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Incidence of Drug-drug Interactions and the Role of Clinical Pharmacists in Neurological Ward

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Abstract— Introduction: Drug-drug interactions (DDIs) present a significant challenge for patients, as concurrent medication use can lead to adverse effects. Early detection can mitigate these complications, and clinical pharmacists play a key role in providing guidance and facilitating communication with physicians. Objective: This study aimed to assess the prevalence of DDIs and evaluate the pharmacist's role in monitoring these interactions at Shar Hospital's neurology department in Sulaimani, using free drug interaction checker mobile applications. Patients and Methods: A prospective observational and interventional study was conducted at Shar Teaching Hospital, Sulaimani, from Nov. 2021 to Feb. 2022. The observational phase assessed DDI incidence and types in patients admitted to the neurology ward. In the interventional phase, clinical pharmacists reviewed high-risk patients' medications, identified potential interactions, and recommended interventions, such as dose adjustments, alternative medications, or additional monitoring. The impact of these interventions on reducing DDIs and improving outcomes was then evaluated. Results: The study found that 41.1% of patients used 3-5 drugs, while 37.4% used 6-10 drugs. Among the cases, 50.5% showed no interactions, 39.5% had minor interactions, and 3.7% had significant interactions. DDIs accounted for 49% of all interactions. Of the prescribed medications, 50.5% required no intervention, while 49.5% did, with 15.8% of these cases being resolved. In terms of drug therapy problems (DTP), 18% of interventions fully resolved the issue, 17% partially resolved it, and 65% had no resolution. Conclusion: The study highlights the increasing prevalence of DDIs, underscoring the need for enhanced recognition of pharmacists' roles, particularly in polypharmacy, and improved communication between specialists and pharmacists.

Keywords*:* Drug-Drug interaction (DDIs), adverse drug reactions, pharmacist intervention, clinical pharmacist, neurological medications

1. Introduction

Drug-drug interactions (DDIs) are a prevalent concern impacting individuals in both inpatient and outpatient settings, with the potential to result in severe health complications and life-threatening outcomes if not addressed [1]. Several clinical factors have been reported to influence the susceptibility of a drug interaction. These include a history of drug allergies, older age, the number of prescription drugs, and the presence of certain medical conditions [2]. The utilization of multiple classes of medications to treat various types of diseases in the same patient (s) elevates the risk of drug-drug interactions (DDIs)[3, 4], and interactions among medications can yield both

advantageous and detrimental outcomes. Positive interactions enhance the efficacy of drugs, diminish the likelihood of adverse events, and facilitate the administration of moderate dosages. Conversely, negative interactions can improve drug fficacy with unwanted and potentially deleterious effects in the body. As a result, Drug-drug interactions (DDIs) can increase or decrease the therapeutic efficacy of several drugs, in addition to enhancing undesirable side effects[5].

The simultaneous intake of more than one drug can have the potential to cause congenital abnormalities, life-threatening conditions, hospitalization, disability in body function, and death[6, 7]. DDIs are divided into pharmacodynamic and pharmacokinetic interactions depending on the mechanism. Pharmacodynamic interactions are synergistic or antagonistic effects of the interacting drugs, whereas pharmacokinetic interactions influence the plasma levels of the interacting drugs. Unforeseen changes in the condition of a patient resulting from administering a combination of drugs can indicate a potentially significant interaction. DDIs are an important cause of drug side effects, accounting for approximately 3-5% of all adverse drug reactions[8, 9]. The inhibition of drug-metabolizing enzymes represents a significant drug-drug interaction (DDI) with serious pharmacological consequences, potentially increasing plasma levels of co-administered drugs [10]. Lack of comprehensive knowledge about potential interactions affecting the patient is creating a potential risk that can cause harm. Producing a simulation method that can find all possible interactions before effecting a new treatment has become vital[11]. A comprehensive study on drug-drug interactions involving metabolism and transport considering the needs of clinical practice is very important in terms of public health, clinical studies on drug-drug interactions have been performed during the past years[12]. Early detection of drug-drug interactions during treatment initiation makes it possible to intervene and reduce the risk of potential adverse effects[13].

Clinical pharmacists play a crucial role in overcoming or managing this challenge. They provide valuable information and recommendations to patients about their medications, e.g., potential interactions like between digoxin and spironolactone. Clinical pharmacists also meet with the treating physicians to provide feedback and recommendations, and ultimately work towards optimal patient outcomes[14]. Clinical pharmacists optimize medical therapy depending on the individual drugs and the patient's disease(s)

selecting the most appropriate drugs for the patient(s). They also bear the responsibility of educating the patients on potential side effects and explaining the effect of the drug. Clinical pharmacists are also pivotal in the prevention, detection, and reporting of drug interactions. In drug interactions, they intervene and prevent drug combinations, control dosages, and space dosing accordingly [15, 16]. The aim of the study was to assess the prevalence of drug-drug interactions and the role of pharmacists in monitoring drug-drug interactions to provide maximum medication safety for hospitalized patients within the neurology department of Shar Hospital in Sulaimani; this was accomplished through free-subscription drug interaction checker mobile apps.

2. Patients and Methods

2.1 Study design and setting:

This prospective observational and interventional study took place at the Neurology Department of Shar Teaching Hospital in Sulaimani, from November 2021 to February 2022. The observational

component focused on assessing the incidence and types of drug-drug interactions (DDIs) among patients admitted to the neurological ward. Data were collected on demographics, medical history, and medications used by the patients, with DDIs identified using established resources like Micromedex and the British National Formulary. The interventional part of the study involved clinical pharmacists conducting medication reviews for patients identified as being at high risk for DDIs. These pharmacists pinpointed potential interactions and suggested interventions, which included dose adjustments, alternative medications, or additional monitoring. The effectiveness of these interventions in reducing DDIs and enhancing patient outcomes was then evaluated.

2.2 Inclusion Criteria:

Patients who were hospitalized in the neurology ward due to neurological issues, classified as having neurological diseases, and who were either currently on drug therapy or had previously received drug therapy for various neurological conditions, must have stayed in the neurology ward for at least 24 hours upon admission during the study period.

2.3 Exclusion Criteria:

Patients admitted to Shar Hospital who did not have neurological issues were not treated in the neurology ward. Additionally, patients with neurological conditions who were admitted to the neurology ward but stayed for less than 24 hours were either transferred to other wards for further care or remained untreated due to specific circumstances. These circumstances may include factors such as the unavailability of specialized resources, changes in clinical priorities, or decisions based on the patients' overall condition and treatment requirements.

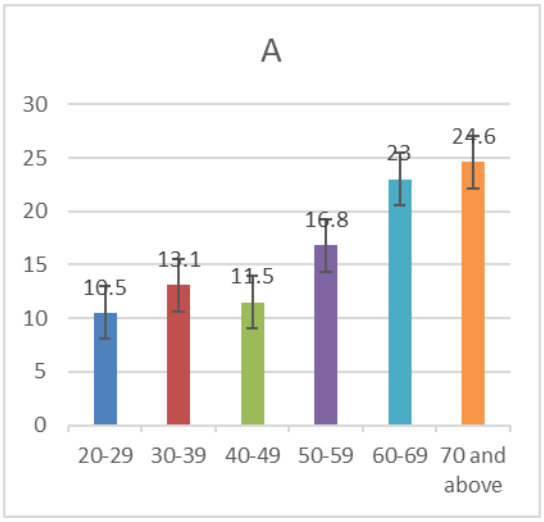
2.4 Statistical Analysis:

The data were analysed using Microsoft office 2024, which used descriptive statistics such as frequency and percentage for categorical variables.

3. Results

During the course of this study, a total of 7,301 patients were admitted to Shar Hospital. Among them, 496 patients were admitted to the neurology department for various neurological conditions. Of those, 203 patients stayed in the neurology ward for more than 24 hours, and these cases were closely monitored and evaluated. Comprehensive data were gathered on their clinical condition, treatment regimens, and the role of clinical pharmacists during their hospitalization.

The study cohort had the following demographic characteristics: 47.6% of the patients were aged 60 or older, with 23% in the 60-69 age range. The majority (91.6%) of patients were married, and 53.9% were female. In terms of residency, 57.6% of participants lived in rural areas, indicating a notable rural representation within the study population (Figure 1).



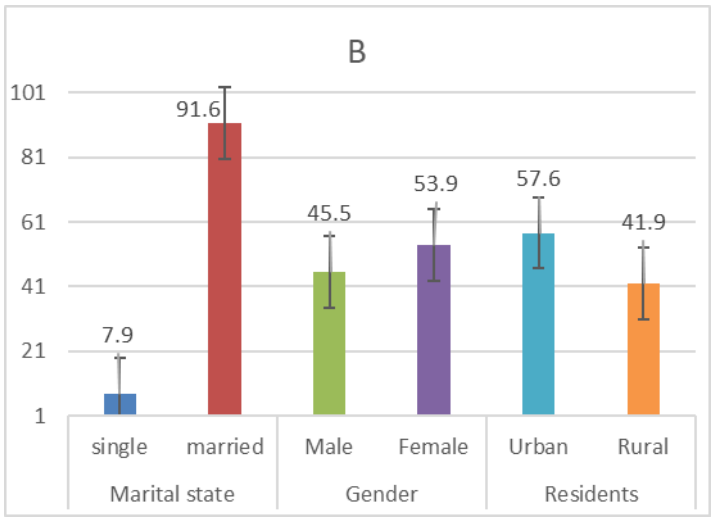
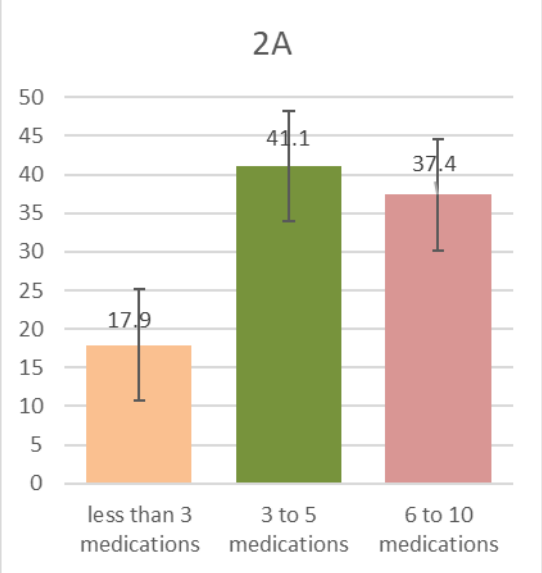


Figure 1A: Age (years).**Figure 1B.** Distribution of patients by gender, marital status, and residency.

The study also examined the number of prescribed medications and the types of diseases affecting the patients. It was found that 41.1% of patients were prescribed between 3 to 5 medications simultaneously, while 37.4% were prescribed 6 to 10 medications, indicating a significant prevalence of polypharmacy within the study population.

In terms of disease types, ischemic stroke was the most common condition, affecting 33% of the patients, making it the leading diagnosis in the cohort. Interestingly, 23% of patients were diagnosed with conditions unrelated to the neurology ward, suggesting the presence of comorbidities. The least common diagnosis was confusion, with only 1% of patients being affected, representing a relatively rare condition within this study population (Figure 2).



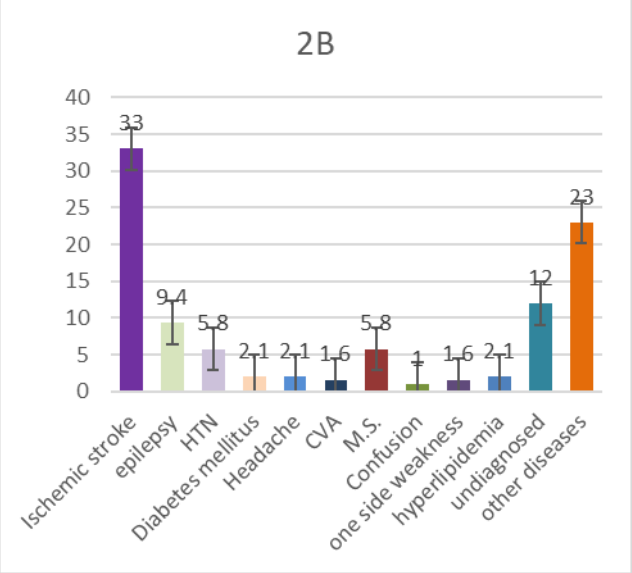


Figure 2A: The number of prescribed medications**Figure 2B:** type of diseases

Despite the primary reasons for patient admission, as illustrated in Figure 2B, a considerable proportion of the cases presented with comorbid conditions, as detailed in Table 1. Specifically, 6.3% of the patients had both hyperlipidemia and diabetes mellitus. The second most common combination involved hyperlipidemia, hypertension, and diabetes mellitus, affecting 5.2% of the patients. In contrast, single conditions such as epilepsy, diabetes mellitus, and hyperlipidemia were less prevalent, each accounting for only 1% of the cases.

It is noteworthy that in approximately 61.8% of the cases, comorbid conditions were not documented. Furthermore, 8.4% of the cases remained undiagnosed, with the primary reasons for admission not recorded in the patients' charts. A more detailed breakdown of the comorbid conditions in the study population is provided in Table 1.

In terms of medication interactions, 50.5% of the prescribed medications showed no interactions, while 39.5% exhibited minor interactions. Additionally, 3.7% of the prescribed medications were associated with significant interactions, and 3.7% had both minor and moderate interactions concurrently, as presented in Figure 3A.

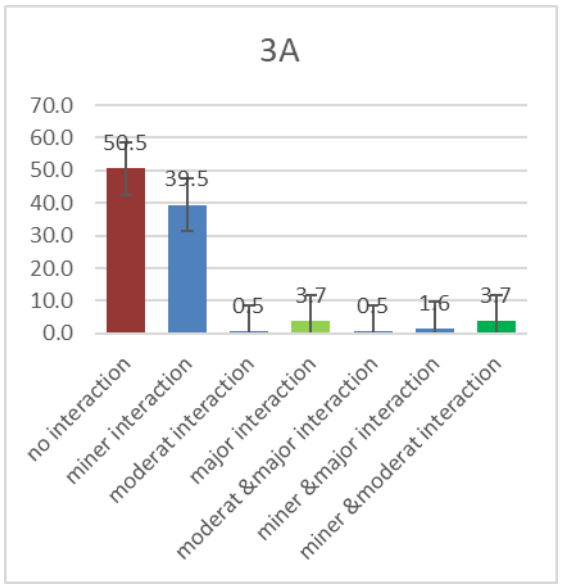
Regarding the nature of these interactions, 49% were classified as drug-drug interactions, as shown in Figure 3B.

Concerning the involvement of clinical pharmacists, 50.5% of the prescribed medications did not necessitate any intervention. Conversely, 49.5% required pharmacist intervention. However, within this subset, only 15.8% of the cases were addressed through direct consultation with a pharmacist, while 84.2% of the medications requiring intervention were not reviewed by a pharmacist, as depicted in Figure 3B.

Table 1: The frequency of Common comorbid diseases among the admitted patients.

Diseases	**Frequency (%)**
HTN and DM	1.6
HTN and Hyperlipidemia	3.7
D.M. and Hyperlipidemia	6.3
D.M, HTN and Hyperlipidemia	5.2
Epilepsy	1
Headache	3.1
CVA	2.6
HTN	3.7
D.M.	1
Hyperlipidemia	1
Undiagnosed	8.4
Comorbid diseases were not mentioned	61.8

Note: HTN: hypertension, DM: diabetes mellitus, CVD: cardiovascular Diseases.



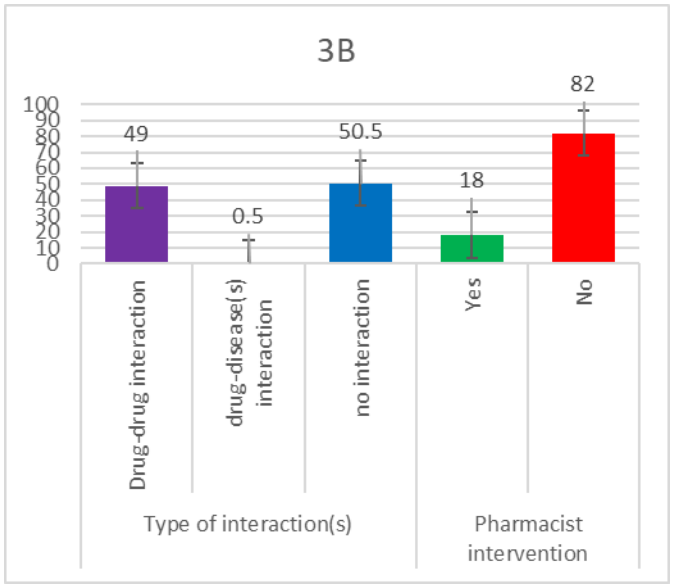
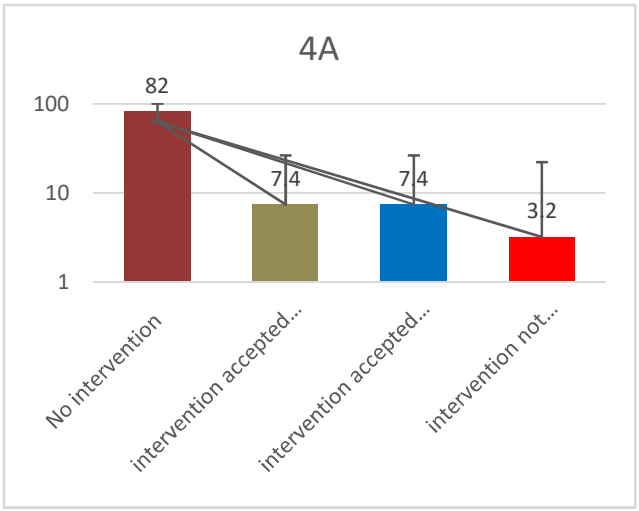


Figure 3A: Percentage of severity of interaction.**Figure3B:** type of interaction, and pharmacist intervention.

Regarding the interventions, 7.4% of the interactions were fully accepted and implemented, while another 7.4% were accepted but only partially implemented. In contrast, 3.2% of the interventions were not accepted, as depicted in Figure 4A.

In terms of the types of interventions, as shown in Figure 4B, 89.6% of the interactions could be resolved through medication changes alone. Additionally, 5.2% of the cases required discontinuation of the medication, while approximately 5% could be addressed by adjusting the doses, either by increasing or decreasing them.



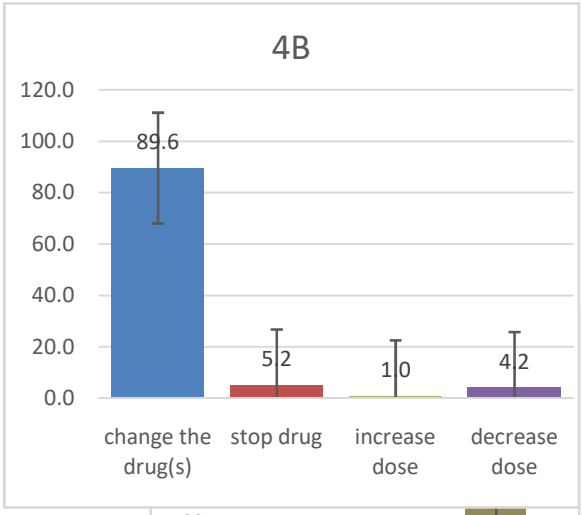
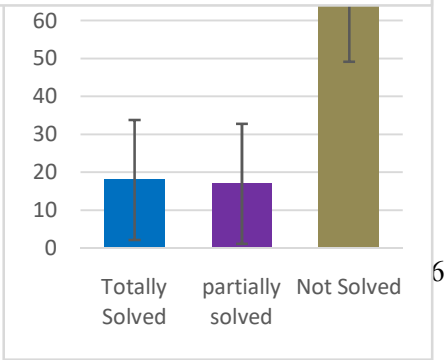


Figure 4A: State of intervention.**Figure 4B:** type of interventions



Regarding drug therapy problems (DTP), 18% of pharmacist interventions resulted in the resolution of the identified issues,

while 17% led to partial acceptance of the proposed solutions. However, a significant 65% of the DTPs remained unresolved, as depicted in Figure 5. This underscores the need for enhanced attention to these problems and suggests that involving a specialist pharmacist could potentially mitigate these undesirable effects.

Furthermore, the limited collaboration between specialist neurologists and pharmacists, coupled with insufficient consideration of pharmacists' recommendations, appears to be contributing factors. As shown in Figure 5, approximately 65% of the interactions remain unresolved, highlighting the need for improved interdisciplinary teamwork and greater integration of pharmacist expertise in the clinical decision-making process.

Figure 5. The state of DTP solving per problem.

4. Discussion:

This observational and interventional study aimed to assess the prevalence of drug-drug interactions (DDIs) in the neurology ward of Shar Teaching Hospital, Sulaimani, and evaluate the role of clinical pharmacists in managing these interactions. The results indicate that DDIs are a significant concern, particularly in the context of polypharmacy and the aging population. The study also highlights the importance of pharmacist interventions in mitigating these risks.

The study sample comprised 203 patients, 47.6% of them were more than 60 years old, highlighting the rising problem of polypharmacy in elderly patients, which is in line with evidence from previous research. For instance, a study by Béjot and Yaffe (2019)[17] noted that an older population is at higher risk for neurological disorders and polypharmacy, making it more susceptible to DDIs. The extremely high polypharmacy rates in this population (41.1% were receiving 3–5 drugs, and 37.4% receiving 6–10 drugs) are similar to analogous efforts in neurology clinics. Farooqui et al. (2018)[5] determined that polypharmacy was a prominent cause of DDIs among inpatients, especially for comorbid patients.

Comorbidity is also a factor that cannot be downplayed in the management of neurological disease and treatment. 61.8% of the patients were said to have unspecified comorbidities, and their frequent pairings were HTN, DM, and hyperlipidemia. This is consistent with the finding of Zafar et al. (2018)[18], where it was observed that comorbid conditions increased drug interaction in patients with neurological disorders to the maximum. Furthermore, the significant rate of undiagnosed comorbidities (8.4%) illustrates the challenge clinicians experience in realizing the complete image of the patient's state of health that can result in missed or unreported DDIs.

As for the concomitant use of the drugs, the majority of the cases (41.1%) involved the use of three to five drugs together, followed by roughly 37.4% of the cases using six to ten drugs at once. These findings are consistent with those shown by Georgiev et al. (2019)[19], Who indicated that the number of prescribed drugs was between three and fourteen, 92% of which have been on over five medications, per patient. The majority of the cases, as observed, are polypharmacy-related, thus indicating the problem that an increase in the number of prescribed drugs may enhance drug adverse interactions. This tendency should be taken seriously, as polypharmacy not only complicates the therapeutic regimen but also leads to a higher risk of adverse clinical effects due to drug-drug interactions[20].

The incidence of DDIs in this study was high, with 39.5% of the drugs experiencing minor interactions and 3.7% experiencing major interactions. This finding is consistent with the risk documented in previous studies, such as that of Jimmy et al. (2023)[21], who also documented that neurological patients are frequently exposed to more than one drug interaction due to the complexity of their treatment regimen.

Besides, the results of this study show that the prevalence of clinically significant drug interactions is lower compared to what was reported by Bose and Sushma (2016)[22], in which approximately 20% of the interactions were deemed to be significant. The comparison reveals a difference in the prevalence of clinically significant interactions between the two studies, which may be attributed to differences in study design, patient population, or drug profile. The level of interaction discovered in this research suggests that a more organized method needs to be employed to monitor and control these interactions for effective management.

The high rate of minor interactions (39.5%) suggests that although these interactions are not directly dangerous, they could accumulate over time to have harmful effects if left unaddressed. The converse is the 3.7% of major interactions, which suggests the need for intervention, particularly in those patients who are at higher risk, e.g., the elderly and those with multiple comorbidities

Clinical pharmacists played a key role within this study by intervening in 49.5% of the cases where DDIs were identified. However, only 18% of these interventions were ever accepted and implemented, signifying an absence of communication or opposition towards pharmacist intervention. This is consistent with Shafiekhani et al. (2019)[1], when they reported that not always were interventions by pharmacists consistently implemented in clinical practice due to factors like no communication with physicians or organizational barriers. Not implementing pharmacist advice in a significant proportion of cases means there is a need for better working collaboration of pharmacists within multidisciplinary teams, particularly on high-risk wards such as neurology. The results of this research differ from those of Jimmy, Nivya, et al. (2023) and Siddiqui (2023)[21, 23]. In Nivya et al.'s and Siddiqui's studies, the percentage of accepted pharmacist interventions was much higher, at approximately 89% and 88%, respectively. The variation can mean differences in the healthcare settings, pharmacists' role, or nature of interventions provided within each study.

The nature of interventions was also studied in the research, with the majority (89.6%) being adjustments of the prescribed medication. This approach is in accordance with the recommendations of Ansari (2010)[6], who emphasized that the role of clinical pharmacists is not only to detect DDIs but also to recommend modifications in medication regimens to avoid harm. Even though the study found some level of success with the resolution of DDIs through interventions by pharmacists, the overall rate of resolution for DTPs remained low at 65% not resolved. This suggests a need for further integration among clinical pharmacists, physicians, and other healthcare professionals. Integration among doctors, pharmacists, and nurses will enhance patient safety as well as optimize medication therapy[24]

When the findings of this study are compared to other studies of a similar type, e.g., Farooqui et

al. (2018) [5] and Zafar et al. (2018)[18], the incidence of DDIs reported in this study is within predicted parameters. The reduced acceptance and implementation rate of pharmacist interventions in this study contrasts with studies where pharmacist intervention has been more impactful.

5. Conclusion

The findings of this study support the involvement of clinical pharmacists in the early detection and prevention of the risks of DDIs, particularly among high-risk groups like neurology ward inpatients. Despite the potential of the pharmacist's contribution, the study finds significant gaps in recognition and implementation of pharmacists' interventions. Better communication among doctors, druggists, and other medical practitioners, as well as the introduction of standardized guidelines, is the solution to reducing DDIs and improving safety for the patient. Additionally, since the prevalence of polypharmacy and comorbidities among this population is high, future research should include intervention for better control of these elements in a move to reduce the prevalence of DDIs.

6. References

[1] M. Shafiekhani, N. Moosavi, D. Firouzabadi, and S. Namazi, "Impact of Clinical Pharmacist's Interventions on Potential Drug-Drug Interactions in the Cardiac Care Units of Two University Hospitals in Shiraz, South of Iran," (in eng), Journal of research in pharmacy practice, vol. 8, no. 3, pp. 143-148, 2019.

[2] M. B. Zazzara, K. Palmer, D. L. Vetrano, A. Carfì, and O. Graziano, "Adverse drug reactions in older adults: a narrative review of the literature," European geriatric medicine, vol. 12, pp. 463-473, 2021.

[3] M. J. Hasan, R. Rabbani, and S. C. Bachar, "Critical Care Pharmacist Using Free Drug-Interaction Checker Mobile Apps Can Ensure Medication Safety in Critically Ill Patients," Jundishapur Journal of Health Sciences, vol. 12, no. 2, 2020.

[4] R. Roberti, C. De Caro, L. F. Iannone, G. Zaccara, S. Lattanzi, and E. Russo, "Pharmacology of cenobamate: mechanism of action, pharmacokinetics, drug–drug interactions and tolerability," CNS drugs, vol. 35, no. 6, pp. 609-618, 2021.

[5] R. Farooqui, T. Hoor, N. Karim, and M. Muneer, "Potential Drug-Drug Interactions among Patients prescriptions collected from Medicine Out-patient Setting," (in eng), Pakistan journal of medical sciences, vol. 34, no. 1, pp. 144-148, Jan-Feb 2018.

[6] J. Ansari, "Drug interaction and pharmacist," Journal of young pharmacists, vol. 2, no. 3, pp. 326-331, 2010.

[7] U. Saha, Clinical Anesthesia for the Newborn and the Neonate. Springer, 2023.

[8] W. W. Benton, A. W. Brothers, C. C. J. Kirk, G. A. L. Irby, and C. M. Rubino, "Adverse drug reactions and drug-drug interactions," in Pediatric Critical Care: Elsevier, 2011, pp. 1569-1589.

[9] S. Polaka, H. P. Koppisetti, M. Tekade, M. C. Sharma, P. Sengupta, and R. K. Tekade, "Drug–drug interactions and their implications on the pharmacokinetics of the drugs," in Pharmacokinetics and toxicokinetic considerations: Elsevier, 2022, pp. 291-322.

[10] M.-K. Choi and I.-S. Song, "Pharmacokinetic Drug–Drug Interactions and Herb–Drug Interactions," vol. 13, ed: MDPI, 2021, p. 610.

[11] S. Gupta, A. Dhawan, J. Dhawan, M. A. McColl, K. M. Smith, and A. McColl, "Potentially harmful drug–drug interactions in the therapeutic regimens of persons with spinal cord injury," The Journal of Spinal Cord Medicine, vol. 47, no. 5, pp. 692-700, 2024.
[12] Z. Očovská, M. Maříková, and J. Vlček, "Potentially clinically significant drug-drug interactions in older patients admitted to the hospital: A cross-sectional study," Frontiers in Pharmacology, vol. 14, p. 1088900, 2023.
[13] D. S. Atmaja, Yulistiani, Suharjono, and E. Zairina, "Detection tools for prediction and identification of adverse drug reactions in older patients: a systematic review and meta-analysis," Scientific Reports, vol. 12, no. 1, p. 13189, 2022.
[14] A. F. Talib and Z. M. Anwer, "The role of clinical pharmacist in reducing drug related problems in hemodialysis patients," Iraqi Journal of Pharmaceutical Sciences (P-ISSN: 1683-3597, E-ISSN: 2521-3512), vol. 29, no. 2, pp. 223-230, 2020.
[15] M. M. Rekha and T. Mubeena, "A study on role of Clinical Pharmacist inidentification and reporting of drug interactions in Physciatric Ward in a Teritary Care Teaching Hospital," PharmaTutor, vol. 5, no. 5, pp. 70-75, 2017.
[16] R. M. Hamadouk, E. D. Albashair, F. M. Mohammed, and B. A. Yousef, "The practice of the community pharmacists in managing potential drug-drug interactions: a simulated patient visits," Integrated Pharmacy Research and Practice, pp. 71-84, 2022.
[17] Y. Béjot and K. Yaffe, "Ageing population: a neurological challenge," Neuroepidemiology, vol. 52, no. 1-2, pp. 76-77, 2019.
[18] A. Zafar et al., "Stroke and seizure continue to be the major brunt of in patient neurology care. An observation from teaching hospital," Neurosciences, vol. 23, pp. 13-17, 01/21 2018.
[19] K. D. Georgiev, N. Hvarchanova, M. Georgieva, and B. Kanazirev, "The role of the clinical pharmacist in the prevention of potential drug interactions in geriatric heart failure patients," International journal of clinical pharmacy, vol. 41, no. 6, pp. 1555-1561, 2019.
[20] J. Wolff et al., "Polypharmacy and the risk of drug–drug interactions and potentially inappropriate medications in hospital psychiatry," Pharmacoepidemiology and Drug Safety, vol. 30, no. 9, pp. 1258-1268, 2021.
[21] N. Jimmy et al., "A Clinical Pharmacist-led Approach on Reducing Drug Related Problems Among Patients with Neurological Disorders: An Interventional Study," Exploratory Research in Clinical and Social Pharmacy, vol. 11, p. 100302, 2023.
[22] d. bose and m. sushma, "pattern & predictors of drug-drug interactions among the patients admitted in neurology at a tertiary care hospital-a cross-sectional study," international journal of pharmaceutical sciences and research, vol. 7, no. 8, p. 3458, 2016.
[23] D.-e.-S. Siddiqui, "Role of healthcare professionals in drug-drug interactions and clinical interventions," European Journal of Clinical and Experimental Medicine, no. 1, pp. 81-89, 2023.
[24] D. Z. Aleksic, S. M. Jankovic, M. N. Mlosavljevic, G. L. Toncev, S. D. Miletic Drakulic, and S. M. Stefanovic, "Potential drug-drug interactions in acute ischemic stroke patients at the Neurological Intensive Care Unit," Open Medicine, vol. 14, no. 1, pp. 813-826, 2019.