

Drug related problems among hospitalized geriatric patients in medicine departments of Misurata Medical Centre

Yousef Omar Erfaida^{1*}, Amna Ahmed Alshaaf², Sameera Abushaala Swayib²

1. Pharmacology Department, Faculty of medicine, Misurata University, Libya.
2. Pharmacology and toxicology Department, Faculty of Pharmacy, Misurata University, Libya.

ABSTRACT

Preventing drug-related problems (DRPs) is one important factor to improve health care and quality of life for elderly patients. The safety of patients could be negatively affected by possible drug-related problems (DRPs). This study aimed to identify and evaluate the drug-related problems among hospitalized elderly patients in the medicine departments of Misurata Medical Centre. This research is a descriptive and retrospective cross-sectional study that was carried out at Misurata Medical Center, Misurata, Libya, from Jan to Jun 2024. The population under study was patients aged ≥ 60 years. In 120 hospitalized in-patient medication charts, cardiovascular diseases were the most common cause for hospitalization (75%), followed by endocrine disorders (55%) and infectious diseases (30 %). A total of 111 drug-related problems were identified in 66 patients with an overall prevalence of 55 %. The present study showed that the need for additional drug therapy (43.2%) was the main category of DRP identified, and drug-drug interactions (39.6%) were the second commonly encountered, followed by unnecessary drugs (17.2%). The most common DRP is the need for additional drug therapy, 43.2% of the total DRPs. The current study showed that DRPs are common among elderly patients, and there is the existence of comorbidities puts elderly people at risk of prescription polypharmacy.

KEYWORDS: Drug related problem, elderly patient,

INTRODUCTION

A drug-related problem (DRP) is defined as an undesirable event involving drug therapy that is considered serious and, if unaddressed, can complicate the healthcare system. DRPs contribute significantly to mortality, morbidity, hospitalization, long-term care admissions, and economic burden on healthcare systems (Amsalu, Baraki and Muche, 2022). Drug therapy problems can originate at any stage of the medicines use process, including prescription, transcription, verification, dispensing, administration, monitoring, and reporting (Bekele et al., 2021).

DRPs are commonly categorized using various classification systems. According to Cipolle, Strand, and Morley (2012), DRPs are divided into seven subgroups (Table 1). The classification includes: unnecessary drug therapy, need for additional drug therapy, ineffective drug therapy, inappropriate dosage (too low or too high), adverse drug reactions, and noncompliance.

All patients, particularly geriatric populations, face a pronounced risk of DRPs, which result in up to 30% of hospitalizations among elderly individuals (Jeffery and Campbell, 2020; Abramsson and Gustafsson, 2020). Due to physiological and pharmacological changes associated with aging, elderly patients are more susceptible to DRPs. Compared to other age groups, the geriatric population accounts for the highest proportion of drug prescriptions annually, leading to higher rates of DRPs, which are associated with high rates of medical comorbidities, overprescribing, and inadequate monitoring (van Poelgeest et al., 2023).

Prescribing medications for geriatric patients is a challenging process for physicians and healthcare providers and poses an economic burden on healthcare systems. Despite the high risk of DRPs in elderly patients, studies in this area are scarce in resource-limited settings such as Libya. This study aimed to investigate the prevalence and types of DRPs and identify factors associated with these problems in elderly patients admitted to medical wards of Misurata Medical Centre in Misurata, Libya.

Table 1. Definition of drug-related problems

DRP	Definition
Unnecessary drug therapy	is a DRP that occurs when there is no valid medical indication for the drug at the time, multiple drug products are used when only single-drug therapy is appropriate, or the condition is best treated with nondrug therapy (3).
Needs additional drug therapy	is a DRP that occurs when there is a medical condition needing new drug therapy, or preventive therapy is needed to reduce the risk of developing a new condition, or a medical condition requires combination therapy for better efficacy (3).
Ineffective drug	is a DRP where the drug is not the most effective for the medical problem, or the condition is refractory to the drug product being used, or the dosage form is inappropriate (3).
Inappropriate dosage Dosage too low,	- refers to dosages both too low and too high (3). is a DRP that occurs when the dose is too low to produce the desired outcome, or the dosage interval is too long, or a drug interaction reduces the amount of active drug available, or the duration of therapy is too short. is a DRP where the dose is too high or the dosing frequency is too short or the duration of therapy is too long for the patient, or a drug interaction causes a toxic reaction to the drug product, or the dose was administered too rapidly.
Adverse drug reaction (ADR)	“an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product.” (09)
Noncompliance	is a DRP that occurs when the patient does not understand the instructions, or the patient prefers not to take or forgets to take the medication, or the cost of the drug product is not affordable for the patient, or the patient cannot swallow or self-administer the medication properly, or the drug product is not available for the patient (3).

2. Materials and Methods

Type of Study: This study is descriptive, retrospective, cross-sectional study

Study Settings: The study was conducted at one of the public hospitals in Misurata (Misurata Medical Centre) for a six-month period from Jan 1 to June 30, 2024.

Study Population: Elderly patients who had been hospitalized in the medicine wards for ≥ 24 hours were included.

Inclusion criteria: Patient records were eligible for inclusion if the patient's age was ≥ 60 years, and Patients were admitted for > 24 hours

Exclusion criteria: Patients who were transferred from critical care units,

Cancer patients, and Patients on dialysis

Data Collection:

Two pharmacy students were trained as data collectors by the principal investigator extensively for two days about the aim of the study, data collection methods, including data extraction from patient charts, as well as data handling, ethical approaches, and DRP identification. They retrieved the documentation of the medication review from the medical records by using the standardized data extraction sheet. They review the medical record, medications and laboratory data to identify and address DRPs.

Data collected from a patient chart includes: (Age, Gender, History of drug allergies, Medical History, Medication history, Diagnosis, Prescribed drugs).

Data Processing:

DRP's assessment based on Cipolle et al classifying system (3). All data with prescribed drugs and identification of DRPs handled by the individual researchers to reviewed the document to categorize and enter information into the data collection sheet. Each documented drug therapy was evaluated for the presence of DRPs using standard textbooks as a pharmacotherapy case book and pathophysiologic approach applied therapeutics. The reliability and accuracy of each drug treatment problem will be evaluated by the supervisor pharmacologist.

Ethical consideration

Ethical clearance was obtained from the ethical review committee of the Faculty of Medicine, Misurata University, and Permission was also obtained from the MMC office for cooperation from the Department of Medical Records at MMC. Privacy of participants was ensured since patients are differentiated with a code (no name) only.

All information obtained from the files was kept confidential, and the data obtained was used for research purposes only.

Statistical analysis:

The collected data was checked for completeness, ensuring accuracy and consistency before processing. All data from the recorded collection sheet were classified and coded, then entered into the computer and analyzed using Statistical Package for Social Studies (SPSS) version 21. Chi-Square tests were used to analyze the associations of risk factors among DRPs. Significance level was set at $p < 0.05$. The result of the analysis was presented by using frequencies, mean and standard deviation, tables, and graphs.

RESULTS

Socio-demographic characteristics of patients

In this study, a total of 120 were selected to conduct study. More than half of the patients were male 65 (54.2%). The mean ($\pm$ SD) age of study patients was 74.05 ± 9.23 years, the majority (21.7 %) lie within the age group of 70-74 years. Socio-demographic characteristics is summarized in Table 2

Table:2 Socio-demographic characteristics of geriatric patients admitting at medicine departments of MMC, Libya, Jan 1 to June 30, 2024

variables	Types of groups	No. of patients	% of total patients
Age group (in years)	60-64	25	20.8%
	65-69	12	10%
	70-74	26	21.7 %
	75-79	15	12.5%
	80-84	23	19.2%
	85-89	9	7.5%
	≥ 90	10	8.3 %
Sex	Male	65	54.2%
	Female	55	45.8%

Clinical data of patients

As it is shown in Table 3 and Figures 3-6, Majority of patients 43 (35.8%) in our study were found suffering with three diseases, 42 patients (35%) were found more than four diseases, 22 patients (18.3%) were found suffering with two diseases, and 13 patients (10.8%) was suffering from one disease. Most of the patients had 1-3 days of hospital stay accounted for 94 (77.5%). Regarding history of chronic illness, 108 (90%) patients were had chronic illness and co-morbidity was present in 101 (84.2%) of the patients.

Table:3 Clinical characteristics of geriatric patients admitting at medicine departments of MMC, Libya, Jan 1 to June 30, 2024.

Variables	Category	Frequency (N=120), (%)
Number of disease condition	1	13 (10.8 %)
	2	22 (18.3 %)
	3	43 (35.8 %)
	≥4	42 (35 %)
Duration of stay	≤3	93 (77.5 %)
	4-6	15 (12.5 %)
	≥7	12 (10 %)
History of chronic illness	Yes	108 (90 %)
	NO	12 (10 %)
Comorbidity	Yes	101 (84.2 %)
	NO	19 (15.8 %)

The morbidity profile shows diseases related cardiovascular system were the most common cause for hospitalization (90; 75%), followed by endocrine disorders (66; 55 %), infectious diseases (36; 30%), respiratory diseases (30; 25%), and gastrointestinal diseases (8; 6.7%). 34 (16.74%) patients were suffering with miscellaneous disorders like diseases of the CNS, and anemia (Table 4).

Table:4 Clinical Conditions for Hospitalization of geriatric patients admitting at medicine departments of MMC, Libya, Jan 1 to June 30, 2024

Disease condition	Number of patients (%)
Cardiovascular diseases	90 (75)
Endocrine disorders	66 (55)
Infectious diseases	36 (30)
Respiratory diseases	30 (25)
Gastrointestinal diseases	8 (6.7)
Others	18 (15)

Drug related problems:

Prevalence and nature of DRPs:

Among the study participants, as it is shown in Table 5, a total of 111 DRPs were identified in 66 patients and an overall prevalence was 55 %, a mean of 1.7 per patient. 45% (54) of the participants did not expose to any event of DRPs. Among the study participants who encountered DRPs, 38 (57.6 %) of them have one drug related problems, 17 (25.7 %)

Table5: Frequency of patients who have drug-related problems

Type of DRPs and its causes	Frequency (%)
Need additional drug therapy	48 (43.2%)
Adverse drug reaction (Drug – drug interaction)	44 (39.6 %)
Unnecessary drug therapy	19 (17.2)

DRP type and its causes

Among the identified DRP types, needs additional drug therapy was the most frequent DRP accounting for 48 (43.2 %), adverse drug reaction (drug interactions) was the second accounting for 44 (39.6%), and unnecessary drug was the third 19 (17.2 %). Among the possible causes of need additional drug therapy were related to a medical condition such as diabetes mellitus, hypertension, and anemia requires the initiation of drug, preventive drug therapy is required for example, prophylactic assessment for ischemic stroke. While drug interaction most frequent causes of adverse drug reaction. and the possible causes of unnecessary drug therapy, multiple drug products are being used and no valid medical indication such as irrational prescribing antibiotics which was the majority of this category (Table 6).

Table:6 Types of DRPs and its causes identified among geriatric patients admitting at medicine departments of MMC, Libya, Jan 1 to June 30, 2024 (N=111).

Variables		DRPs (count)		P value
		Yes	NO	
Duration of stay	≤3	49	44	0.602
	4-6	9	6	
	≥7	8	12	
Polypharmacy	Yes	86	8	0.000
	NO	26	0	
Comorbidity	Yes	93	8	0.000
	NO	19	0	

Factors associated with DRPs

The factors associated with DRPs included duration of stay and polypharmacy and comorbidity were shown in figure 1 and 2

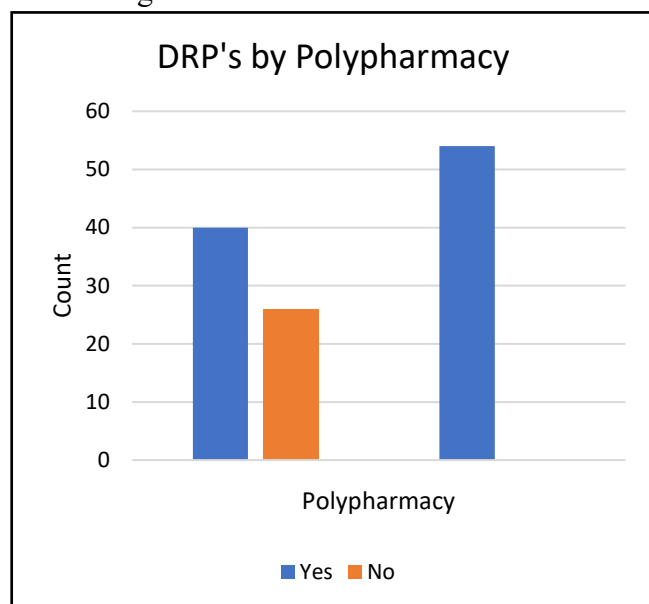


Figure:1 Polypharmacy associated with DRPs among geriatric patients admitting at medicine departments of MMC, Libya, Jan 1 to June 30, 2024

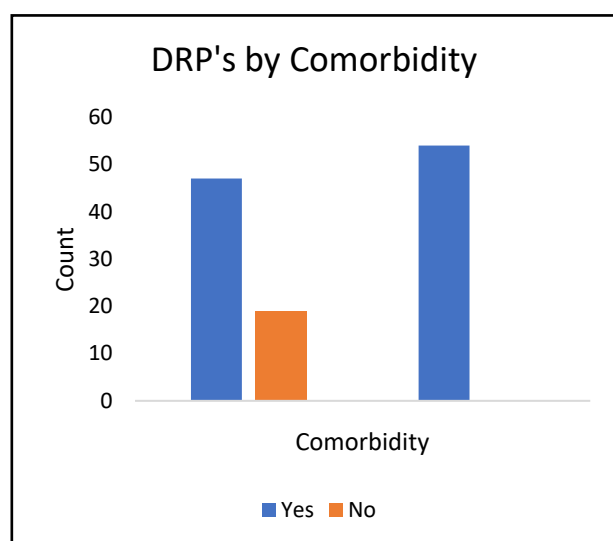


Figure:2 Comorbidity associated with DRPs among geriatric patients admitting at medicine departments of MMC, Libya, Jan 1 to June 30, 2024

DISCUSSION

DRPs are serious events that, if unaddressed, can complicate the healthcare system. They are common among people living with chronic illnesses, particularly geriatric patients. Appropriate detection

and prevention of DRPs is a cornerstone of pharmaceutical care to provide safe and effective healthcare and ensure patients achieve optimal therapeutic goals (Sheleme, Sahilu and Feyissa, 2021; Babelghaith et al., 2020).

The results of this study indicate that a significant proportion of hospitalized geriatric patients experience DRPs, which represent a major barrier to achieving optimal therapeutic outcomes. The current study found that 55% of geriatric patients had at least one DRP. This finding is similar to a study conducted in Northern Sweden (66%) (Peterson, 2017) but lower than findings from Southern Sweden (93%) (Milos et al., 2013) and Norway (81%) (Blix et al., 2004). These differences may be attributed to variations in study settings, sample sizes, and the presence of clinical pharmacists in medical wards. The benefits of pharmacist involvement and active participation appear significant when directly involved in ward rounds, rapidly identifying DRPs and providing real-time recommendations to prescribers. Additionally, discrepancies may be due to differences in DRP classification methods; our study used Cipolle's classification, while other studies utilized the PCNE classification system.

The present study showed that the need for additional drug therapy (43.2%) was the main category of DRP identified, with drug-drug interactions (39.6%) being the second most commonly encountered, followed by unnecessary drug therapy (17.2%). A similar trend of inappropriate treatment requiring additional therapy has been demonstrated in other studies (Alssageer et al., 2023; Koh, Kutty and Li, 2005).

A lower prevalence was reported in a South Indian study (Adepu and Adusumilli, 2016), which may be due to differences in study duration, population, and design. Diabetes mellitus, anemia, appropriate antibiotics for infections, and prophylactic assessment for ischemic stroke were health-related issues left untreated in some patients.

DDIs were implicated in 39.6% of DRPs. The mean number of medications prescribed in this study was 6.6 drugs per patient, comparable to data from Northern Ethiopia (6 drugs per patient) (Teka et al., 2016) and Taiwan (5.8 drugs per patient) (Lin, Wang and Bai, 2011). A lower mean number of drugs prescribed was reported in southern Brazil (4.4 drugs per patient) (Teixeira et al., 2012), Gujarat, India (4.3 drugs per patient) (Vegada et al., 2020), and Germany (3.7 drugs per patient) (Junius-Walker, Theile and Hummers-Pradier, 2007). A higher mean number of medications was reported in India (9.2 drugs per patient) (Kashyap et al., 2013) and South Africa (7.7 drugs per patient) (Kapp, Klop and Jenkins, 2013). The most commonly observed DDIs involved ciprofloxacin, heparin, furosemide, warfarin, omeprazole, clopidogrel, atorvastatin, and aspirin in combination with each other or with other medicines. Different variations could be attributable to differences in study design, comorbidity profile,

and medication usage patterns. Notable drug combinations with significant interactions included clopidogrel + omeprazole, heparin + aspirin, atorvastatin + clopidogrel, omeprazole + iron, and omeprazole + ciprofloxacin.

The interaction between clopidogrel and omeprazole was classified as 'major' in severity, potentially causing decreased effectiveness of clopidogrel. The interaction between aspirin and heparin was classified as 'moderate' in severity, potentially increasing bleeding risk, necessitating close monitoring. The interaction between aspirin and warfarin was also classified as 'moderate' severity, with increased bleeding risk.

In the present study, 19% of total DRPs were identified as unnecessary drug use, a phenomenon frequently reported in developing countries. The prevalence of unnecessary drug therapy is more frequent than problems due to prescribing drugs for elderly patients (Joshi, Sugimoto and Santoso, 1997; Haider, Mazhar and Ahmed, 2017). Additionally, physicians are often not fully updated on their patients' actual drug use. The rising costs of drug therapies represent a significant financial burden, particularly for developing countries such as Libya. This issue is especially acute among hospitalized geriatric patients, who are often prescribed multiple medications due to age-related comorbidities. Prevention of unnecessary drug therapies is a critical strategy to mitigate healthcare costs and reduce drug-related complications.

This study showed that comorbidity and polypharmacy were the main factors associated with increased DRPs among elderly hospitalized patients, consistent with previous studies conducted in Ethiopia (Dagne et al., 2022). The elderly are significantly more prone to comorbidities due to aging and physiological changes; the majority suffer from chronic illnesses (Acurcio et al., 2006). Consequently, they are more likely to have greater drug utilization to manage chronic conditions. In geriatric patients, administration of multiple medications does not necessarily indicate improper use; rather, it often reflects the complexity of managing various medical conditions concurrently. Medicines are prescribed for various purposes, including achieving therapeutic synergy, reducing resistance risk, and mitigating adverse drug reactions (Teka et al., 2016). Given that elderly patients commonly present with multiple comorbidities,

polypharmacy is often unavoidable. Ultimately, the goal is to balance therapeutic benefits of each medication while minimizing risks associated with polypharmacy and drug interactions, thereby optimizing care for geriatric patients (Bista et al., 2009).

Conclusion

This study demonstrated that DRPs are common among elderly patients, and the presence of comorbidities puts elderly individuals at risk of prescription polypharmacy. Need for additional drug therapy, drug interactions, and unnecessary drug therapy were the identified DRPs among hospitalized geriatric patients at MMC. DRPs were significantly associated with polypharmacy but not with duration of hospital stay. Elderly patients on polypharmacy regimens are at risk of medicine overuse and adverse effects. While polypharmacy is often unavoidable due to multiple comorbid conditions, a multidisciplinary approach is required to avoid potentially inappropriate medications in the elderly.

Recommendations

The study recommends the need for qualified clinical pharmacists to evaluate drug use in geriatric patients. Clinical pharmacists should play an active role in detecting and resolving DRPs. Strengthening clinical pharmacy services in hospitals is essential to ensure patients receive safe and effective drug therapy.

Clinical pharmacists should be encouraged to contribute to formulating policy and evidence-based clinical guidelines focusing on essential drugs, generic prescribing, appropriate antibiotic use, and controlling polypharmacy.

Regular medication reviews and reconciliation should be implemented for all geriatric patients.

Educational programs for healthcare providers on geriatric pharmacotherapy and DRP prevention should be established.

Limitations of the Study

The exclusion of intensive care unit and oncology patients limits the generalizability of results to the entire geriatric population.

The study was conducted at a single institution using a cross-sectional design with a relatively small sample size, limiting generalizability to other hospitals.

Some data were obtained from patients' medical records, which may have affected data quality due to potential documentation errors or incomplete records.

The retrospective nature of the study limited the ability to assess causality and may have introduced information bias.

References

- 1- Amsalu, A., Baraki, A.G. and Muche, E.A., 2022. Drug-related problems and associated factors among hospitalized pediatric patients at the university of Gondar comprehensive and specialized hospital. *medRxiv*, pp.2022-09.
- 2- Bekele F, Fekadu G, Bekele K, Dugassa D, Sori J. Drug-related problems among patients with infectious disease admitted to medical wards of Wollega University Referral Hospital: Prospective observational study. *SAGE open medicine*. 2021 Jan; 9:2050312121989625
- 3- Cipolle RJ, Strand LM, Morley PC. Pharmaceutical care practice: the patient-centered approach to medication management. New York: McGraw-Hill Medical; 2012 Apr 22.
- 4- Jeffery SM, Campbell N. Medication-related problems in surgical patients. *Principles and Practice of Geriatric Surgery*. 2020:159-87.
- 5- Abramsson L, Gustafsson M. Prevalence of drug-related problems using STOPP/START and medication reviews in elderly patients with dementia. *Research in Social and Administrative Pharmacy*. 2020 Mar 1;16(3):308-14.
- 6- van Poelgeest E, Seppala L, Bahat G, Ilhan B, Mair A, van Marum R, Onder G, Ryg J, Fernandes MA, Cherubini A, Denkinger M. Optimizing pharmacotherapy and deprescribing strategies in older adults living with multimorbidity and polypharmacy: EuGMS SIG on pharmacology position paper. *European Geriatric Medicine*. 2023 Dec;14(6):1195-209.
- 7- Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. *The lancet*. 2000 Oct 7;356(9237):1255-9.
- 8- Sheleme T ,Sahilu T, and Feyissa D. Identification and resolution of drug-related problems among diabetic patients attending a referral hospital: a prospective observational study *J of Pharm Policy and Pract* (2021) 14:50.
- 9- Babelghaith SD, Wajid S, Alrabiah Z, Othiq MAM, Alghadeer S, Alhossan A, et al. Drug-related problems and pharmacist intervention at a general hospital in the Jazan Region, Saudi Arabia. *Risk Manage Healthc Policy*. 2020;13:373–8.
- 10- Peterson, Cecilia. "Characterization of drug related problems and associated factors at a clinical pharmacy-naïve hospital in the northern part of Sweden." (2017).
- 11- Milos V, Rekman E, Bondesson Å, Eriksson T, Jakobsson U, Westerlund T, et al. Improving the Quality of Pharmacotherapy in Elderly Primary Care Patients Through Medication Reviews: A Randomised Controlled Study. *Drugs Aging*. 2013 Apr 1;30(4):235–46.
- 12- Blix HS, Viktil KK, Reikvam Å, Moger TA, Hjemaas BJ, Pretsch P, et al. The majority of hospitalised patients have drug-related problems: results from a prospective study in general hospitals. *Eur J Clin Pharmacol*. 2004 Oct 2;60(9):651–8.
- 13- Alssageer MA, Sherif FM, Mohammed ES, Abd Alsalm SA. Pattern of drug prescribed and drug related problems among hospitalized elderly patients. *Mediterranean Journal of Pharmacy and Pharmaceutical Sciences*. 2023 Oct 21;2(2):66-78.
- 14- Koh Y, Kutty FBM, Li SC (2005) Drug-related problems in hospitalized patients on polypharmacy: the influence of age and gender. *Therapeutic and Clinical Risk Management*. 1 (1): 39-48. doi:10.2147/tcrm.1.1.39.53597.
- 15- Adepu R, Adusumilli PK (2016) Assessment of drug related problems in patients with chronic diseases through health status survey in a South Indian rural community setting. *Indian Journal of Pharmaceutical Science*. 78: 537- 541. doi: 10.4172/pharmaceutical-sciences.1000149.
- 16- Teka F, Teklay G, Ayalew E, et al. Potential drug–drug interactions among elderly patients admitted to medical ward of Ayder Referral Hospital, Northern Ethiopia: a cross sectional study. *BMC Res Notes* 2016; 9(1): 431.
- 17- Lin CF, Wang CY, Bai CH. Polypharmacy, aging and potential drug–drug interactions in outpatients in Taiwan: a retrospective computerized screening study. *Drugs Aging*. 2011;28(3):219–25.
- 18- Teixeira JJ, Crozatti MT, Dos Santos CA, et al. Potential drug–drug interactions in prescriptions to patients over 45 years of age in primary care, southern Brazil. *PLoS One* 2012; 7(10): e47062.
- 19- Vegada BN, Shah AM, Shah D, et al. Polypharmacy and potential drug–drug interactions among geriatric patients. *Natl J Physiol Pharm Pharmacol* 2020; 10(5): 393–399.
- 20- Junius-Walker U, Theile G and Hummers-Pradier E. Prevalence and predictors of polypharmacy among older primary care patients in Germany. *Fam Pract* 2007; 24(1): 14–19
- 21- Kashyap M, D'Cruz S, Sachdev A, Tiwari P. Drug–drug interactions and their predictors: results from Indian elderly inpatients. *Pharm Pract*. 2013;11(4):191–5.
- 22- Kapp PA, Klop A and Jenkins L. Drug interactions in primary health care in the George subdistrict, South Africa: a cross sectional study. *S Afr Fam Pract* 2013;

- 55(1): 78–84.
- 23- Joshi, M. P., SUGIMOTO, T. B., and SANTOSO, P. (1997) Geriatric Prescribing in the Medical Wards of a Teaching Hospital in Nep. PHARMACOEPIDEMIOLOGY AND DRUG SAFETY, (6): 417–421.
- 24- Haider N, Mazhar F, Ahmed M (2017) Drug use without indication in elderly hospitalized patients. Journal of Postgraduate Medicine. 63 (2): 138-139. doi:10.4103/jpgm.JPGM_675_16
- 25- Dagnew, Samuel Berihun, Tesfaye Yimer Tadesse, Mulugeta Molla Zeleke, Tesfagegn Gobezie Yiblet, Getu Tesfaw Addis, Gashaw Binaga Mekonnen, Samuel Agegneu Wondm, and Erkihun Assefa Negash. "Drug–drug interactions among hospitalized elderly in patients at medical wards of Northwest Ethiopia’s Comprehensive Specialized Hospitals: A multicenter observational study." *SAGE open medicine* 10 (2022): 20503121221135874.
- 26- Acurcio FdA, et al. Use of medications by elderly Brazilian retirees: methodology and response rates of a multicenter survey. *Cadernos de Saúde Pública*. 2006;22(1):87–96.
- 27- Bista D, Saha A, Mishra P, Palaian S, Shankar PR. Impact of educational intervention on the pattern and incidence of potential drug-drug interactions in Nepal. *Pharm Pract (Granada)*. 2009;7(4):242-247).