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EVALUATION AND MANAGEMENT OF DRUG–DRUG INTERACTIONS IN STROKE PATIENTS

Dr. Pooja V. Salimath[1]*, Dr. Vanishree Babaladi[2], Dr. Syed Afzal Uddin Biyabani[3], Mrudulla M. Patil[4], Siddiqui Sabakarim[4], S. V. Divya[4], Vaibhavi Kattimani[4]

*[1,2]Associate Professor, Department of Pharmacy Practice, Matoshree Taradevi Institute of Pharmaceutical Sciences, Kalaburagi – 585105, Karnataka, India.
[3]Research Scholar, Department of Pharmacy Practice, Matoshree Taradevi Institute of Pharmaceutical Sciences, Kalaburagi – 585105, Karnataka, India.
[4]Pharm D Intern, Department of Pharmacy Practice, Matoshree Taradevi Institute of Pharmaceutical Sciences, Kalaburagi – 585105, Karnataka, India.

***Corresponding Author: Dr. Pooja V. Salimath**

Associate Professor, Department of Pharmacy Practice, Matoshree Taradevi Institute of Pharmaceutical Sciences, Kalaburagi – 585105, Karnataka, India.

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ABSTRACT

Background: Stroke patients frequently require multiple medications for the management of acute neurological events and associated comorbidities, leading to polypharmacy and an increased risk of potential drug–drug interactions (pDDIs). These interactions may compromise therapeutic outcomes and patient safety, particularly in critically ill and elderly populations. **Objective:** To evaluate the prevalence, severity, and clinical significance of potential drug–drug interactions among stroke patients and to assess the impact of clinical pharmacist interventions in their management. **Materials and Methods:** A prospective interventional study was conducted over six months in the Department of General Medicine at HKE's Basaveshwar Teaching and General Hospital, Kalaburagi. A total of 102 hospitalized stroke patients receiving at least two medications were included. Patient demographic details, comorbidities, and medication profiles were reviewed. Potential drug–drug interactions were identified and classified using Micromedex® based on severity and documentation. Identified pDDIs were communicated to prescribers, and pharmacist interventions were recorded along with acceptance rates. **Results:** Among the 102 stroke patients evaluated, 65.7% of prescriptions contained at least one pDDI, with a total of 236 interactions identified. Hyper-polypharmacy (>10 drugs) was observed in 75.5% of patients. The majority of pDDIs were classified as major (61.2%), followed by moderate (37.3%) and contraindicated (1.5%) interactions. Most interactions were supported by fair documentation. Of the identified pDDIs, 48 were communicated to prescribers, and 77.1% of pharmacist recommendations were accepted. Dose adjustment and regular monitoring were the most common interventions. Ondansetron and clopidogrel were the most frequently involved drugs. **Conclusion:** The study demonstrates a high prevalence of clinically significant pDDIs among stroke patients, largely driven by advanced age, comorbidities, and polypharmacy. Clinical pharmacist involvement played a crucial role in identifying, preventing, and managing pDDIs, thereby enhancing medication safety. Early pharmacist participation in prescription review and multidisciplinary care is essential to minimize drug-related risks in stroke management.

KEYWORDS: Stroke; Polypharmacy; Drug–Drug Interactions; Clinical Pharmacist; Micromedex; Patient Safety.

INTRODUCTION

Stroke is a major public health problem and remains one of the leading causes of mortality and long-term disability worldwide. It is clinically defined as a sudden onset of focal neurological dysfunction lasting more than 24 hours or leading to death, with a vascular origin. Stroke places a substantial burden on patients, families, and healthcare systems due to its associated physical, cognitive, and psychosocial consequences.[1]

Globally, stroke accounts for millions of deaths annually and is a leading cause of adult disability. The increasing prevalence of aging populations, urbanization, sedentary lifestyles, and chronic diseases has further escalated the incidence and recurrence of stroke, particularly in low- and middle-income countries.[2]

Based on etiology, stroke is broadly classified into ischemic stroke and hemorrhagic stroke. **Ischemic stroke** constitutes approximately 85–88% of all cases and occurs due to obstruction of cerebral blood flow caused by thrombus formation or embolic occlusion of cerebral arteries.[3] Cerebral atherosclerosis is the most common underlying pathology; however, nearly one-third of ischemic strokes remain cryptogenic despite extensive diagnostic evaluation.[4]

Embolic strokes may arise from extracranial or intracranial arterial sources, while the heart is responsible for approximately 20% of embolic events, particularly in patients with atrial fibrillation, valvular heart disease, or cardiomyopathy. Cardioembolic strokes are often more severe and associated with higher recurrence rates.[5]

Hemorrhagic stroke, accounting for nearly 12–15% of all strokes, results from rupture of cerebral blood vessels and includes intracerebral hemorrhage, subarachnoid hemorrhage, and subdural hematoma. Although less frequent than ischemic stroke, hemorrhagic stroke carries a higher risk of early mortality and poor neurological outcomes.[6]

Several **risk factors** contribute to stroke development. Non-modifiable risk factors include increasing age, male gender, ethnicity, and genetic predisposition. Modifiable risk factors such as hypertension, diabetes mellitus, atrial fibrillation, dyslipidemia, cigarette smoking, excessive alcohol consumption, obesity, and sickle cell disease play a crucial role in both primary and secondary prevention strategies.[7,8]

Stroke patients frequently present with multiple comorbidities that require long-term pharmacological management. This often results in polypharmacy, commonly defined as the concurrent use of multiple medications. Polypharmacy is categorized as minor (2–4 drugs), moderate (5–9 drugs), and severe (≥10 drugs) based on medication count.[9]

The prevalence of polypharmacy is particularly high among elderly stroke patients due to the coexistence of cardiovascular diseases, diabetes, and other chronic conditions. Studies report that more than half of stroke patients aged 65 years or older are prescribed five or more medications.[10]

Polypharmacy has been associated with adverse clinical outcomes including increased risk of adverse drug reactions, medication non-adherence, functional decline, hospital readmissions, cognitive impairment, and mortality.[11] In stroke survivors, polypharmacy has also been linked to increased post-stroke fatigue and poorer rehabilitation outcomes.[12]

One of the most clinically significant consequences of polypharmacy is the occurrence of drug–drug interactions (DDIs). DDIs are defined as alterations in the pharmacokinetics, pharmacodynamics, or adverse effect profile of a drug when administered with another drug. Stroke patients are particularly vulnerable due to narrow therapeutic index drugs such as anticoagulants and antiplatelets.[13]

Early identification of potential drug–drug interactions (pDDIs) is critical in preventing medication-related harm. pDDIs may lead to therapeutic failure, toxicity, increased bleeding risk, or worsening neurological outcomes if not promptly recognized and managed.[14]

Various electronic drug-interaction screening tools such as Micromedex®, Lexi-Interact®, Drug Interaction Facts®, EpocratesRx®, and Pharmavista® are widely used to detect and classify pDDIs according to severity and clinical relevance. Although these databases differ in sensitivity and specificity, they play an important role in routine clinical decision-making.[15]

Based on their mechanism of action, DDIs are broadly classified into pharmacodynamic and pharmacokinetic interactions. Pharmacodynamic interactions involve additive, synergistic, or antagonistic effects at the site of action, whereas pharmacokinetic interactions affect drug absorption, distribution, metabolism, or excretion.[16]

In stroke management, pharmacodynamic interactions such as enhanced bleeding with antiplatelet–anticoagulant combinations and pharmacokinetic interactions involving cytochrome P450 enzymes are of particular clinical concern.[17]

The clinical pharmacist plays a pivotal role in identifying, preventing, and managing polypharmacy and DDIs in stroke patients. Through comprehensive medication review, therapeutic optimization, dose adjustment, and patient counseling, pharmacists significantly contribute to improved safety and therapeutic outcomes.[18]

Pharmacist-led interventions have been shown to reduce inappropriate prescribing, minimize DDIs, improve medication adherence, and enhance quality of life in patients with chronic neurological conditions, including stroke.[19]

Effective strategies to prevent inappropriate polypharmacy include regular medication reconciliation, deprescribing unnecessary drugs, simplifying dosing regimens, screening for drug–drug and drug–disease interactions, and adopting a multidisciplinary, patient-centered approach to care.[20]

MATERIALS AND METHODS

This prospective interventional study was conducted in the Department of General Medicine at HKE's Basaveshwar Teaching and General Hospital, Kalaburagi, over a period of six months. The primary objective of the study was to evaluate and manage potential drug–drug interactions (pDDIs) among stroke patients. The specific objectives included assessing patient demographic characteristics, evaluating their disease conditions, determining the extent of polypharmacy, identifying potential drug–drug interactions, and assessing the severity of these interactions. Data for the study were obtained from the case sheets and medication records of inpatients admitted to the general medicine department. Patients who met the eligibility criteria during the study period were enrolled. The inclusion criteria consisted of patients of either sex, patients admitted to the general medicine department, prescriptions containing at least two drugs, patients above 18 years of age, and stroke patients with or without comorbidities who were willing to participate. Patients who were terminally ill, discharged against medical advice, or receiving treatment as outpatients were excluded from the study.

RESULTS

A total of 102 stroke patients were evaluated during the study period. Of these, 65 patients (63.7%) were male and 37 (36.3%) were female. The majority of patients belonged to the 58–77 years age group (48.0%), followed by the 38–57 years group (33.3%). Only a small proportion of patients were younger than 37 years or older than 78 years.

Regarding medication burden, hyper-polypharmacy (>10 drugs) was observed in 77 prescriptions (75.5%), while major polypharmacy (5–9 drugs) was noted in 24 prescriptions (23.5%). Moderate polypharmacy (2–4 drugs) was seen in only one prescription (1.0%), indicating a high overall medication load among stroke patients.

Demographic Characteristics and Polypharmacy Distribution

Table 1 presents the demographic profile of the study population along with the distribution of polypharmacy status. This table provides baseline information on age, gender, and medication burden among the enrolled stroke patients.

Table No. 1: Demographic and Polypharmacy Distribution of Study Population (N = 102).

Category	Sub-Category	Number of Patients
Age Group (years)	18–37	9
	38–57	34
	58–77	49
	78–97	10
Gender	Male	65
	Female	37
Polypharmacy Status	Hyper (>10 drugs)	77
	Major (5–9 drugs)	24
	Moderate (2–4 drugs)	1
Total Patients	—	102

Distribution of Potential Drug–Drug Interactions per Prescription

Out of 102 prescriptions evaluated, 67 prescriptions (65.7%) contained at least one potential drug–drug interaction (pDDI), accounting for a total of 236 pDDIs. Thirty-five prescriptions (34.3%) showed no pDDIs. The number of pDDIs per prescription ranged from 1 to 16, with most patients experiencing two or more interactions.

Table 2 illustrates the frequency distribution of pDDIs per prescription, highlighting the extent of interaction risk associated with polypharmacy.

Table No. 2: Distribution of Potential Drug–Drug Interactions per Prescription (N = 102).

Number of pDDIs	Number of Prescriptions
0	35
1	10
2	27
3	9
4	5
5	4
6	4
7	3

8	1
9	1
13	1
14	1
16	1
Total	102

Severity, Documentation, and Error Reach of pDDIs
Based on severity assessment, 41 pDDIs (61.2%) were classified as major, 25 (37.3%) as moderate, and 1 (1.5%) as contraindicated. Documentation analysis using Micromedex® revealed that most interactions were supported by fair evidence.

Regarding error reach, 46 pDDIs reached the patient, while 21 interactions did not reach the patient due to timely intervention.

Table 3 summarizes the severity classification, documentation levels, and error reach status of identified pDDIs.

Table No. 3: Severity, Documentation, and Error Reach of pDDIs (N = 67).

Category	Sub-Category	Number
Severity of pDDIs	Contraindicated	1
	Major	41
	Moderate	25
Documentation (Micromedex®)	Excellent	6
	Good	16
	Fair	45
Error Reach	Error Reached Patient	46
	Error Did Not Reach Patient	21
Total pDDIs	—	67

Communication of pDDIs and Prescriber Acceptance
Among the identified pDDIs, 48 interactions were communicated to prescribers, while 19 were not reported. Of the 48 reported pDDIs, 37 (77.1%) recommendations were accepted by prescribers, demonstrating a high level of interdisciplinary collaboration.

Table 4 details prescriber communication and acceptance of pharmacist-reported pDDIs.

Table No. 4: Prescriber Communication and Acceptance of pDDIs (N = 67).

Category	Sub-Category	Number
pDDIs Reported to Prescriber	Yes	48
	No	19
Prescriber Response (N = 48)	Accepted	37
	Not Accepted	11

Pharmacist Interventions and Timing
Pharmacist recommendations included dose adjustment, alteration in administration timing, therapeutic substitution, and regular monitoring. Most interventions occurred after drug administration, indicating delayed detection of pDDIs in several cases.

Table 5 outlines the types of pharmacist interventions provided and the timing of these interventions.

Table No. 5: Pharmacist Interventions and Timing of Intervention (N = 67).

Category	Sub-Category	Number
Pharmacist Suggestions (N = 37)	Dose Adjustment	13
	Change in Administration Time	6
	Alternate Drug Suggested	5
	Metoclopramide instead of Ondansetron	1
	Reduce KCl Dose	1
	Regular Monitoring	11
Timing of Intervention	After Administration	47
	During Administration	2
	During Prescription	18

DISCUSSION

The present study was conducted to evaluate the prevalence, severity, and management of potential drug–drug interactions (pDDIs) among stroke patients and to assess the impact of clinical pharmacist interventions in a tertiary care hospital setting. Over a six-month period, a total of 102 stroke patients admitted to the General Medicine ward, ICCU, MICU, and AMC wards were analyzed. The findings highlight a substantial burden of polypharmacy and pDDIs in stroke patients, emphasizing the need for vigilant medication review and interdisciplinary collaboration.[21]

In the present study, male patients (63.7%) predominated over females (36.3%). This male preponderance aligns with epidemiological evidence suggesting a higher incidence of stroke among males, particularly in middle and older age groups, possibly due to greater exposure to modifiable risk factors such as smoking, alcohol consumption, and cardiovascular disease.[22] the observed gender distribution is consistent with findings reported by Johnson et al., who documented a similar male-to-female ratio among stroke patients.[23]

Age-wise distribution revealed that the majority of patients (48%) belonged to the 58–77 years age group, followed by those aged 38–57 years. This trend underscores the strong association between advancing age and stroke risk, which may be attributed to progressive vascular changes, increased comorbidities, and cumulative exposure to risk factors. Similar age distributions have been reported in previous stroke-related pharmacotherapy studies.[24]

Polypharmacy was highly prevalent in the study population. Hyper polypharmacy was observed in 77 prescriptions, while major and moderate polypharmacy were noted in 24 and 1 prescriptions, respectively. This high prevalence reflects the complex therapeutic requirements of stroke patients, who often require antiplatelets, anticoagulants, antihypertensives, statins, antidiabetics, and supportive medications. Previous studies have consistently demonstrated a direct association between polypharmacy and increased risk of adverse drug events and DDIs.[25]

Out of 102 prescriptions evaluated, 67 (65.7%) contained at least one pDDI, accounting for a total of 236 identified interactions. This high prevalence of pDDIs is comparable with findings from Acharya et al., who reported that a significant proportion of hospitalized patients experienced at least one potential interaction.[26] The increasing number of pDDIs with rising medication count further reinforces the established relationship between polypharmacy and drug interaction risk.

Severity analysis showed that the majority of pDDIs were classified as major (61.2%), followed by moderate (37.3%) and contraindicated interactions (1.5%). These findings are consistent with earlier studies that reported a predominance of moderate-to-major interactions in hospitalized patients.[23] Major interactions are clinically significant and may result in serious adverse outcomes if left unmanaged, highlighting the importance of early identification and timely intervention.

Regarding the level of documentation, most interactions were supported by fair evidence, while a smaller proportion had good or excellent documentation. This distribution is consistent with published literature, where many clinically relevant interactions rely on observational data or pharmacological plausibility rather than randomized trials.[27]

In the present study, 46 patients experienced medication-related errors associated with DDIs, whereas 21 patients did not progress to error outcomes. Notably, 48 pDDIs were communicated to prescribers, of which 37 interventions were accepted. This relatively high acceptance rate underscores the value of pharmacist-led recommendations and reflects growing recognition of the clinical pharmacist's role in optimizing drug therapy.[28]

Pharmacist interventions included dose adjustments, changes in administration timing, therapeutic substitutions, and enhanced monitoring. Dose adjustment was the most frequent intervention, followed by regular monitoring and scheduling changes. Such interventions have been shown to significantly reduce adverse drug events and improve therapeutic outcomes in hospitalized patients.[29]

The majority of interventions were made after drug administration, indicating the need for earlier pharmacist involvement during prescription and dispensing stages. Integrating clinical pharmacists into multidisciplinary ward rounds may help identify and prevent pDDIs at earlier stages of patient care.[30]

Drugs most commonly involved in pDDIs included ondansetron, tramadol, telmisartan, clopidogrel, levofloxacin, theophylline, atorvastatin, metformin, potassium chloride, and heparin. Ondansetron, atorvastatin, levofloxacin, and clopidogrel were the most frequently interacting drugs. Similar patterns have been reported by Venkateswaramurthy et al., highlighting the recurrent involvement of cardiovascular and supportive medications in DDIs among hospitalized patients.[31]

Overall, the findings of this study emphasize the high prevalence of pDDIs in stroke patients and reinforce the critical role of clinical pharmacists in identifying, preventing, and managing medication-related problems to enhance patient safety and clinical outcomes.

CONCLUSIONS

Among 102 cases analysed, 67 Different pDDIs found, Our study reveals that majority of pDDIs were majorly based on severity and majority of interactions which falls under Micromedex. The possible factors that cause pDDIs are age, co-morbid conditions and polypharmacy. As length of stay increases the polypharmacy increases, resulting in more number of pDDIs. The majority of pDDIs can be avoided just by changing the time of administration and the rest of pDDIs require monitoring.

In a nutshell, we conclude that, clinical pharmacist can play important role in critical care unit in reducing and avoiding these pDDIs. The population in critical care unit have multiple co morbidities which often require high risk medication and need of time sensitive medication decisions. Routine ward rounds, frequent monitoring of drugs and lab data, assisting the physician to select the drugs and dosage forms reduces such pDDIs.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

ETHICAL APPROVAL

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee prior to the initiation of the study.

INFORMED CONSENT

Written informed consent was obtained from all participants or their legally authorized representatives before inclusion in the study.

AUTHORS' CONTRIBUTIONS

All authors contributed significantly to the conception and design of the study. Data collection, analysis, and interpretation were performed collaboratively. The manuscript was drafted and critically revised by the authors, and all authors approved the final version for publication.

LIMITATIONS OF THE STUDY

The study was conducted at a single centre with a limited sample size, which may restrict the generalizability of the findings. Additionally, potential DDIs were identified using interaction-checking databases and may not always translate into clinically significant outcomes.

CLINICAL SIGNIFICANCE

This study highlights the high prevalence of potential drug–drug interactions among stroke patients and underscores the critical role of clinical pharmacists in identifying, preventing, and managing medication-related problems to improve patient safety and therapeutic outcomes.

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