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Provision of information and recommendation by pharmacists regarding drug-related problems in hospitalized dyslipidemia patients: A pre-experimental pre-post design research

Rizky Nurhikmah^{1*}, Retnosari Andrajati², Santi Purna Sari³

^{1,2,3}*Faculty of Pharmacy, University of Indonesia, Depok, West Java, Indonesia.*

Corresponding author: Rizky Nurhikmah (Email: rizkynurhikmah93@gmail.com)

Abstract

Dyslipidemia is a condition of imbalance in the lipid profile of the body and a risk factor for atherosclerotic disease. In this context, the administration of statin as the main choice in the therapy has been proven safe. However, the method can cause drug-related problems that affect the effectiveness and safety of treatment. This drug-related problem is reduced and resolved through drug therapy monitoring activities by pharmacists. Therefore, this research aims to describe the characteristics of hospitalized dyslipidemia patients and identify drug-related problems, as well as analyze the effect of providing information and recommendation by pharmacists on changes in the number of statin drug-related problems. This research was conducted with a pre-experimental design before and after the interventions prospectively including 102 hospitalized dyslipidemia patients. Drug therapy monitoring was carried out while patients were hospitalized and the problems were identified using the Indonesian PCNE version 9.00 classification. Additionally, the data obtained were analyzed statistically to determine the effect of providing information and recommendations by pharmacists on changes in the number of drug-related problems. The number of drug-related problems in 102 hospitalized dyslipidemia patients identified and intervened was 307, consisting of 83% safety and 17% effectiveness, respectively. The provision of information by pharmacists had a significant effect (p -value $0.000 < 0.05$), reducing the number of drug-related problems by 90%. The provision of information and recommendations by pharmacists reduced the number of drug-related problems in hospitalized dyslipidemia patients.

Keywords: Drug-Related Problems, Dyslipidemia, Information, Pharmacists' Interventions.

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1. Introduction

In the world, a leading cause of death is atherosclerotic cardiovascular disease and dyslipidemia (hyperlipidemia) is a risk factor closely related to the incidence [1]. Dyslipidemia is characterized by an imbalance in lipid levels, specifically high low-density lipoprotein (LDL) and low high-density lipoprotein (HDL) cholesterol as well as triglycerides [2]. The prevalence of dyslipidemia worldwide varies. According to World Health Organization (WHO) [3] the increase in total cholesterol in adults globally is 39%, with 40% in women and 37% in men. The prevalence in Southeast Asia is 30.3% lower than in America at 47.7%. Meanwhile, in Indonesia, the prevalence according to WHO statistics in adults aged 25 years is 36% (33.1% in men and 38.2% in women) [4]. Based on the 2018 Riskesdas data, the proportion of Indonesian population with very high LDL cholesterol (≥ 190 mg/dL) in men is 2.4% lower than in women at 4.4%. In the 35-75 year age group, a total of 21.4% have very high LDL cholesterol compared to the 15-34 of 2.5% [5]. This shows that adults experience more dyslipidemia.

Based on the description above, statin therapy is the main choice for controlling and reducing lipid levels [2]. Statin (HMG-CoA reductase enzyme inhibitors) work by reducing cholesterol synthesis in the liver through competitive inhibition of HMG-CoA reductase enzyme responsible for cholesterol biosynthesis [6]. In general, the use of statin is safe and well tolerated but there is the potential to cause drug-related problems such as interactions and side effects [7]. Retrospective research conducted at Jazan Hospital, Saudi Arabia, showed that 9.4% of drug-related problems were caused by the use of statin therapy [8].

The most common problem encountered in hospitalized patients is drug-related. The incidence of drug-related problems in hospitalized patients is reported to be 15.5 to 81.0% and some cases have the potential to be prevented [9]. This problem is associated with a tendency for inappropriate drug use due to several factors such as ignorance, inappropriate prescription writing, and inadequate pharmaceutical service facilities [10]. Drug-related problems are also influenced by the choice of drug type, dose selection, and treatment duration [11]. These problems include non-guideline-compliant and guideline-compliant drugs with contraindications, inappropriate combinations, omitted treatments, underdosing or overdosing, and incorrect or unclear dose instructions. This should be considered to ensure drugs are effective and safe for patients [12].

Drug-related problems can be minimized by the role of pharmacists. Research showed that pharmacists could help identify, solve, and reduce the incidence of drug-related problems [13]. Clinical pharmacy activities carried out through therapy monitoring identify drug-related problems and provide recommendations for solving problems [14]. Research on pharmacists' interventions showed that 77.36% of interventions are accepted and implemented as well as to reduce the risk of drug-related problems [15]. Identification of drug-related problems can be performed using instruments, such as PCNE (Pharmaceutical Care Network Europe) classification. This classification is used to distinguish actual and potential problems affecting the occurrence. Drug-related problems in PCNE classification are divided into 3 categories, 9 cause categories, 5 intervention categories, 3 intervention acceptance categories, and 4 drug-related problem status categories [11].

University of Indonesia Hospital (RSUI) is a Type A and referral hospital in Depok City that collaborates with BPJS Kesehatan (Indonesian national health insurance agency). This hospital serves internal medicine, neurology, and heart polyclinics, hence, many patients use statin drugs. The use of atorvastatin and rosuvastatin at RSUI is often found in therapy of dyslipidemia patients. However, the research on drug-related problems in dyslipidemia patients at RSUI is still limited. The role of pharmacists in clinical pharmacy activities, specifically drug therapy monitoring at RSUI has been running but is not optimal. Therefore, this research aims to analyze statin drug-related problems and to determine the influence of pharmacists in terms of drug therapy monitoring activities (providing information and recommendations) in hospitalized dyslipidemia patients at RSUI.

2. Methods

This research used a prospective pre-experimental pre-post design to determine the effect of providing information and recommendations on changes in the number of drug-related problems using statin at RSUI from April to July 2024. The subjects were patients who fulfilled the inclusion and exclusion criteria. The inclusion criteria were patients with dyslipidemia as a primary or secondary diagnosis, regular check-ups at the hospital, over 30 years old, drug-related problems, and cholesterol laboratory values. Meanwhile, the exclusion criteria were patients who were unwilling to be respondents. Sample collection used the consecutive sampling method where each subject who fulfilled the inclusion criteria was selected until the required sample size was reached [16]. The sample calculation used the one-proportion estimation formula by Lemeshow and obtained a minimum size of 96. The provision of information and recommendations served as independent variables, while changes in the number of drug-related problems were the dependent variables. The confounding variables include age, gender, comorbidities, drug type, number of drugs, dose, treatment duration, and allergy history. This research obtained an ethical review permit from RSUI Ethics Committee with permit number: S-033/KETLIT/RSUI/II/2024. Data collection was carried out in 3 stages, where the pre-intervention included respondent recruitment, collection of primary and secondary data, as well as identification of drug-related problems based on Indonesian PCNE v9.00 classification and related literature. Meanwhile, the intervention stage comprised the determining and implementing interventions with RSUI pharmacists to doctors and patients/families. The post-intervention stage included evaluating the results and the status of drug-related problems based on Indonesian PCNE v9.00 classification. Data processing was also carried out with statistical analysis using univariate to obtain an overview regarding the frequency distribution of age, gender, comorbidities, drug type, drug dose, number of drugs, treatment duration, and allergy history. Bivariate analysis used the Wilcoxon test to determine the difference in the number of drug-related problems before and

after the intervention as well as chi-square analysis to check the effect of providing information and recommendations. The relationship was significant when the significance value was less than 0.05. Meanwhile, multivariate analysis was carried out when there were significant confounding variables ($p < 0.25$) in the bivariate analysis.

3. Results

3.1. Patient Characteristics

A total of 102 respondents were willing to take part in the research, experiencing drug-related problems, and receiving interventions by pharmacists before and after was 102 (Table 1).

Table 1.

Characteristics of 102 Hospitalized Dyslipidemia Patients Using Statin Identified as Drug-Related Problems and Receiving Pharmacists' Interventions.

| Characteristics | Number | Percentage (%) |
|----------------------------|--------|----------------|
| Age | | |
| Adults (30-60 years) | 50 | 49.0 |
| Elderly (>60 years) | 52 | 51.0 |
| Gender | | |
| Male | 66 | 64.7 |
| Female | 33 | 35.3 |
| Comorbidities | | |
| Yes | 99 | 97.1 |
| No | 3 | 2.9 |
| Drug Type | | |
| Simvastatin | 15 | 14.7 |
| Atorvastatin | 79 | 77.5 |
| Rosuvastatin | 8 | 7.8 |
| Drug Dose | | |
| 10 mg/day | 4 | 3.9 |
| 20 mg/day | 80 | 78.4 |
| >20 mg/day | 18 | 17.6 |
| Number of Drugs | | |
| Polypharmacy (>5 drugs) | 100 | 98.0 |
| Nonpolypharmacy (<5 drugs) | 2 | 2.0 |
| Treatment Duration | | |
| 1-6 weeks | 68 | 66.7 |
| 7-12 weeks | 14 | 13.7 |
| >12 weeks | 20 | 19.6 |
| Allergy History | | |
| Yes | 17 | 16.7 |
| No | 85 | 83.3 |
| Total | 102 | 100.0 |

3.2. Identification of Drug-Related Problems (DRP)

The number of drug-related problems in 102 hospitalized dyslipidemia patients using statin before pharmacists' interventions was 307 (Table 2). In this context, 27.5% of patients experienced drug-related problems associated with statin.

Table 2.

Number of Drug-Related Problems in 102 Hospitalized Dyslipidemia Patients Using Statin at RSUI

| Primary DRP* | Secondary DRP* | Number (%) |
|-----------------------------|---|------------|
| P1. Treatment Effectiveness | P1.1 No therapeutic effect | 0 (0%) |
| | P1.2 Suboptimal therapeutic effect | 48 (16%) |
| | P1.3 Untreated symptoms or indications | 3 (1%) |
| P2. Treatment Safety | P2.1 Adverse drug events (possible) occur | 256 (83%) |
| P3. Others | P3.1 Cost-effectiveness-related drug problems | 0 (0%) |
| | P3.2 Unnecessary drugs | 0 (0%) |
| | P3.3 Unclear drug-related problems need further clarification (alternatives only) | 0 (0%) |
| Total | | 307 (100%) |

Note: *DRP classification based on Indonesian PCNE version 9.00, DRP: Drug-Related Problems.

3.3. Causes of Drug-Related Problems

Causes of drug-related problems in 102 dyslipidemia patients were dominated by interactions (Table 3). Drug interactions could occur because most patients suffer from heart disease, hypertension, and dyslipidemia, thereby receiving combination therapy of antihypertensives, antiplatelets, and anticholesterol.

Table 3.

Causes of Drug-Related Problems in 102 Hospitalized Dyslipidemia Patients Using Statin at RSUI.

| Causes of Primary DRP* | Sub-Causes of DRP* | Number (%) |
|------------------------|--|------------|
| C1. Drug selection | C1.1 Non-guideline-compliant drugs | 0 (0%) |
| | C1.2 Guideline-compliant drugs with contraindications | 0 (0%) |
| | C1.3 No indication for drugs | 0 (0%) |
| | C1.4 Inappropriate combinations (drug-drug, drug-herbal, drug-supplement) | 0 (0%) |
| | C1.5 Inappropriate therapeutic class or active ingredient duplication | 12 (4%) |
| | C1.6 Omitted or incomplete treatments despite indications | 2 (1%) |
| | C1.7 Excessive prescribing for a single indication | 2 (1%) |
| C9. Others | C9.1 Lack of appropriate drug therapy monitoring (including TDM/Therapeutic Drug Monitoring) | 0 (0%) |
| | C9.2 Other causes; specify... (Drug Interactions) | 291 (95%) |
| | C9.3 No clear cause | 0 (0%) |
| Total | | 307 (100%) |

Note: *classification of DRP Causes based on Indonesian PCNE version 9.00.

3.4. Pharmacists' Interventions for Drug-Related Problems

Pharmacists' interventions were in the form of providing information and recommendations. The number of interventions carried out on 102 hospitalized dyslipidemia patients was 344 (Table 4). The number of interventions received by each patient varied depending on the problem. Meanwhile, some types of problems could receive more than an intervention.

Table 4.

Pharmacists' Interventions in 102 Hospitalized Dyslipidemia Patients Using Statin at RSUI.

| Interventions | Intervention Form | Number | Percentage |
|-------------------|--|--------|------------|
| Doctors | Information on potential drug interactions | 148 | 43% |
| | Recommended intervals for taking medication and additional therapy | 52 | 15% |
| Patients/Families | Information on drugs used by patients | 144 | 42% |
| | Monitoring of patient conditions regarding potential drug interactions and possible side effects | | |
| Total | | 344 | |

3.5. Acceptance of Interventions and Status of Drug-Related Problems

From the 344 interventions carried out, 318 (92%) interventions were accepted and implemented (Table 5). The information provided by pharmacists was accepted by the doctor and follow-up was carried out to resolve the problem. The status of drug-related problems was completely resolved after the interventions was received before conducting follow-up. Meanwhile, the status of drug-related problems was unresolved when the interventions received was less effective in solving (Table 6).

Table 5.

Acceptance of Pharmacists' Interventions.

| Acceptance of Interventions | Number | Percentage |
|--|--------|------------|
| Accepted and implemented interventions | 318 | 92% |
| Accepted but not implemented interventions | 26 | 8% |
| Not accepted interventions | 0 | 0% |
| Total | 344 | 100% |

Table 6.

Status of Drug-Related Problems.

| Status of Drug-Related Problems | Number | Percentage |
|--|--------|------------|
| Completely resolved problems | 318 | 92% |
| Partially resolved problems | 22 | 6% |
| Unresolved problems due to ineffective interventions | 4 | 1% |
| Total | 344 | 100% |

3.6. Analysis of Information and Recommendations by Pharmacists on Changes in the Number of Drug-Related Problems

The success of pharmacists' interventions was reported in the number of drug-related problems. Based on the Wilcoxon test (Table 7), a significant value was obtained between the number of drug-related problems before and after pharmacists' interventions ($p > 0.05$). The decrease in the number of drug-related problems could be seen from the negative rank value.

Table 7.

Wilcoxon Test Analysis Results.

| Number of DRP post – Number of DRP pre | Ranks | N | Rerata | Sig |
|--|--------------|----------|---------------|------------|
| | Negative | 98 | 49.50 | 0.000 |
| | Positive | 0 | 0.00 | |
| | Ties | 4 | | |
| Total | | 102 | | |

Bivariate chi-square analysis (Table 8) was conducted to see the effect of information and recommendations provided by pharmacists on changes in the number of drug-related problems.

Table 8.

Chi-Square Bivariate Analysis Results.

| Information and Recommendations | Changes in the Number of DRP | | Sig | OR | 95% CI | |
|--|-------------------------------------|---------------|------------|-----------|---------------|--------------|
| | Decrease | Stable | | | Lower | Upper |
| For doctors and patients | 89 (100%) | 0 (0%) | 0.000 | 1.444 | 1.005 | 2.075 |
| For doctors only | 9 (69.2%) | 4 (30.8%) | | | | |

Descriptively, changes in the number of drug-related problems in 102 hospitalized dyslipidemia patients before and after interventions are as follows:

Table 9.

Drug-Related Problems Before and After Pharmacists' Interventions.

| Primary DRP | Sub-DRP | Σ pre (%) | Σ post (%) |
|-------------------------|---|------------------|-------------------|
| Treatment Effectiveness | No therapeutic effect | 0 | 0 |
| | Suboptimal therapeutic effect | 48 (16%) | 2 (7%) |
| | Untreated symptoms or indications | 3 (1%) | 1 (3%) |
| | Total | 51 (17%) | 3 (10%) |
| Treatment Safety | Adverse drug events (possibly) occur | 256 (83%) | 27 (90%) |
| | Total | 256 (83%) | 27 (90%) |
| Others | Cost-effectiveness-related drug problems | 0 | 0 |
| | Unnecessary drugs | 0 | 0 |
| | Unclear drug-related problems need further clarification (alternative only) | 0 | 0 |
| | Total | 307 | 30 |
| DRP pre-post difference | 307-30 = 277 | | |
| Percentage | 90% | | |

3.7. Analysis of Risk Factors/Confounding Variables on Changes in the Number of Drug-Related Problems

Table 10.

Bivariate Analysis Results of Risk Factors on Changes in the Number of Drug-Related Problems.

| Risk Factors | Category | Changes in the Number of DPR | | OR value* | P value* |
|--------------------|----------------------|------------------------------|-----------|-----------|----------|
| | | Decrease | Stable | | |
| Age | Adults (30-60 years) | 48 (96.0%) | 2 (4.0%) | 0.960 | 1.000 |
| | Elderly (> 60 years) | 50 (96.2%) | 2 (3.8%) | | |
| Gender | Male | 62 (93.9%) | 4 (6.1%) | 0.939 | 0.330 |
| | Female | 36 (100.0%) | 0 (0.0%) | | |
| Comorbidities | Yes | 96 (97.0%) | 3 (3.0%) | 16.000 | 0.114 |
| | No | 2 (66.7%) | 1 (33.3%) | | |
| Drug Type | Simvastatin | 15 (100.0%) | 0 (0.0%) | reff | 1.000 |
| | Atorvastatin | 75 (94.9%) | 4 (5.1%) | 1.396 | 1.000 |
| | Rosuvastatin | 8 (100.0%) | 0 (0.0%) | 1208.508 | 0.999 |
| Drug Dose | 10 mg/day | 4 (100.0%) | 0 (0.0%) | reff | 0.997 |
| | 20 mg/day | 77 (96.3%) | 3 (3.8%) | 0.000 | 0.999 |
| | >20 mg/day | 17 (94.4%) | 1 (5.6%) | 0.1091 | 0.942 |
| Number of Drugs | Polypharmacy | 96 (96.0%) | 4 (4.0%) | 0.960 | 0.923 |
| | Non polypharmacy | 2 (100.0%) | 0 (0%) | | |
| Treatment Duration | 1-6 weeks | 64 (94.1%) | 4 (5.9%) | reff | 1.000 |
| | 7-12 weeks | 14 (100.0%) | 0 (0.0%) | 1253.529 | 0.998 |
| | >12 weeks | 20 (100.0%) | 0 (0.5%) | 1.350 | 1.000 |
| Allergy History | Yes | 17 (100.0%) | 0 (0.0%) | 1.049 | 0.820 |
| | No | 81 (95.3%) | 4 (4.7%) | | |

Note: *p-value of chi-square results, 1-way fisher exact and logistic regression; DPR: Drug-Related Problems; *OR value: odd ratio.

4. Discussion

Age characteristics are dominated by the elderly at 51%. This was in accordance with previous research where the prevalence of dyslipidemia in the elderly is 30% higher than in adults at 10% [17]. Gender characteristics are dominated by males at 64.7% compared to the female group at 35.3%. This is different from previous research where 55% of female patients experience dyslipidemia compared to 45% of male [18]. The prevalence of dyslipidemia in women is higher than in men and is influenced by the hormone estrogen. The hormone plays a role in regulating cholesterol balance and blood lipid profiles. This is the factor influencing older women to experience more dyslipidemia because estrogen levels will decrease after the end of menopause [19]. A total of 97.1% patients were characterized with comorbidities in this research. Secondary dyslipidemia was experienced due to other diseases such as ischemic stroke, diabetes mellitus, nephrotic syndrome, and hypertension. This is consistent with previous research where hyperlipidemia patients were accompanied by complications such as hypertension, diabetes mellitus, kidney failure, and other diseases. Therefore, combination therapy was received to increase the risk of drug interactions [20]. The most common drug types were atorvastatin, simvastatin, and rosuvastatin at 77.5%, 14.7%, and 7.8%, respectively. This is different from previous research where hospitalized dyslipidemia patients used simvastatin and atorvastatin therapy at 67% and 6%, respectively [18]. The most commonly prescribed drug dose was 20 mg/day at 78.4% and the selection was adjusted to the target therapy. Meanwhile, the most commonly used statin therapy was atorvastatin at a dose of 20 mg/day. Atorvastatin is recommended as the primary therapy of choice to reduce the risk of atherosclerotic cardiovascular disease [21]. In this research, the dose of more than 20 mg/day given was 40 mg - 80 mg/day. This dose was prescribed by doctors for lipid levels of more than 160 mg/dL, while patients with optimal levels <100 mg/dL used a dose of 20 mg/day. This was consistent with dyslipidemia guidelines, where the maximum recommended dose of statin use was 80 mg/day [1]. The number of dominant drugs was polypharmacy at 98%. This was because patients with comorbidities receive therapy with more than 5 types of drugs. A goal of providing polypharmacy therapy is to produce optimal therapeutic effects [20]. The dominant treatment duration in this research was 1-6 weeks at 66.7% since most of patients were new statin users. Patients were subjected to statin therapy when admitted to the hospital but previously received oral antihypertensive or antidiabetic drugs. Statin therapy was given after laboratory examination of the lipid profile (LDL cholesterol and triglycerides). Based on the literature, the duration of routine use for 4-12 weeks can show the effectiveness of therapy and the occurrence of side effects [6].

Patients without allergy history dominate this research at 83.3%. Documentation of allergy history is important because the possibility of medication errors due to a lack of information leads to changes in drug therapy [22]. The number of drug-related problems before pharmacists' interventions was 307. The category of treatment effectiveness problems consisted of 48 suboptimal drug therapy effects (16%) and 3 untreated symptoms/indications (1%). The category of medication safety problems, namely adverse drug events reported 256 problems (83%). This was different from previous research where drug-related problems in prolans patients with dyslipidemia and hypertension were dominated by treatment effectiveness problems at 95% [17]. The number of drug-related problems was the identification result of all drugs during hospitalization. Dyslipidemia experienced by patients is a secondary diagnosis, hence, statin were used with other drugs such as antiplatelets, antidiabetics, and antihypertensives.

The causes of drug-related problems are dominated by the category of others, specifically interactions at 95%. This is followed by the category of selection, including inappropriate therapeutic duplication at 4%, as well as omitted or incomplete treatment despite indications and excessive prescribing for a single indication at 1%. This was consistent with previous research on statin drug-related problems, namely potential interactions at 39.2% [23]. Statin drugs include rosuvastatin, simvastatin, and atorvastatin interactions with clopidogrel, amlodipine, and sacubitril valsartan at 2.3%, 2.0%, and 0.7%, respectively. This was different from previous research where potential statin drug interactions were experienced by 72% of patients. The most frequently interacting drugs were statin with amlodipine and diltiazem [24]. The interaction of rosuvastatin and clopidogrel increased blood levels of rosuvastatin to improve the level of myopathy and rhabdomyolysis. In this context, the dose should be reduced to avoid toxicity [25]. Simvastatin is used as cholesterol therapy, while amlodipine serves as antihypertensive therapy and is prescribed in patients with dyslipidemia accompanied by hypertension [26]. The interaction of simvastatin and amlodipine increases serum concentrations of simvastatin to improve the side effects of muscle disorders such as muscle pain. The dose of simvastatin is less than 20 mg per day and laboratory values, such as creatinine kinase as well as rhabdomyolysis signs and symptoms need to be monitored [25]. The use of sacubitril with atorvastatin increases the risk of toxicity such as rhabdomyolysis and myopathy. The dose of atorvastatin must be reduced or replaced with a statin possessing less potential for interactions such as simvastatin [25].

Pharmacists' interventions carried out are in the form of providing information and treatment recommendations for identified drug-related problems. The intervention plan is given to the prescribing doctor, who is only informed at 43%. The information given to the doctor is that there is a potential drug interaction problem in the use of amlodipine and simvastatin. In theory, this interaction can be overcome by providing a time interval for taking drug, and the dose of simvastatin given is no more than 20 mg/day. The information is provided through integrated patient records to remind the prescribing doctor of potential drug interactions. Another intervention carried out by pharmacists is an intervention proposed to the prescribing doctor at 15%. In this context, there is a potential drug interaction in the use of clopidogrel and rosuvastatin simultaneously which increases the risk of myopathy or rhabdomyolysis. The time to take clopidogrel and rosuvastatin listed on the medication card is 06:00 p.m. Information is also provided regarding the increased risk of statin side effects when used together. There is a time gap between the administration of clopidogrel and rosuvastatin, taken after dinner at approximately 6:00 p.m., and before bedtime, as reported in the integrated medical records, respectively.

Approximately 42% of pharmacists' interventions is provided to patients and families. Pharmacists' visits patients in the inpatient room to provide information about drugs used during treatment, deliver information regarding side effects, as well as monitor the conditions related to potential interactions and side effects. The accepted and implemented interventions in this research were 92%. This was consistent with previous research where 77.36% of pharmacists' interventions were fully accepted and implemented [15]. The implementation of interventions was in the form of information received and followed-up. An example of implementation carried out on the problem of rosuvastatin and clopidogrel interactions was changing the time of taking medication while patient is hospitalized. This can be seen by analyzing the medical records and medication cards of patients. The form of implementation is carried out by interviews regarding the condition after taking medication to ascertain signs and symptoms of side effects such as muscle pain, cramps, or weakness. Patients do not feel any signs and symptoms of side effects or drug interactions during treatment. Furthermore, 8% of interventions were received and unimplemented in this research. The form of interventions received but unimplemented is the interaction of simvastatin and atorvastatin with amlodipine and rifampicin, respectively. Pharmacists have provided information and confirmation regarding potential drug interactions to doctors through integrated patient records. However, there is no follow-up such as spacing for taking or stopping drugs because the interventions only reminds the doctor about the interference with clinical outcomes. In clinical practice, not all interventions can be accepted and implemented. Collaboration factors between doctors and pharmacists or other health workers determine the acceptance of interventions [15]. Drug-related problem status shows completely and partially resolved, as well as unresolved problems [11]. The status of resolved drug-related problems was 92% concerning potential interactions after information and treatment recommendations were received and follow-up was performed. The status of partially resolved drug-related problems was 6%, namely issues related to potential drug interactions receiving information and recommendations. Moreover, the status of unresolved drug-related problems was 1%, namely issues identified and given recommendations but were unresolved because the recommendations were considered ineffective. For example, problems related to the effectiveness of treatment in the category of symptoms but not treated. Patient complains of difficulty defecating since being admitted to the hospital for about 2 days. Subsequently, pharmacists proposed the administration of laxative therapy to overcome constipation, but the doctor disagreed because patient was given fruit rather than prescribing medication.

The success of interventions in providing information and recommendations by pharmacists can be seen from changes in the number of drug-related problems. The data before and after interventions is in the form of numbers. Therefore, a paired t-test is conducted with the condition that the data on the number of drug-related problems before and after interventions is normally distributed ($p > 0.05$). The Wilcoxon test is used as an alternative when the data is not normally distributed. Based on the results, a significance value of 0.000 is obtained. This shows a significant difference between the number of drug-related problems before and after interventions ($p < 0.05$). The decrease in the number of drug-related problems is obtained from the negative rank mean value of 49.50 ($N=98$). Bivariate chi-square analysis is conducted to determine the relationship between the provision of information and recommendations for changes in the number of problems. Drug-related problems decreased to 89 after the provision of information and recommendations by pharmacists to doctors and patients. A significance value of 0.000 shows a relationship between the provision of information and recommendations for a decrease in the number of drug-related problems ($OR=1.44$). The difference in the decrease after the provision of information and recommendations by pharmacists is 90%.

Based on the bivariate analysis, no confounding variables significantly influence changes in the number of drug-related problems due to a significance value of >0.05 . Multivariate analysis is performed on comorbidities with a significance value of 0.114 ($p < 0.25$). Meanwhile, comorbidities have no significant effect on changes in the number of drug-related problems. In this context, changes in the number of drug-related problems are not influenced by confounding variables.

5. Conclusion

In conclusion, dominant patient characteristics were elderly age (> 60 years), male gender, presence of comorbidities, use of atorvastatin statin therapy at a dose of 20 mg/day, polypharmacy, treatment duration of 1–6 weeks, and no allergy history. Approximately 307 drug-related problems in hospitalized dyslipidemia patients using statin were identified, consisting of 17% and 83% of treatment effectiveness and safety problems, respectively. The dominant treatment safety problems were potential drug interactions. The success of providing information and recommendations was known from the decrease in the number of drug-related problems. The decrease from 307 to 30 problems with a percentage of 90% was obtained from the number of resolved issues after providing information and recommendations. The provision of information and recommendations had a significant effect ($p = 0.000 < 0.05$). However, no dominant risk factors had a significant effect ($p < 0.05$) on changes in the number of drug-related problems.

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