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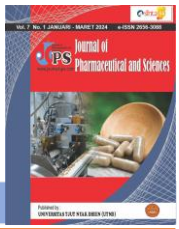

Identification of Drug-Related Problems (DRPs) in Ischemic and Hemorrhagic Stroke Inpatients: A Retrospective Observational Study at a Referral Hospital

Identifikasi Drug-Related Problems (DRPs) pada Pasien Rawat Inap Stroke Iskemik dan Hemoragik: Studi Observasional Retrospektif di Rumah Sakit Rujukan

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Abstract

Stroke remains a leading cause of mortality and long-term disability worldwide, requiring complex pharmacotherapy regimens that significantly increase the risk of Drug-Related Problems (DRPs). This study aimed to identify, categorize, and analyze the prevalence and patterns of DRPs among stroke inpatients using a retrospective observational approach. Data were collected from medical records of 98 hospitalized stroke patients treated between January and December 2025 at a referral hospital. DRPs were classified based on the Pharmaceutical Care Network Europe (PCNE) V9.1 system. The patient cohort comprised 55.1% males and 44.9% females, with 57.1% aged ≥ 60 years. Ischemic stroke accounted for 91.8% of cases, while hemorrhagic stroke constituted 5.1%. Hypertension (69.4%) and Type 2 Diabetes Mellitus (28.6%) were the predominant comorbidities. A total of 135 DRP events were identified in 82 patients (83.7%). The most frequent categories were potential drug–drug interactions (36.3%), untreated indications or need for additional therapy (29.6%), inappropriate drug selection (19.3%), and inappropriate dosing, including absent renal-dose adjustment (14.8%). Critical potential interactions included co-administration of clopidogrel with omeprazole and NSAIDs with antihypertensives. Untreated indications mainly involved the absence of high-intensity statin therapy in ischemic stroke patients. In conclusion, DRPs are highly prevalent among stroke inpatients, particularly driven by polypharmacy and complex comorbidities. Clinical pharmacist interventions are crucial to optimize therapeutic outcomes and minimize adverse drug events.

***Keywords:** Stroke, Drug-Related Problems, PCNE V9.1, Polypharmacy, Retrospective Study.*

Abstrak

Stroke tetap menjadi penyebab utama kematian dan disabilitas jangka panjang di seluruh dunia, yang membutuhkan regimen farmakoterapi kompleks sehingga meningkatkan risiko Drug-Related Problems (DRPs). Penelitian ini bertujuan untuk mengidentifikasi, mengategorikan, dan menganalisis prevalensi serta pola DRPs pada pasien stroke rawat inap menggunakan pendekatan observasional retrospektif. Data diperoleh dari rekam medis 98 pasien stroke rawat inap periode Januari hingga Desember 2025 di rumah sakit rujukan. DRPs diklasifikasikan berdasarkan sistem Pharmaceutical Care Network Europe (PCNE) V9.1. Kohort pasien terdiri dari 55,1% laki-laki dan 44,9% perempuan, dengan 57,1% berusia ≥ 60 tahun. Stroke iskemik mencakup 91,8% kasus, sedangkan stroke hemoragik sebesar 5,1%. Hipertensi (69,4%) dan Diabetes Melitus Tipe 2 (28,6%) merupakan komorbiditas dominan. Sebanyak 135 kejadian DRP teridentifikasi pada 82 pasien (83,7%). Kategori yang paling sering ditemukan adalah potensi interaksi obat (36,3%), indikasi yang belum diterapi atau kebutuhan terapi tambahan (29,6%), pemilihan obat yang kurang tepat (19,3%), dan dosis yang tidak tepat, termasuk tidak dilakukannya penyesuaian dosis berdasarkan fungsi ginjal (14,8%). Interaksi obat potensial yang krusial antara lain penggunaan bersamaan clopidogrel dengan omeprazole serta NSAID dengan antihipertensi. Indikasi yang tidak diterapi sebagian besar berupa ketiadaan terapi statin intensitas tinggi pada pasien stroke iskemik. Kesimpulannya, DRPs sangat prevalen pada pasien stroke rawat inap, terutama didorong oleh polifarmasi dan komorbiditas kompleks. Intervensi apoteker klinik sangat penting untuk mengoptimalkan luaran terapi dan meminimalkan efek samping obat.

***Kata kunci:** Stroke, Drug-Related Problems, PCNE V9.1, Polifarmasi, Studi Retrospektif.*

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Introduction

Stroke represents one of the major global health burdens, ranking as the second leading cause of death and a primary contributor to severe adult disability worldwide [1]. In Indonesia, the prevalence of stroke has shown an escalating trend, driven by an aging population and an increasing incidence of metabolic and cardiovascular risk factors [2]. The clinical management of stroke—comprising both acute ischemic stroke (AIS) and intracerebral hemorrhage (ICH)—requires rapid, multidimensional therapeutic strategies aimed at brain tissue reperfusion, secondary prevention, and the control of systemic comorbidities such as hypertension, hyperglycemia, and cerebral edema [3].

Consequently, stroke inpatients are frequently exposed to complex polypharmacy regimens involving antiplatelets, anticoagulants, antihypertensives, neuroprotective agents, osmotic diuretics, and broad-spectrum antibiotics [4]. While multi-drug regimens are clinically indispensable for managing severe acute stroke and associated complications, polypharmacy substantially escalates the vulnerability to Drug-Related Problems (DRPs) [5]. A DRP is defined by the Pharmaceutical Care Network Europe (PCNE) as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes [6]. Unresolved DRPs in stroke care are associated with prolonged hospital length of stay (LOS), elevated healthcare expenditure, increased risk of adverse drug reactions (ADRs), treatment failure, and heightened mortality rates [7]. Despite the established clinical guidelines provided by the American Heart Association/American Stroke Association (AHA/ASA) and the Indonesian Neurological Association (PERDOSSI), variations in real-world clinical practice frequently lead to potential DRPs, including inappropriate drug selection, drug-drug interactions, unaddressed clinical indications, and improper dosing in patients with organ dysfunction [8].

Although several studies have investigated DRPs in cardiovascular diseases, detailed retrospective evaluations specifically examining DRP patterns among stroke inpatients in Indonesian regional referral hospitals remain limited. Therefore, this study aimed to evaluate the demographic and clinical profiles of stroke inpatients, identify and categorize the prevalence and types of DRPs according to the PCNE V9.1 classification, and analyze critical drug interaction patterns to provide evidence-based recommendations for clinical pharmacy practice.

Methods

Study Design and Patient Selection

This research employed a descriptive, observational, retrospective cross-sectional design. Medical records of all stroke patients admitted to the inpatient wards and intensive care units (ICU/HCU/RICU) of a referral hospital between January 1, 2025, and December 31, 2025, were reviewed. The inclusion criteria were: (1) hospitalized patients aged ≥ 18 years, (2) diagnosed with acute stroke confirmed by brain MSCT/CT scan or clinical evaluation (ICD-10 codes: I63, I61, I60, I64, or I69), and (3) complete inpatient medical records containing demographic data, diagnostic imaging, laboratory results, and daily medication administration records. Exclusion criteria included patients with incomplete medical records, length of stay < 24 hours, or those discharged against medical advice upon admission before complete pharmacotherapy initiation.

Ethical Approval and Data Collection

Ethical approval for this retrospective study was obtained from the Research Ethics Committee of Andalas University (Komite Etik Penelitian Universitas Andalas), Padang, Indonesia, under Ethical

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Approval/Description of Ethical Approval Number 8/UN16.19/KEP/2026, dated June 29, 2026. The approved research protocol was entitled "Evaluasi Drug Related Problems (DRP) pada Pasien Stroke Iskemik di Ruang Rawat Inap Rumah Sakit Dr. Bratanata Jambi" and was declared approved for implementation. The ethical approval was valid for one year from the date of approval. In accordance with the approved protocol, the study used retrospective medical-record data, and patient confidentiality was strictly protected throughout data collection and analysis. All personal identifiers and medical record numbers were anonymized and were not included in the research dataset or manuscript. Data were collected from eligible inpatient medical records and included patient demographics (age, gender), clinical diagnosis (ICD-10 classification), length of stay, intensive care unit utilization, diagnostic imaging findings (MSCT scan, chest X-ray), physiological and laboratory parameters (serum creatinine, blood urea nitrogen, HbA1c, random blood glucose, electrolyte levels, full blood counts, arterial blood gases), and daily administered medications (drug name, dosage, frequency, route, and administration duration). Any serious adverse event related to the research, if identified, was to be reported to the Research Ethics Committee in accordance with the provisions stated in the ethical approval.

Identification and Classification of DRPs

Pharmacotherapy regimens were evaluated independently against established evidence-based clinical practice guidelines, including the AHA/ASA Guidelines for the Management of Ischemic and Hemorrhagic Stroke, PERDOSSI Stroke Management Guidelines, Eighth Joint National Committee (JNC 8) guidelines for hypertension management, and the American Diabetes Association (ADA) Standards of Medical Care. Potential Drug-Drug Interactions (DDIs) and organ-specific dose adjustments were analyzed using the Lexicomp® Drug Interactions database, Micromedex®, and the Drug Information Handbook (DIH). DRPs were systematically categorized using the Pharmaceutical Care Network Europe (PCNE) V9.1 classification system, focusing on primary domains: P1 (Treatment Effectiveness: unnecessary therapy, untreated indication), P2 (Adverse Events), C1 (Drug Selection), C3 (Dose Selection: excess/inadequate dose, renal adjustment), and C8 (Other / Interaksi: potential drug-drug interactions).

Data Analysis

Extracted data were digitized and analyzed using SPSS statistical software version 26.0. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR) based on normality testing. Categorical variables were presented as absolute frequencies (n) and percentages (%). Bivariate comparisons between patient characteristics (e.g., age, polypharmacy status, comorbidities) and the presence of DRPs were analyzed using the Chi-Square test (χ^2), where a p-value < 0.05 was considered statistically significant.

Results and Discussion

Demographic and Clinical Characteristics

A total of 98 stroke inpatients met the eligibility criteria and were evaluated in this study. The demographic and clinical characteristics of the study population are summarized in Table 1.

Table 1. Demographic and Clinical Characteristics of Stroke Inpatients (N = 98)

Parameter	Subcategory	Frequency (n)	Percentage (%)
Gender	Male	54	55.1
	Female	44	44.9
Age Group	< 45 years	4	4.1
	45–59 years	38	38.8
	≥ 60 years	56	57.1
Stroke Type (ICD-10)	Ischemic Stroke (I63.9, I63, I69.3)	90	91.8
	Hemorrhagic Stroke (I61, I60)	5	5.1
	Stroke Unspecified (I64)	3	3.1
Comorbidities	Essential / Secondary Hypertension	68	69.4
	Type 2 Diabetes Mellitus	28	28.6
	Cardiovascular Diseases (AF, CAD, HHD, MI)	18	18.4

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The cohort showed a modest male predominance (55.1%), while 57.1% of patients were aged ≥60 years. These findings are compatible with the concentration of stroke burden in older adults and the substantial contribution of vascular risk factors, although this descriptive study cannot attribute the sex distribution to smoking or atherosclerosis because those exposures were not reported in Table 1 [1,11,13]. Ischemic stroke accounted for 91.8% of admissions; hypertension (69.4%) and type 2 diabetes (28.6%) were the most common recorded comorbidities. The predominance of these conditions reinforces the need for medication review that simultaneously addresses acute stroke treatment and long-term vascular-risk reduction [4,12,14].

Prevalence and Distribution of Drug-Related Problems (DRPs)

Out of 98 patients, 82 patients (83.7%) experienced at least one DRP during their hospital stay. A total of 135 DRP events were identified, corresponding to 1.65 events per affected patient (or 1.38 events per patient in the full cohort). Because the source data did not provide the patient-level dispersion required to calculate a standard deviation, no SD is reported. The distribution of DRP problems and causes mapped to PCNE V9.1 is presented in Table 2.

Table 2. Classification and Frequency of Identified Drug-Related Problems (DRPs) (N = 135 events)

PCNE V9.1 problem/cause category	DRP Subcategory	Frequency (n)	Percentage (%)
Potential drug interaction (cause C8.1)	Antiplatelet + Proton Pump Inhibitor (Omeprazole)	21	15.6
	Antihypertensive + NSAID / Analgesic	16	11.9
	Anticoagulant (Warfarin) + Broad-Spectrum Antibiotic	12	8.9
Untreated indication / additional therapy required (problem P1.3)	Absence of Statin Therapy in Ischemic Stroke	26	19.3
	Uncontrolled Glycemia / Missing Anti-diabetic Agent	14	10.4
Inappropriate drug selection (cause C1)	Unnecessary Neuroprotective Therapy (Citicoline/Piracetam)	18	13.3
	Stress Ulcer Prophylaxis in Non-High-Risk Patients	8	5.9
Inappropriate dose selection (cause C3)	Failure to Adjust Dose in Renal Impairment (CKD)	13	9.6
	Inadequate Glycemic Management / Hypoglycemia Events	7	5.2

In-Depth Analysis of Major DRP Domains

Potential drug–drug interactions were the largest category (49/135; 36.3%). The clopidogrel–omeprazole pair was recorded in 21 events. Omeprazole inhibits CYP2C19 and can reduce formation of clopidogrel's active metabolite; however, the magnitude of clinical harm is not uniform across studies. Therefore, the finding should trigger an individualized review of gastrointestinal risk, indication for acid suppression, treatment duration, and availability of a PPI with less CYP2C19 inhibition rather than an automatic substitution in every patient [15–17]. The 16 NSAID–antihypertensive/diuretic combinations are also clinically relevant because NSAIDs may attenuate blood-pressure control and increase acute kidney-injury risk, particularly in older patients, those with diabetes or kidney dysfunction, and those receiving renin–angiotensin system inhibitors plus diuretics [18,19].

Untreated indications or need for additional therapy accounted for 40/135 events (29.6%). The most frequent finding was absent statin therapy in 26 patients with ischemic stroke. Contemporary secondary-prevention recommendations support high-intensity or maximally tolerated statin therapy for appropriate patients, commonly atorvastatin 80 mg, with treatment individualized according to stroke mechanism, LDL-C, drug interactions, tolerability, and contraindications; the original statement that all non-cardioembolic cases require atorvastatin 20–40 mg regardless of LDL-C was therefore too absolute [4,14,20]. The 14 events involving uncontrolled glycemia or missing glucose-lowering therapy likewise require interpretation alongside nutritional intake, acute illness, renal function, and hypoglycemia risk rather than glucose concentration alone [21].

Inappropriate drug selection represented 26/135 events (19.3%). Eighteen involved citicoline or piracetam categorized as unnecessary neuroprotective therapy. This classification should be interpreted

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cautiously: evidence for routine functional benefit of neuroprotective agents in acute stroke remains uncertain, and prescribing may also reflect local protocols or case-specific considerations. A defensible stewardship response is to document the intended indication, measurable treatment goal, planned duration, and stopping criteria, and then reassess continuation when benefit is not demonstrated [22,23]. Stress-ulcer prophylaxis in eight patients without documented high-risk features similarly supports periodic reassessment because unnecessary acid suppression adds cost and potential harm [24].

Dose-selection problems accounted for 20/135 events (14.8%), including 13 instances without documented renal-dose adjustment. In acute stroke, renal function may change during hospitalization; dose assessment should therefore use a consistent estimate of kidney function, current rather than isolated laboratory values, and drug-specific recommendations. Pharmacist-led renal-dosing protocols and multidisciplinary review can improve detection and resolution of such discrepancies [25–27]. The seven glycemic-management or hypoglycemia-related events also indicate the importance of linking dose decisions to oral intake, concurrent medicines, and serial glucose measurements [21].

Table 3. Association Between Clinical Factors and DRP Occurrence

Clinical Parameter	Category	DRP Present (n=82)	DRP Absent (n=16)	χ^2 Value	p-value
Age	< 60 years	31	11	5.235	0.022*
	≥ 60 years	51	5		
Number of Medications	< 8 drugs	18	12	17.737	< 0.001*
	≥ 8 drugs (Polypharmacy)	64	4		
Comorbidities	≤ 1 comorbid	22	10	7.746	0.005*
	≥ 2 comorbidities	60	6		
Length of Stay	< 5 days	30	12	8.067	0.005*
	≥ 5 days	52	4		

In unadjusted bivariate analyses, DRP occurrence was associated with receiving ≥8 medicines (p<0.001), having ≥2 comorbidities (p=0.005), age ≥60 years (p=0.022), and length of stay ≥5 days (p=0.005). The strongest crude separation was observed for the number of medicines: 78.0% of patients with a DRP received ≥8 medicines compared with 25.0% of those without a DRP. Similar associations between treatment complexity and DRP burden have been reported in stroke cohorts [8–10]. Nevertheless, these comparisons do not establish independent "determinants." Medication count and length of stay may partly reflect disease severity and may also increase after a DRP occurs. Multivariable modeling with confidence intervals and prespecified covariates would be required before claiming independent risk factors.

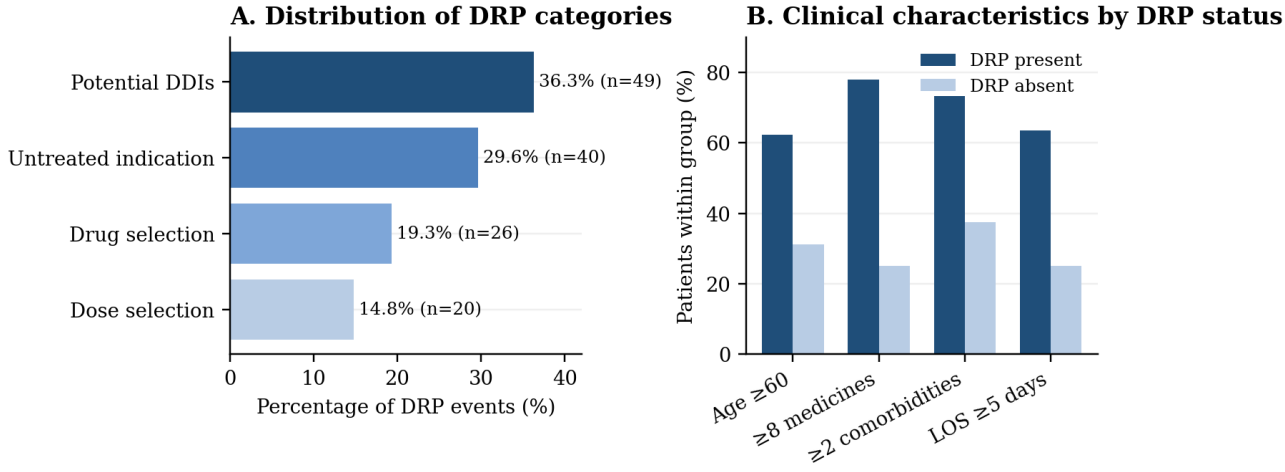

Figure 1. Distribution of identified DRP categories and clinical characteristics according to DRP status. Panel A is derived from Table 2 (N=135 events); Panel B is derived from Table 3 (N=98 patients). LOS, length of stay; DDI, drug–drug interaction.

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Limitations

This study has several limitations. Its retrospective, single-center design depends on the completeness of medical records and limits generalizability. Potential DDIs were identified from reference databases and were not necessarily accompanied by observed adverse outcomes. The analysis did not report inter-rater agreement for DRP classification, pharmacist intervention acceptance, clinical severity, stroke-severity scores, or patient-level outcomes. The bivariate analyses were unadjusted and may be confounded by disease severity, medication burden, and duration of hospitalization. Finally, the ethics-approval date post-dated the data-collection period; the manuscript should explicitly confirm that the committee authorized retrospective access to the records and any applicable consent waiver before publication.

Conclusions

In this single-center retrospective cohort, 82 of 98 stroke inpatients (83.7%) had at least one identified DRP, with 135 events documented. Potential DDIs and untreated indications were the most frequent categories. Receipt of ≥8 medicines, multiple comorbidities, older age, and longer hospitalization were associated with DRP occurrence in unadjusted analyses, but should not be interpreted as independent causal factors. The findings support structured medication reconciliation, indication and duration review, renal-dose surveillance, and guideline-informed secondary-prevention assessment by a multidisciplinary team that includes a clinical pharmacist. Prospective multicenter studies should evaluate DRP severity, intervention acceptance, preventable adverse drug events, and patient-centered outcomes.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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