RESEARCH ARTICL

# The Implementation and Evaluation of Pharmaceutical Care Plan in Stroke Patients at Tertiary Care Hospital

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## ABSTRACT

**Objective:** To assess the pattern and prevalence of adverse drug reactions (ADRs) reported by the neurology department and review the benefits of the pharmaceutical care plan.

**Materials and Methods:** A total of 148 stroke cases with previous medication history correlated with current complaints leading to hospitalization were included in the prospective study for one year in the neurology department.

**Results:** This study identified non-adherence (50%) and ADRs (38%). Ignorance of the disease, its complications, and the possible adverse effects of self-medication have been identified as risk factors. The medication-related problems were mainly observed with antimicrobials, central nervous system (CNS), central venous system (CVS), and inflammatory and immune modulators.

**Conclusion:** The risk factors involved are illiteracy regarding prescribed therapy benefits. In the patient's medication therapy, warfarin has more adverse events, and an observation of the patient's plasma concentration levels increased.

**Keywords:** Adverse events, Drug-related problems, Hospitalization, Pharmaceutical care plan, Warfarin.

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## INTRODUCTION

In the present scenario, drug-related problems are more prominent in overall treatment. When drug-related problems are not observed or eliminated at the right time, it affects the patient's quality of life and causes an economic burden. Mainly, the problems arise when there is polypharmacy, lack of knowledge of health practitioners, negligence of hospital staff, and lack of clinical pharmacists. All these significant concerns lead to morbidity and mortality.[1] In today's hair care system, drug-related problems have become a primary concern and a great challenge to improve the quality of treatment.[2] In the research literature, many drug categorization systems are available, and most of those systems focus on the problems associated with the patient drug-related problems. The most frequently occurring adverse drug reaction (ADR) are non–adherence to the prescribed therapy, sub-therapeutic dose, overdosage of the drug, and therapeutic duplication.[3] Evaluation of drug-related problems and their risk factors are essential for eliminating drug-related problems and, primarily, the economic burden on patients. The study mainly focuses on the benefits of pharmaceutical care plans in reducing adverse effects, highly possible drug-related problems, and drug interaction complications. High-risk patients such as geriatrics, patients with co-morbidities, and polypharmacy are needed with special monitoring on drug-related problems.

## MATERIALS AND METHODS

The study type is a retrospective observational study performed in the South Indian population. During the study period, the patients' data helps determine the occurrence of drug-related problems. Mainly the patients or their caretakers who can communicate adequately are included in the study.[4] Ambulatory patients, patients using herbal medicines, and substance abuse patients are excluded.

### Plasma Warfarin Determination

*Collection and preparation of samples*

The blood from veins (5 mL) is withdrawn from the patient and placed in the sodium ethylene diamine tetra acetic acid tubes. The plasma separation from the sample is done by centrifugation technique (3000 rpm) for 10 minutes and stored at 70°C.

*Standard preparation*

Warfarin standard solution, 7-hydroxy warfarin, and internal standard of carbamazepine are prepared at a concentration (1-µg/mL) in methanol. Then, warfarin and 7-hydroxywarfarin

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standard solution in human plasma is analyzed at specific concentrations. All the samples are stored well in standard conditions. The standard curves for solutions were calibrated before analysis. The six standard analyte solutions were arranged by diluting MilliQ water for 100% control.

*Procedure for extraction*

Solid-phase extraction is done to bring out the drug mainly from the collected plasma samples. For the 1-mL standard solution, carbamazepine (10 µL of 1-mg/mL) is added. The C18 cartridges are utilized for the process of extraction. One percent methanol (2 mL) is adjusted with ortho-phosphoric acid at a pH of 2.8 to condition cartridges. The plasma samples were introduced into the columns, which were retained with 7-hydroxywarfarin and warfarin, and then it was eluted with acetonitrile (2 mL). In the next step, the organic phase is introduced into glass tubes and evaporated to dryness under the influence of nitrogen gas at 60ºC in the water bath. The sample solutions were remade with MilliQ water (200 mL), with 50 µL of the solution was administered into HPLC columns.

*Chromatography technique*

The mobile phase consists of (60:40) potassium phosphate buffer (dipotassium hydrogen phosphate) and isopropanol. The pH was adjusted to 7.0 with potassium phosphate buffer. The HPLC constituted of the Shimadzu SPD-10A UV/VIS detector, the Shimadzu LC-10AD solvent delivery module, and a 100 µl injection loop. The flow rate is adjusted to 1-mL/min, the analyte is identified at 308 nm, the absorbance is set at 0.005 Aufs, and the separation is done on the C18 column. The retention time of 7-hydroxywarfarin, warfarin, and carbamazepine was 2.9, 3.6, and 5.9 minutes, respectively. The chromatographs obtained are examined using CLASS-VP version 6.14 SP2 software. The reproducibility method, accuracy, and precision were determined by quality control samples containing warfarin and 7-hydroxywarfarin at the concentration range from 0.1 to 5.0 mg/mL. Six replicates observe the assay accuracy and precision at 2.5 and 5 mg/mL. The precision and accuracy were identified over 15 days utilizing similar concentration ranges. The analysis of the standard solution is done on the same day as the sample analysis to calculate the concentrations of 7-hydroxywarfarin and warfarin standard solution. The established detection limit is done by serial extractions of plasma samples containing a reduced concentration of 7-hydroxywarfarin and warfarin standard solution

## RESULTS AND DISCUSSION

A total of 452 cases with prior medical histories were examined for the study. The patient history is taken by using medical charts and enquiring patients or care takers. 148 cases were allocated for the study, while 304 instances were excluded based on the exclusion criteria. 159 drug-related issues were found in the patients who were enrolled. The various metrics are assessed in relation to drug-related issues. Patients with prior medical histories are more likely to experience drug-related issues than the general population. The patients with various past medical histories who are more likely to prone drug related problems are listed in Table 1.

**Table 1:** Distribution according to past medical history

| *Sl. No* | *Past medical history* | *Frequency* | *Percentage (%)* |
|---|---|---|---|
| 1 | Cardiovascular disease | 35 | 23.65 |
| 2 | Central Nervous disease | 31 | 20.94 |
| 3 | Skin disorders | 20 | 13.51 |
| 4 | Metabolic disease | 17 | 11.50 |
| 5 | Renal disease | 12 | 8.11 |
| 6 | Immune disease | 10 | 6.76 |
| 7 | GI disease | 06 | 4.05 |
| 8 | Respiratory disease | 03 | 2.03 |
| 9 | Others | 14 | 9.45 |
| | Total | 148 | 100 |

**Table 2:** Distribution according to risk factor frequency and percentage

| *Sl. No* | *Risk factors* | *Frequency* | *Percentage (%)* |
|---|---|---|---|
| 1 | Illiteracy | 89 | 39.73 |
| 2 | Inappropriate use of medication | 35 | 15.65 |
| 3 | Hypersensitivity | 33 | 14.73 |
| 4 | Self-medication | 22 | 9.82 |
| 5 | Age | 17 | 7.59 |
| 6 | Narrow therapeutic index drugs | 12 | 5.35 |
| 7 | Parasitic and Infectious diseases | 8 | 3.57 |
| 8 | Social habits | 6 | 2.67 |
| 9 | Economic status | 2 | 0.89 |
| | Total | 225 | 100 |

### Distribution Based on Past Medical History

Table 1 represents 225 risk factors responsible for 159 drug-related problems as assessed. Among patients with past medical history, 148 cases have a higher prevalence of drug-related problems. CVS diseases are 35 (23.65%), CNS diseases are 31 (20.94%), skin diseases are 20 (13.51%), metabolic diseases are 17 (11.50%), renal diseases are 12 (8.11%), immune diseases are 10 (6.76%), GI disease is 06 (4.05%), respiratory disease is 03 (2.03%), and others are 14 (9.45%).

### Risk Factors

Among 159 drug-related problems are illiteracy 89 (39.73%), inappropriate use of medication 35 (15.65%), hypersensitivity 33 (14.73%), self-medication 22 (9.82%), age 17 (7.59%), narrow therapeutic index drugs 12 (5.35%), parasitic and Infectious diseases 8 (3.57%), social habits 6 (2.67%), economic status 2 (0.89%). The following table distributed 225 risk factors contributing to each identified drug-related problem in 148 patients (Table 2).

### Risk Factors and Drug-Related Problems Distribution

Illiteracy 71 (31.70%) was predominant for non-adherence, and hypersensitivity 33 (14.73%) was found to be predominant for Adverse drug reactions. Among overuse of drugs, therapeutic

**Table 3:** Drug-related problems and risk factors

| *Sl. No* | *DRP* | *Risk factor* | *Frequency* | *Percentage* |
|---|---|---|---|---|
| 1 | Non-adherence | Lack of knowledge | 71 | 31.70 |
| | | Inappropriate medication use | 18 | 8.04 |
| | | Age | 7 | 3.12 |
| | | Social habits | 6 | 2.67 |
| | | Economic status | 2 | 0.89 |
| | | Infectious diseases | 2 | 0.89 |
| 2 | Adverse drug reaction | Hypersensitivity and pharmacology | 33 | 14.73 |
| | | Self –medication | 17 | 7.58 |
| | | Narrow therapeutic index | 10 | 4.50 |
| | | Inappropriate medication use | 10 | 4.50 |
| | | Age | 6 | 2.67 |
| | | Infectious diseases | 6 | 2.67 |
| | | Lack of knowledge | 6 | 2.67 |
| 3 | Overuse of the drug | Inappropriate medication use | 8 | 3.57 |
| | | Self –medication | 6 | 2.67 |
| | | Lack of knowledge | 6 | 2.67 |
| | | Age | 1 | 0.45 |
| 4 | Therapeutic duplication | Lack of knowledge | 3 | 1.33 |
| | | Narrow therapeutic index | 2 | 0.89 |
| | | Inappropriate medication use | 1 | 0.45 |
| 5 | Wrong administration | Lack of knowledge | 2 | 0.89 |
| | | Inappropriate medication use | 1 | 0.45 |
| Total | | | 225 | 100 |

**Table 4:** Assessment of significant risk factors in non-adherence

| *Non-adherence* | | | | | |
|---|---|---|---|---|---|
| | | Yes | No | RR | CI |
| | | 81 | 67 | | |
| Lack of knowledge | Yes | 71 | 18 | 3.26 | 2.17 to 4.85 |
| | No | 10 | 49 | | |
| Inappropriate medication use | Yes | 18 | 17 | 0.87 | 0.49 to 1.56 |
| | No | 63 | 50 | | |
| Age | Yes | 7 | 10 | 0.57 | 0.23 to 1.43 |
| | No | 74 | 57 | | |
| Infectious diseases | Yes | 2 | 6 | 0.27 | 0.05 to 1.32 |
| | No | 79 | 61 | | |

**Table 5:** Assessment of significant risk factors in adverse drug reaction

| *Adverse drug reaction* | | | | | |
|---|---|---|---|---|---|
| | | *Yes* | *No* | *RR* | *CI* |
| | | *61* | *87* | | |
| Hypersensitivity | Yes | 29 | 4 | 11.57 | 4.29 to3.19 |
| | No | 28 | 87 | | |
| Self-medication | Yes | 17 | 5 | 4.84 | 1.89 to 12.43 |
| | No | 44 | 82 | | |
| Narrow therapeutic indexw | Yes | 10 | 2 | 7.13 | 1.61 to 31.40 |
| | No | 51 | 5 | | |
| Inappropriate medication use | Yes | 10 | 25 | 0.57 | 0.29 to 1.09 |
| | No | 51 | 62 | | |
| Age | Yes | 11 | 6 | 2.61 | 1.02 to 6.68 |
| | No | 50 | 81 | | |
| Infectious diseases | Yes | 6 | 2 | 1.27 | 0.89 to 20.49 |
| | No | 55 | 85 | | |
| Lack of knowledge | Yes | 6 | 83 | 0.10 | 0.04 to 0.22 |
| | No | 55 | 4 | | |

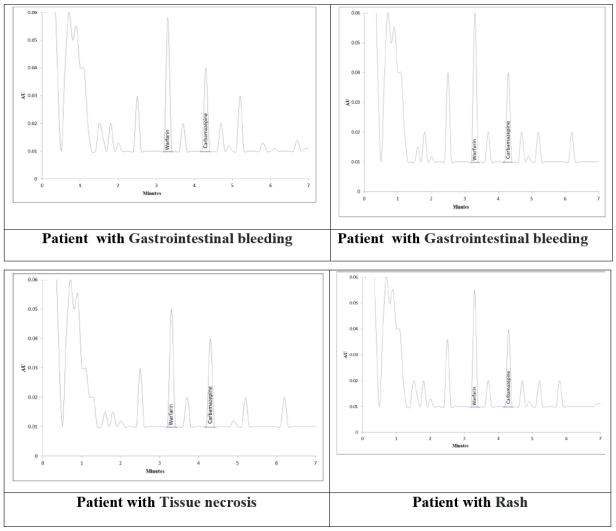
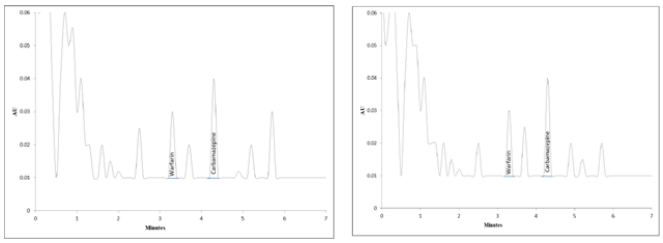



**Figure 1:** Estimation of plasma levels of warfarin in adverse events Patients

duplication, and wrong administration above mentioned risk factors have approximately the same impact on developing respective drug problems (Table 3).

## Assessment of Significant Risk Factors in Adverse Drug Reaction

Hypersensitivity shows an 11.57 times higher risk for adverse drug reactions than other risk factors. A narrow therapeutic index, self-medication, age, and infectious diseases in the order of relative risk follow hypersensitivity. Inappropriate medication use and lack of knowledge need 175 and 1000 more cases of drug-related problems to attain significant relative risk. Among 142 patients, four severe adverse events were observed.[6] The events are due to the narrow therapeutic drug warfarin. Moreover, two patients have gastrointestinal bleeding, one with tissue necrosis and one with a rash.[7]




No Adverse Events Patients Warfarin Concentration levels

**Figure 2:** Estimation of plasma levels of warfarin in non-adverse events patients

Warfarin concentration levels were estimated in four patients and two patients (no adverse events) (Tables 4 and 5).

### Estimation of Plasma Levels

Two patients had gastrointestinal bleeding and adverse events. Among them, plasma concentrations of warfarin were found to be 6 and 5.8 µg/mL. In non-adverse events patients (two), warfarin plasma concentrations were 3 and 2.8 µg/mL in gastrointestinal bleeding patients, almost double plasma concentrations of regular patients.

In tissue necrosis patients, the plasma concentrations of warfarin were 5 µg/mL in non-adverse events patients, (two) plasma concentrations of warfarin were found to be 3 and 2.8 µg/mL. In tissue necrosis, patient plasma concentrations of warfarin are 1.72 times more than in regular patients.

In rash patients, the plasma concentrations of warfarin were 5.2 µg/mL, and in non-adverse events patients, (two) plasma concentrations of warfarin were 3 and 2.8 µg/mL. In rash conditions, patient plasma concentrations of warfarin were 1.79 times more than regular patients.

Overall, among four patients have adverse events, four patients' plasma concentrations of warfarin were found to be 5, 5.2, 5.8, and 6 µg/mL, mean ± Sd 5.5 ± 0.17 µg/mL, in non-adverse event patients plasma concentrations of warfarin were found to be 3, and 2.8 µg/mL, mean ± Sd was 2.9 ± 0.01 µg/mL, *p-value* is 0.001. Warfarin levels were very high in gastrointestinal bleeding patients compared to non-adverse events. Patient details are shown in Figures 1 and 2. Warfarin plasma concentration levels were also increased in tissue necrosis and rash patients.

## DISCUSSION

The 452 cases with past medical history were included in the study and observed. The number of cases is 148 allotted in the study, and the cases excluded are 304, depending on exclusion criteria. In the cases excluded, 110 patients have nil inter-relationship between current reasons for admission and past medical history, The identified results are that DRP is more common with age of 1–10 years, and males have an increased risk of drug-related problems than females due to social habits, as Kumar BPS (2013). The non-adherence is (50.94%), and ADR is (38.36%) in the identified drug-related problems, as same stated by, which showed ADR (39.3%) and a higher incidence of non-compliance (44.3%). To avoid the risk of ADR, patients should be alert and have knowledge of the therapy they are receiving and should inform the suspected ADRs as soon as possible. The management of ADR will be easier for a physician, as reported. The study also stated that geriatrics and children have an increased risk of non-adherence to the medications, leading to different complications.[8] ADRs have more incidences in adults. It also observed that risk factors like lack of knowledge, inappropriate medication use, hypersensitivity towards drugs, and pharmacology of certain drugs have a higher impact on drug-related problems. Illiteracy about the disease and the need for pharmacological management are the main risk factors for the development of non-adherence. In contrast, hypersensitivity to drugs and pharmacology of drugs are the main risk factors for developing ADR, which are unavoidable.[9] Similar findings were reported by. The study also explains that the increased incidence of drug-related problems is mainly noticed in a patient with a previous medical history of CNS and CVS disease, as stated by. Similar findings were reported by patients with inadequate awareness and improper use of medications has more risk of DRP. It is also observed that patients who have past medical history have a higher chance of drug-related problems, as stated. In a study of 501 outpatients, 41 patients experienced 51 hemorrhagic episodes (incidence 4.3–8.2% per treatment year), and the risk of hemorrhage was unrelated to age. In patients with aortic valve prosthesis, there is an increased risk of bleeding between the fifth to seventh years with oral anticoagulants.[10] The clinician faced with the anticoagulated patient experiencing bleeding is often tempted to label the bleeding a "normal side effect" of anticoagulant therapy.[11] However, bleeding episodes encountered in anticoagulated patients with unmasked tumours are not uncommon.[12] The discovery of urinary tract infections, renal stones, peptic ulcer disease, and other more innocuous lesions is even more frequent.[13] Gastrointestinal and genitourinary bleeding commonly occurs at prothrombin times (PTs) which are considered within the normal therapeutic range; spontaneous soft tissue haemorrhage is more likely associated with supra-therapeutic patient.[14] The purple toe syndrome, characterized as the dark purplish or mottled colour of the toes, occurs between 3- and 20-weeks following warfarin therapy initiation.[15]

## CONCLUSION

Non-adherence to prescribed treatment is the main cause of drug-related problems, leading to an adverse drug reaction. The most often involved risk factors are illiteracy about the disease, prescribed treatment, and therapeutic benefits.

## ETHICAL APPROVAL

VISTAS SPS IEC approves the Ethical committee and approval reference number is VISTAS-SPS/IEC/VI/2021/12.

## REFERENCES

1. Acheampong F, Nkansah FA, Anto BP. Drug-related problems and their clinical interventions in a Ghanaian teaching hospital. Safety in Health. 2016 Dec;2(1).

2. Pk A, Adepu R. DRUG RELATED PROBLEMS: AN OVERVIEW OF VARIOUS CLASSIFICATION SYSTEMS. 2014;7.
3. Randhawa M, Al-Wahhas M, Al-Jumaan M, Alghamdy M. Admissions for drug-related problems at the Emergency Department of a University Hospital in the Kingdom of Saudi Arabia. J Family Community Med. 2015;22(1):44.
4. Randhawa M, Al-Wahhas M, Al-Jumaan M, Alghamdy M. Admissions for drug-related problems at the Emergency Department of a University Hospital in the Kingdom of Saudi Arabia. J Family Community Med. 2015;22(1):44.
5. Andreazza RS, Silveira De Castro M, Sippel Köche P, Heineck I. Causes of drug-related problems in the emergency room of a hospital in southern Brazil. Gac Sanit. 2011 Nov;25(6):501–6.
6. Easton KL, Parsons BJ, Starr M, Brien JAE. The incidence of drug-related problems as a cause of hospital admissions in children. Medical Journal of Australia. 1998 Oct 5;169(7):356–9.
7. Li M, Fan Y, Zhang X, Hou W, Tang Z. Fruit and vegetable intake and risk of type 2 diabetes mellitus: Meta-analysis of prospective cohort studies. BMJ Open. 2014;4(11).
8. Forfar JC. A 7-year analysis of haemorrhage in patients on long-term anticoagulant treatment [Internet]. Vol. 42, British Heart journal. 1979. Available from: http://heart.bmj.com/
9. Hsu WT, Shen LJ, Lee CM. Drug-related problems vary with medication category and treatment duration in Taiwanese heart failure outpatients receiving case management. Journal of the Formosan Medical Association. 2016 May 1;115(5):335–42.
10. Kroovand RL, Bell TE, Kohler HH. Coumadin induced hematuria simulating a renal pelvic tumor: case presentation and review of the literature. Journal of Urology. 1974;111(2):223–4.
11. Mannheimer B, Ulfvarson J, Eklöf S, Bergqvist M, Andersén-Karlsson E, Pettersson H, et al. Drug-related problems and pharmacotherapeutic advisory intervention at a medicine clinic. Eur J Clin Pharmacol. 2006 Dec;62(12):1075–81.
12. Michaels MM. Bleeding from Occult Tumors during Anticoagulant Therapy [Internet]. Available from: http://circ.ahajournals.org/
13. Dahal P, Venkataraman R. Assessment of clinical pharmacist intervention in tertiary care teaching hospital of Southern India Community pharmacy staff's perception and dispensing practice of herbal products in eastern, Nepal: A cross-sectional study View project THE RELATION BETWEEN INTERNET, DEPRESSION, SELF-ESTEEM AND SOCIAL ATTACHMENT ON COGNITIVE FUNCTION OF HEALTH CARE INDIVIDUALS View project [Internet]. 2013. Available from: https://www.researchgate.net/publication/323677493
14. Rashed AN, Wilton L, Lo CCH, Kwong BYS, Leung S, Wong ICK. Epidemiology and potential risk factors of drug-related problems in Hong Kong paediatric wards. Br J Clin Pharmacol. 2014;77(5):873–9.
15. Singh H, Kumar BN, Sinha T, Dulhani N. The incidence and nature of drug-related hospital admission: A 6-month observational study in a tertiary health care hospital. J Pharmacol Pharmacother. 2011 Jan;2(1):17–20.