 8-10 hours). So, in this study, a maintenance dose of 3x 500 can be given.

4. *Treatment Duration*

This research indicates that treatment therapy is too short when using metformin therapy. Considering that metformin is the first line choice in the presence of T2DM, there is a minimum risk of hypoglycemia, 25%, and without consideration of body weight. Long-term use of metformin minimises complications for the kidneys and eyes (RACCP, 2021). Initiation of the first dose of metformin is 500-850 mg per day, but in the patient's medical records, there is no initiation of dose continuation; the therapeutic dose is generally individualised and can be started first with a low amount of 500 mg per day which is then increased gradually after 2-3 weeks with additional 500 mg per week or 850 mg per two weeks until blood sugar control is achieved or does not exceed the maximum dose of 2,550 mg per day or by administering metformin 500 mg in the form of a slow-release preparation (Nathan et al., 2009)

Based on research conducted on patients with type 2 diabetes mellitus at Undata Regional Hospital, Central Sulawesi Province, 18 people (100%) found that the drug that was widely used was the biguanide group, namely the drug metformin. According to (Jonathan & Natalia, 2017), 25 patients (21,7%) only used metformin at the Bandung City Regional Hospital. Metformin is the first-line therapy for type 2 DM patients, which mainly reduces gluconeogenesis and increases glucose uptake in peripheral tissues by 10-40%.

Meanwhile, in research conducted by Porter *et al*. (2014) At Pekanbaru District Hospital, respondents used metformin 500 mg twice a day with a daily dose of 1000-1500 mg/day with a total of 53 respondents (55.2%). Research (Almasdy et al., 2015) shows that metformin can reduce LDL (Low-Density Lipoprotein) levels. Evaluating LDL levels using single metformin showed an average initial LDL of 148.22 mg/dl and a decrease in evaluation of 133.56 mg/dl. There was a significant reduction in LDL levels in patients who received metformin alone at a P value (0.0001). Initial LDL levels were 111 mg/dl, and final LDL levels were 102 mg/dl. Metformin could reduce LDL levels by 9%, whereas in this study, metformin reduced levels of LDL by 14.66%; this was because the number of samples used was different.

5. *Problems with the Drug Use Process*

There is no indication that the time of administration or dosing interval is incorrect, the drug is not given, the drug is given excessively, the drug is not given at all, the wrong drug is given, and the drug is given via the wrong route. However, there are indications that the patient used medication for self-consumption before arriving at the hospital. The geriatric population is at high risk for drug-related problems (DRPs) due to age-related changes in pharmacokinetics and pharmacodynamics. Additionally, a higher incidence of drug-related problems may result from the increasing prevalence of age-related chronic diseases, leading to the use of complex therapeutic regimens. (Vos et al., 2016). According to the Pharmaceutical Care Network of Europe (PCNE), DRP is defined as "an event or circumstance involving drug therapy that actually or

has the potential to interfere with a desired health outcome" (PCNE 2019). DRPs are associated with increased health care and hospitalisation costs, more extended hospital stays, reduced quality of life, and increased mortality (Naples et al., 2016; Salvi et al., 2012). Therefore, the prescribing and use of medications in older patients requires special considerations, including avoidance of inappropriate medicines, rational use of indicated drugs, monitoring for side effects, prevention of drug-drug interactions, and evaluation of patient compliance and engagement.

Problems with the drug use process in the study, as many as 2% of respondents, were due to digestive issues due to previous self-medication with herbal medicines. This was written in the medical records of respondents whose elderly age made it possible for them to be unable to tolerate herbal preparations well. The use of medicinal plants or their metabolites has increased significantly worldwide: research by scientific groups has also progressed, demonstrating their effectiveness in treating diseases with minimal or no side effects. People are convinced that natural products are less dangerous than synthetic drugs because they are of natural origin; that is, "if it is not good, it is not bad." However, herbal medicines and supplements contain chemical compounds whose interactions may produce the same benefits or risks as other pharmacologically active compounds, both natural and synthetic (Asher et al., 2017). Therefore, individuals, especially patients exposed to polypharmacy regimens, should be alert to drug-drug, herb-herb, herb-food, or herb-drug interactions.

The relationship between the type of DRPs and LOS in this study is found in the problem of drug selection, the problem of the duration of the drug given, and problems related to the dose of the medicine given. Issues with drug selection in this study can be caused by inappropriate use of drugs as a problem in geriatric patients; geriatrics are the target of wrong prescribing errors such as Adverse Drug Reactions, Drug-Drug interactions, Adverse Drug Events, etc. Improper drug administration increases the incidence of ADEs, treatment failure, hospitalisation, death, and medical costs (Hamilton et al., 2009). Generally, the elderly drug selection is the key to minimising DRPs.

Polypharmacy also influenced interactions between drugs in this study due to the presence of comorbid coronary kidney failure (CKD) in 4%, atrial fibrillation in 3%, stroke (2%), hypertension (28%), heart failure (2%), and cervical cancer (1%). Polypharmacy, generally defined as the concurrent use of 5 or more medications (Gnjidic et al., 2012; Masnoon et al., 2017), is increasingly prevalent as the population ages. A recent population-based study estimated the prevalence of polypharmacy among older Australians to be high (36%), with the most senior elderly (aged 85 years or older) most affected. Polypharmacy rates were even higher in hospitalised patients (76%)(Hubbard et al., 2015). The Centers for Medicare and Medicaid Services (CMS) defines polypharmacy as concurrent prescriptions for inappropriate use of medications, medications without a clinical indication, or patients receiving 3 to 5 or more pills in the elderly population due to duplication of illnesses requiring more of one drug for treatment (Hoel et al., 2021). Problems in choosing the duration of

the drug occurred due to errors related to the treatment given in this study; there were 16 incidents caused by too small a dose or the absence of a maintenance dose for antidiabetic drugs.

CONCLUSIONS AND RECOMMENDATIONS

Demographic characteristics of type 2 DM patients are age, gender, length of stay and comorbidities. Treatment patterns are monotherapy, combination therapy, and therapy according to comorbidities. The types of DRPs in treating type 2 DM patients through the PCNE version 9.1 study are errors in drug selection, drug preparation selection, dose selection, treatment duration, and the drug administration process. There is a correlation between the type of DRP's duration of drug use, drug dose, and drug selection on the LOS of therapy for type II DM patients.

FURTHER STUDY

Every research is subject to limitations; thus, you can explain them here and briefly suggest further investigations.

ACKNOWLEDGMENT

I want to express my thanks for this research to Dr Moewardi Surakarta and all parties involved in the study. This research did not receive funding from any party and used personal funds to carry out the research.

REFERENCES

Ahmed, K. O., Muddather, H. F., & Yousef, B. A. (2021). Pharmaceutical Care Network Europe (PCNE) Drug-Related Problems Classification Version 9.1: First Implementation in Sudan. *Journal of Pharmaceutical Research International*, 699–706. https://doi.org/10.9734/jpri/2021/v33i59a34321

American Diabetes Association. (2022). Standards of Medical Care in Diabetes - Abridged for Primary Care Providers. *Clinical Diabetes*, *40*(1), 10–38. https://doi.org/10.2337/cd22-as01

Annani-Akollor, M. E., Addai-Mensah, O., Fondjo, L. A., Sallah, L., Owiredu, E.-W., Acheampong, E., & Akamugri, S. (2019). Predominant Complications of Type 2 Diabetes in Kumasi: A 4-Year Retrospective Cross-Sectional Study at a Teaching Hospital in Ghana. *Medicina*, *55*(5), 125. https://doi.org/10.3390/medicina55050125

Asher, G. N., Corbett, A. H., & Hawke, R. L. (2017). Common Herbal Dietary Supplement-Drug Interactions. *American Family Physician*, *96*(2), 101–107.

Chen, J. Y., Ma, Q., Chen, H., & Yermilov, I. (2012). New Bundled World: Quality of Care and Readmission in Diabetes Patients. *Journal of Diabetes Science and Technology*, *6*(3), 563–571. https://doi.org/10.1177/193229681200600311

Claire L Preston. (2015). *Stockley's Drug Interactions Pocket Companion*.

Dryden, M., Baguneid, M., Eckmann, C., Corman, S., Stephens, J., Solem, C., Li, J., Charbonneau, C., Baillon-Plot, N., & Haider, S. (2015). Pathophysiology and burden of infection in patients with diabetes mellitus and peripheral vascular disease: focus on skin and soft-tissue infections. *Clinical Microbiology and Infection*, *21*, S27–S32. https://doi.org/10.1016/j.cmi.2015.03.024

Dungan, K. M. (2012). The Effect of Diabetes on Hospital Readmissions. *Journal of Diabetes Science and Technology*, *6*(5), 1045–1052. https://doi.org/10.1177/193229681200600508

Endokrinologi Indonesia PEDOMAN PENGELOLAAN DAN PENCEGAHAN DIABETES MELITUS TIPE, P. (n.d.). *PEDOMAN PENGELOLAAN DAN PENCEGAHAN DIABETES MELITUS TIPE 2 DEWASA DI INDONESIA-2021 PERKENI i Penerbit PB. PERKENI*.

Enomoto, L. M., Shrestha, D. P., Rosenthal, M. B., Hollenbeak, C. S., & Gabbay, R. A. (2017). Risk factors associated with 30-day readmission and length of stay in patients with type 2 diabetes. *Journal of Diabetes and Its Complications*, *31*(1), 122–127. https://doi.org/10.1016/j.jdiacomp.2016.10.021

Fullerton, B., Siebenhofer, A., Jeitler, K., Horvath, K., Semlitsch, T., Berghold, A., & Gerlach, F. M. (2018). Short-acting insulin analogues versus regular human insulin for adult, non-pregnant persons with type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD013228

Furqani, W. H., Zazuli, Z., Nadhif, N., Saidah, S., Abdulah, R., & Lestari, K. (2015). Drug Related Problems in the Management of Chronic Kidney Disease with Coronary Artery Disease. *Indonesian Journal of Clinical Pharmacy*, *4*(2), 141–150. https://doi.org/10.15416/ijcp.2015.4.2.141

Fusco, S., Fusco, S., Cariati, D., Schepisi, R., Ganzetti, R., Sestili, M., David, S., Ferrara, L., Gatto, M. L., Vena, S., Corsonello, A., & Corica, F. (2015). *Management of oral drug therapy in elderly patients with dysphagia*.

Hamilton, H. J., Gallagher, P. F., & O'Mahony, D. (2009). Inappropriate prescribing and adverse drug events in older people. *BMC Geriatrics*, *9*(1), 5. https://doi.org/10.1186/1471-2318-9-5

Harreiter, J., & Roden, M. (2019). Diabetes mellitus – Definition, Klassifikation, Diagnose, Screening und Prävention (Update 2019). *Wiener Klinische Wochenschrift*, *131*(S1), 6–15. https://doi.org/10.1007/s00508-019-1450-4

Hoel, R. W., Giddings Connolly, R. M., & Takahashi, P. Y. (2021). Polypharmacy Management in Older Patients. *Mayo Clinic Proceedings*, *96*(1), 242–256. https://doi.org/10.1016/j.mayocp.2020.06.012

Huang, D., Xie, L., & Qiu, Y. (2015). Analysis of Factors Affecting the Length of Hospital Stay for Patients with Diabetes. *Experimental and Clinical Endocrinology & Diabetes*, *124*(01), 5–10. https://doi.org/10.1055/s-0035-1565059

Hubbard, R. E., Peel, N. M., Scott, I. A., Martin, J. H., Smith, A., Pillans, P. I., Poudel, A., & Gray, L. C. (2015). Polypharmacy among inpatients aged 70 years or older in Australia. *Medical Journal of Australia*, *202*(7), 373–377. https://doi.org/10.5694/mja13.00172

International Diabetes Federation (IDF) 9th Atlas. (2019). *International Diabetes Federation*. https://diabetesatlas.org/atlas/ninth-edition/

International Diabetes Federation. (2021). *IDF Diabetes Atlas, 10th edn*.

Joddy, R., Putra, S., Achmad, A., & Rachma, H. (n.d.). PHARMACEUTICAL JOURNAL OF INDONESIA Kejadian Efek Samping Potensial Terapi Obat Anti Diabetes Pasien Diabetes Melitus Berdasarkan Algoritma Naranjo. In *PHARMACEUTICAL JOURNAL OF INDONESIA* (Vol. 2017, Issue 2). http://.pji.ub.ac.id

Jonathan, K., & Natalia Mulyani Soetedjo, N. (n.d.). *Nanny Natalia Mulyani Soetedjo. Pattern of Oral Antidiabetics Use in Type 2 Diabetes Mellitus Patients in Department of Internal Medicine*.

Koubaity, M., Lelubre, M., Sansterre, G., Amighi, K., & de Vriese, C. (2019). Adaptation and validation of PCNE drug-related problem classification v6.2 in French-speaking Belgian community pharmacies. *International Journal of Clinical Pharmacy*, *41*(1), 244–250. https://doi.org/10.1007/s11096-018-0773-y

Linkeviciute-Ulinskiene, D., Kaceniene, A., Dulskas, A., Patasius, A., Zabuliene, L., & Smailyte, G. (2020). Increased Mortality Risk in People with Type 2 Diabetes Mellitus in Lithuania. *International Journal of Environmental Research and Public Health*, *17*(18), 6870. https://doi.org/10.3390/ijerph17186870

Lipska, K. J., Krumholz, H., Soones, T., & Lee, S. J. (2016). Polypharmacy in the Aging Patient. *JAMA*, *315*(10), 1034. https://doi.org/10.1001/jama.2016.0299

Madsen, K. S., Chi, Y., Metzendorf, M. I., Richter, B., & Hemmingsen, B. (2019). Metformin for prevention or delay of type 2 diabetes mellitus and its associated complications in persons at increased risk for the development of type 2 diabetes mellitus. In *Cochrane Database of Systematic Reviews* (Vol. 2019, Issue 12). John Wiley and Sons Ltd. https://doi.org/10.1002/14651858.CD008558.pub2

Masnoon, N., Shakib, S., Kalisch-Ellett, L., & Caughey, G. E. (2017). What is polypharmacy? A systematic review of definitions. *BMC Geriatrics*, *17*(1), 230. https://doi.org/10.1186/s12877-017-0621-2

Mengesha, A. Y. (2007). Hypertension and related risk factors in type 2 diabetes mellitus (DM) patients in Gaborone City Council (GCC) clinics, Gaborone, Botswana. *African Health Sciences*, *7*(4), 244–245.

Michelle, H. S. (2011). Management of dysphagia in stroke patients. *Nursing Older People*, *23*(3), 21–24. https://doi.org/10.7748/nop2011.04.23.3.21.c8420

Mortazavi, S. S., Shati, M., Keshtkar, A., Malakouti, S. K., Bazargan, M., & Assari, S. (2016). Defining polypharmacy in the elderly: a systematic review protocol. *BMJ Open*, *6*(3), e010989. https://doi.org/10.1136/bmjopen-2015-010989

Naples, J. G., Hanlon, J. T., Schmader, K. E., & Semla, T. P. (2016). Recent Literature on Medication Errors and Adverse Drug Events in Older Adults. *Journal of the American Geriatrics Society*, *64*(2), 401–408. https://doi.org/10.1111/jgs.13922

Nathan, D. M., Buse, J. B., Davidson, M. B., Ferrannini, E., Holman, R. R., Sherwin, R., & Zinman, B. (2009). Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy. *Diabetes Care*, *32*(1), 193–203. https://doi.org/10.2337/dc08-9025

Noale, M., Veronese, N., Cavallo Perin, P., Pilotto, A., Tiengo, A., Crepaldi, G., & Maggi, S. (2016). Polypharmacy in elderly patients with type 2 diabetes receiving oral antidiabetic treatment. *Acta Diabetologica*, *53*(2), 323–330. https://doi.org/10.1007/s00592-015-0790-4

Raval, A. D., Zhou, S., Wei, W., Bhattacharjee, S., Miao, R., & Sambamoorthi, U. (2015). 30-Day Readmission Among Elderly Medicare Beneficiaries with Type 2 Diabetes. *Population Health Management*, *18*(4), 256–264. https://doi.org/10.1089/pop.2014.0116

Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S., Unwin, N., Colagiuri, S., Guariguata, L., Motala, A. A., Ogurtsova, K., Shaw, J. E., Bright, D., & Williams, R. (2019). Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Research and Clinical Practice*, *157*, 107843. https://doi.org/10.1016/j.diabres.2019.107843

Salvi, F., Marchetti, A., D'Angelo, F., Boemi, M., Lattanzio, F., & Cherubini, A. (2012). Adverse Drug Events as a Cause of Hospitalization in Older Adults. *Drug Safety*, *35*(S1), 29–45. https://doi.org/10.1007/BF03319101

Setacci C, Sirignano A Ricci G, Spagnolo AG, Pugliese F, & Speziale F. (2015). *A new ethical and medico-legal issue: vascular surgery and the postoperative cognitive dysfunction. J Cardiovasc Surg (Torino). . 56*(4), 607–615. https://pubmed.ncbi.nlm.nih.gov/25216219/

Soeatmadji, D. W., Rosandi, R., Saraswati, M. R., Sibarani, R. P., & Tarigan, W. O. (2023). Clinicodemographic Profile and Outcomes of Type 2 Diabetes Mellitus in the Indonesian Cohort of DISCOVER: A 3-Year Prospective Cohort Study. *Journal of the ASEAN Federation of Endocrine Societies*, *38*(1), 68–74. https://doi.org/10.15605/jafes.038.01.10

Sutkowska, E., Fortuna, P., Wisniewski, J., Sutkowska, K., Hodurek, P., Gamian, A., & Kaluza, B. (2021). Low metformin dose and its therapeutic serum concentration in prediabetes. *Scientific Reports*, *11*(1). https://doi.org/10.1038/s41598-021-91174-7

Tharanon, V., Putthipokin, K., & Sakthong, P. (2022). Drug-related problems identified during pharmaceutical care interventions in an intensive care unit at a tertiary university hospital. *SAGE Open Medicine*, *10*, 205031212210908. https://doi.org/10.1177/20503121221090881

Zhao, Q., Li, H., Ni, Q., Dai, Y., Zheng, Q., Wang, Y., Ke, T., Li, L., Zhao, D., Dong, Q., Ji, B., Shi, J., Peng, Y., Zhang, Y., Xu, F., & Wang, W. (2022). Follow-up frequency and clinical outcomes in patients with type 2 diabetes: A prospective analysis based on multicenter real-world data. *Journal of Diabetes*, *14*(5), 306–314. https://doi.org/10.1111/1753-0407.13271