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ORIGINAL RESEARCH

Drug Therapy-related Problems Detected by Clinical Pharmacists in a Closed Loop Medication Management; A Cross-sectional Study in UAE

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Abstract: **Introduction:** Drug therapy-related problems (DTRP) can lead to avoidable negative health consequences, particularly during hospital admissions. This study aimed to assess the frequency, causes, and associated factors of DTRPs, which are detected by clinical pharmacists' interventions. **Methods:** This is a prospective cross-sectional study of patients admitted to the medical wards of Fakeeh University Hospital, UAE, over a three-month period from September 2022 to December 2022. The data of patients who were assessed by clinical pharmacists regarding the pretense and causes of DTRPs were collected and analyzed using SPSS version 27.0. **Results:** 310 patients with the mean age of 33.43 ± 19.98 years were studied (53.9% male). The highest percentage of patients were Asian (31.0%) and Arabs (30.6%). 79 (25.4%) cases had no DTRPs, while 231 (74.6) had DTRPs. The surgical ward had the highest frequency of DTRPs (41.0%). Improper drug selection with 79 cases, drug use without indication with 73 cases, and sub-therapeutic dosage with 26 cases were among the most common causes of DTRPs. Alcohol intake (p= 0.03), food allergy (p = 0.02), age group 31-40 years (p = 0.04), presence of co-morbidities (p = 0.01), family history of diseases (p = 0.02), and admission to the intensive care unit (ICU) (p = 0.01) were amongst the significantly associated factors of DTRPs. The acceptance status for clinical pharmacists' interventions were complete in 90.0% of cases, partial in 4.1 %, and rejection in 5.9%. **Conclusion:** The study findings show a high prevalence of DTRPs due to drug/dose selection and drug use without indication. It seems that the participation of clinical pharmacists in multidisciplinary teams together with the presence of closed loop medication management facilitates the detection and correction of DTRPs.

Keywords: Drug therapy; Medication therapy management; Pharmaceutical services; Drug-related side effects and adverse reactions; Clinical pharmacy information systems

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1. Introduction

Clinical pharmacists are integral to the multidisciplinary healthcare team, where they are tasked with assessing patients' conditions, evaluating the suitability and efficacy of prescribed medication regimens, identifying any unresolved health issues, and monitoring patient outcomes. Their role is critical in ensuring optimal medication management and enhancing patient care. The American College of Clinical Pharmacy (ACCP) defines these responsibilities as essential for preventing adverse drug events and improving the Pharmaceutical Care process (1). In addition to that, the Closed Loop Medication Management (CLMM) System is a groundbreaking method that combines automated and intelligent technology to shut the inpatient medication management and administration loop, improving patient safety and efficiency (2). The process involves a physician's electronic prescription, review by clinical pharmacists, release for unit-dose manufacture at the hospital pharmacy, and medicine administration and electronic documentation by nurses (3).

Drug Therapy-Related Problems (DTRPs) can lead to significant patient harm, reduced quality of life, increased healthcare costs, and even mortality. The complexity of modern pharmacotherapy, with multiple medications often prescribed to patients with chronic conditions, has heightened the risk of DTRPs. In response, there has been a growing global emphasis on the integration of clinical pharmacists into healthcare teams to mitigate these risks.

Several studies worldwide have demonstrated the essential role of clinical pharmacists in identifying, resolving, and preventing DTRPs across various hospital settings, including internal medicine, surgery, and intensive care units. These studies often use a range of classification systems, such as the

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Hepler-Strand classification (4), one of the earliest systems, which organizes DTRPs into eight distinct categories based on the nature of the issue. The Pharmaceutical Care Network Europe (PCNE)(5) Classification offers a more structured and detailed approach, categorizing drug-related problems into domains like problems, causes, and interventions. Another prominent system, the Strand et al. (6) classification, divides DTRPs into four primary categories: indication, effectiveness, safety, and compliance, providing a clear framework for resolving drug-related issues to achieve optimal therapeutic outcomes. Although these classification systems differ in structure and focus, they share a common goal of enhancing patient outcomes by systematically addressing DTRPs. Notably, the Hepler-Strand classification offers broader coverage of drug-related needs compared to others.

Enhancing our understanding of these issues may facilitate the implementation of universal approaches across diverse settings and serve as a basis for future research into these interactions (7).

Previous researches in the UAE focused only on clinical pharmacists' intervention in preventing DTRPs (8). These studies highlighted the underutilization of pharmacists within healthcare teams. Limited comparisons with international practices revealed that the UAE's clinical pharmacy services lag behind those in the USA and Sweden (9).

Many of these studies highlight that clinical pharmacists are underutilized, often due to a lack of awareness among healthcare providers regarding the importance of their role (10).

This study aimed to assess the frequency, causes, and associated factors of DTRPs, which are detected by clinical pharmacists' interventions.

2. Methods

2.1. Study design and setting

This prospective cross-sectional study was conducted in Fakeeh University Hospital a tertiary care hospital that provides care to a population of 500,000 people in Dubai, UAE, over a three-month period from September 2022 to December 2022. The data of patients who were assessed by clinical pharmacists regarding the presence of DTRPs as well as DTRP causes were collected and analyzed.

Tertiary care hospitals often have specialized services and multi-disciplinary teams, providing a rich environment to assess the collaboration between clinical pharmacists and other healthcare providers.

This research obtained the approval of the Medical Research and Ethics Committee of Dubai Pharmacy College and the Institutional Review Board (IRB) of the hospital before the commencement of the study (Ethics code: FUH/RES/005/023). In addition to that, the identity of the patients was kept anonymous for confidentiality.

2.2. Participants

Patients admitted to surgical, pediatric, intensive care unit (ICU), obstetrics and gynecology, and internal medicine wards from September 2022 to December 2022 were included in the study using convenient sampling technique. Oncology patients, long-term patients, and organ transplant patients were excluded from the study. These patients (Long-term patients/Organ transplant patients) were excluded as they are more of a stable case with a pattern of acute infections coming on top of a chronic condition. The acute infection is usually treated, and the patient goes back to baseline chronic condition.

2.3. Data gathering

Data was collected using a data collection form developed specifically for this project. This form included all the information acquired from the hospital database. The data collection sheets were divided into two sections. The first part primarily focused on including the subject's demographics such as age, body mass index (BMI), nationality, social history, family history of disease, allergy, chief complaint, diagnosis, medical history, past medications, and history of present illness. The second part of the data collection sheet addressed current medications, DTRPs, and acceptance rate of clinical pharmacists' interventions by physicians.

The data collection forms were adapted from the literature review and validated through face and content validation by a group of experts, professionals, physicians, and other healthcare professionals. Regarding the reliability of instruments, A pilot study was done on 10% of the sample population, and outcomes were assessed.

According to the Hepler and Strand classification system DTRPs were classified into the following 8 classes: (1) Untreated indications, (2) Improper drug selection, (3) Subtherapeutic dosage, (4) Failure to receive drugs, (5) Overdosage, (6) Adverse reactions, (7) Drug interactions, and (8) Drug use without indication.

2.4. Statistical analysis

A convenient sampling technique was used. The sample size was calculated using an online sample size calculator, which was 300 patients based on the capacity of the hospital (11) and considering z score 1.96 (z for a 95% confidence level is 1.96) and margin of error 5%.

The data were analyzed using IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 27.0 programs (IBM Corp., Armonk, New York). Statistical significance was set at a value of less than 0.05 for all the analyses. The sociodemographic data were analyzed using descriptive analysis. The association between baseline characteristics and presence of DTRPs were analyzed using Chi-square test.

3. Results

3.1. Baseline characteristics of the studied population

310 patients with the mean age of 33.43 ± 19.98 years (range: 1 month old (infant) – 89 years old) were studied (53.9% male). The highest percentage of patients were Asian (31.0%) and Arabs (30.6%). Table 1 summarizes the baseline characteristics of studied patients. The largest portion (31.6%) of the population fell within the 31-40 years age range. Kids (aged 12 years and below) made up 11.6% of the population, while teenagers (aged 13-18 years) were the least frequent, with only 10 patients falling within this age group. 64.8% of the samples were smokers and 18% reported consuming alcohol. About 42% of patients had a family history of disease. Most of the study participants (80%) had no allergies. Among the 20% with allergies, the majority had food allergies (16.5%). Moreover, the BMI of the population indicates that the majority of the population were overweight and obese.

79 (25.4%) of cases had no DTRPs, while 231 (74.6) had DTRPs. The surgical ward had the highest frequency of DTRPs with 41% frequency, followed by: internal medicine ward (19.6%), pediatric ward (16.1%), ICU (13.9%), and obstetric gynecology ward (9.6%).

3.2. DTRPs' classifications

Improper drug selection with 79 case, drug use without indication with 73 cases, and sub-therapeutic dosage with 26 cases were among the most common causes of DTRPs (Figure 1). In the surgical department, the most frequent DTRP was drug use without indication followed by improper drug selection. Improper drug selection was the most prominent DTRP in surgical, internal medicine, and ICU departments. Drug use without indication was mostly observed in the surgical, pediatrics, and obstetric gynecology departments (Figure 2).

3.3. Associated factors of DTRP

Table 1 compares the baseline characteristics of patients between cases with and without DTRPs. Alcohol intake (p= 0.03), food allergy (p = 0.02), age group 31-40 years (p = 0.04), presence of co-morbidities (p = 0.01), family history of diseases (p = 0.02), and admission to the ICU (p = 0.01) were amongst the significantly associated factors of DTRPs presence.

The acceptance status for clinical pharmacists' interventions were complete in 90.0% of cases, partial in 4.1 %, and rejection in 5.9% (figure 3).The highest acceptance rate was in internal medicine ward (25.7%) followed by surgical department (24.8%).

4. Discussion

This study examines the prevalence and probable associated factors of DTRPs during hospital admissions at Fakeeh University Hospital in Dubai, which has implemented CLMM and clinical pharmacy. The study found a high prevalence of DTRPs due to drug/dose selection and drug use without indication with a diverse sample reflecting multimorbidity and polypharmacy. These findings align with the latest Middle East and North Africa (MENA) Hospital Projects Forum in 2023, which emphasizes the significant role that clinical pharmacists can play in healthcare management by rationalizing and optimizing drug therapy (12) .

In terms of age group, our analysis revealed that individuals in the age category of 31-40 years were at a higher risk for experiencing DTRPs.

This finding contrasts with previous studies that typically associate DTRPs with elderly age groups (>60 years) (9, 13) or pediatrics (14, 15).

The prevalence of this age group in our study can be attributed to the demographic characteristics of Dubai, as our sample reflects a bell-shaped distribution encompassing all age groups, which is representative of the population in Dubai (16). Furthermore, additional factors (sedentary lifestyle, poor nutritional habits, and high-stress occupations) may explain the higher prevalence of DTRPs in this age group (16). In our study, we observed that 41% of patients were classified as overweight (BMI = 25-29.9 kg/m2), while 30% fell into the obese category (BMI > 29.9 kg/m2). Similar results regarding BMI have been reported in other studies (16, 17).

Additionally, approximately 35% of patients were smokers, and around 20% were alcohol consumers. However, no statistically significant association was found between these factors and the occurrence of DTRPs. The presence of comorbid conditions contributes to the occurrence of DTRPs due to the complexity of diseases, polypharmacy, altered drug metabolism, the need for dose adjustments, adverse drug reactions, and non-compliance. Within the study group with comorbid conditions, improper drug selection was the most frequently detected DTRP, while drug use without indication was more prevalent in the study group without comorbid conditions. Our study revealed significant correlations between comorbid conditions and the occurrence of DTRPs, which aligns with findings from other studies (9, 17-19).

Additionally, family history of disease emerged as an associated factor for the occurrence of DTRPs in our analysis. This finding is supported by similar literature (13), although some studies did not specifically measure family history as a factor in clinical pharmacist interventions (13, 17).

Our study revealed a high proportion of admissions with DTRPs, accounting for 75% of cases. While much of the existing evidence at the hospital level focuses on specific medical fields (20-22), often limited to ambulatory patients (23), there are studies that have investigated DTRP prevalence in various medical specialties, which reported prevalence rates ranging from 15% to 81% (24-26).

In terms of medical specialty, the surgical department had the highest proportion of interventions in our analysis.

Improper drug selection and drug use without indication

were the most detected DTRPs. Many studies have supported the same outcome whether the study was only done in the surgical department (19) or surgical patients were included in the studied population (27, 28). These findings are consistent with some recent studies. For example, two studies by Berger et al. and Tefera et al. found that the surgical department had the highest proportion of medication errors compared to other departments, and inappropriate drug selection was identified as one of the most common types of medication errors (29). Moreover, based on the aforementioned information, there is a need for further regulation of antibiotic use in the surgical department. The ASHP stewardship program guidelines (30) recommend the establishment of a Surgical Site Infection (SSI) bundle protocol for each hospital or institute. This protocol should be developed by an antimicrobial stewardship committee consisting of an infectious disease clinical pharmacist, a surgical doctor, a microbiologist, and an infectious disease officer. The committee should conduct daily reviews of all inpatients scheduled for surgery to ensure adherence to the SSI bundle protocol and review the appropriate use of pre-and post-surgical antibiotics (31, 32).

The Internal medicine (IM) ward comes in second place regarding clinical pharmacist interventions and medication errors detected, with improper drug selection, sub-therapeutic dosage, and drug use without indication being the most frequently reported DTRPs. This reflects the nature of patients in IM wards in terms of comorbid conditions, polypharmacy, and age. Similar results are supported by several articles (17, 18, 33, 34).

Clinical pharmacists have an integrated role in the management of chronic conditions such as diabetes mellitus (DM), cardiovascular disease (CVD), chronic kidney disease (CKD), and palliative care, which includes optimization of chronic medications upon discharge, medication reconciliation and counseling, patient education regarding lifestyle modifications required upon discharge, criteria for switching from intravenous to oral medications, and optimization of the patient pharmaceutical plan by review of medication history and newly prescribed medication and creating a most suitable pharmaceutical plan. This process is called Medication Therapy Management (MTM) (35-37).

The pediatric ward is the third most common place where DTRPs are detected, with drug use without indication being the most commonly reported DTRP. Recent studies have shown that the average proportion of children in hospital settings who receive at least one antibiotic is between 33 % and 78 %. (32, 38-42). Antimicrobials are prescribed during approximately 20% of pediatric ambulatory visits (43). It is important to implement formal antimicrobial stewardship (AS) programs in pediatrics due to the extensive use of antibiotics in children and the distinctive antimicrobial resistance patterns observed in this population. Collaboration between the clinical pharmacy department and pediatric physicians is essential in the development of such a program to reduce the overprescription of antimicrobials, particularly in this vulnerable population (38).

The Intensive Care Unit (ICU), including cardiovascular intensive care unit (CICU) and Cardiovascular intensive care unit (NICU), comes in fourth place in terms of clinical pharmacist interventions. Improper drug selection and subtherapeutic dosage are the most common DTRPs detected. Improper drug selection is mainly for antimicrobials, proton pump inhibitors (PPIs), and analgesics. Subtherapeutic dosage is mainly indicated for drugs that need pharmacokinetic monitoring or in cases of dialysis (dose adjustment required). Hemodynamic instability, drug interactions, and organ dysfunction can also lead to these outcomes. The role of clinical pharmacists in this field has been extensively studied in literature from countries all over the world. Studies have emphasized the role of clinical pharmacists in ICU with drug selection and dosage adjustment (44-46), as well as multiple studies done on the role of clinical pharmacists in CICU (47-49). On the contrary, some literature (44, 45) has ranked ICU as the department with the highest DTRPs detected. In our analysis, ICU came in 4th position due to the low flow of cases and the high number of long-term cases during the study interval.

The Obstetrics and Gynecology ward came in 5th place with drug use without indication as the main DTRP detected. To the best of our knowledge, this is one of the few studies to evaluate the role of clinical pharmacists in women's health as most studies either combine this ward together with the Internal medicine ward or they don't include it in the study. The complex medical histories of pregnant women necessitate a multidisciplinary approach for managing chronic diseases such as epilepsy, autoimmune diseases, hypertension (HTN), and DM, and reducing the risk of unfavorable maternal and fetal outcomes (50). This results in quality patient care and education, as well as medication reconciliation. In conclusion, our key recommendations focus on public health concerns, antimicrobial resistance programs, and the critical importance of antimicrobial stewardship, infection control, and early detection of medication errors.

The majority of pharmacist interventions in the current study were accepted effectively, preventing potential negative health outcomes, consistent with our study findings, clinical pharmacists have been successful in reducing adverse drug events by identifying DTRPs before they affect the patients, and the closed-loop electronic prescribing system facilitates more efficient medication reviews within shorter timeframes in many countries (7, 40). Therefore, these interventions should be regarded as effective tools that complement pharmacy practice as it aids in the reduction of medication errors and better patient outcomes.

5. Limitations and strengths

Our study has several notable strengths, including large sample size, the utilization of a validated DTRP classification system (Hepler Strand classification) (51), the assessment of a

comprehensive set of potential associated factors, the inclusion of relevant medical specialties, and the implementation of closed-loop medication management.

Some possible biases appeared due to the short study period including seasonal variations. The findings of this study may have limited applicability and may not be generalizable to populations beyond Dubai, because of the limited study duration and the frequent turnover of patients, particularly in the surgical department where a significant portion of patients were managed.

6. Conclusions

The study findings show a high prevalence of DTRPs due to drug/dose selection and drug use without indication. It seems that the participation of clinical pharmacists in multidisciplinary teams together with the presence of closed loop medication management facilitates the detection and correction of DTRPs.

7. Declarations

7.1. Acknowledgments

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7.2. Authors' Contributions

F.S wrote the concept/study design, performed data collection, interpretation of the data, contributed to statistical analysis, edited, and prepared the manuscript. M.B contributed to the concept/study design, provided clinical and procedural input, interpretation of the data, statistical analysis, and revision of manuscript .M.M and W.A organized the data collection and the database. M.A.M critically reviewed the paper, provided critical comments and prepared the final version of the manuscript. All authors contributed to the manuscript revision and approved the final version of the manuscript.

7.3. Funding

This research received no external funding.

7.4. Institutional Review Board Statement

The study was approved by the Ethics Committee of Dubai Pharmacy College, and by the Institutional Review Board of Fakeeh University Hospital Dubai. (Reference number FUH/RES/005/023).

7.5. Conflicts of Interest

The authors declare no conflict of interest.

7.6. Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request. Due to privacy and ethical considerations, raw patient data cannot be shared publicly, but anonymized and aggregated data are available upon request. Additionally, all relevant processed data supporting the findings of this study are included in this published article and its supplementary information files.

7.7. Using artificial intelligence chatbots

In this study, we utilized artificial intelligence (AI) chatbots, specifically OpenAI's GPT-based models, to assist with language generation tasks. The AI was employed to expedite certain repetitive processes such as summarizing large texts and providing grammar checks for the manuscript. AI was used as a supportive tool, and all interpretations, decisions, and conclusions drawn in the research are those of the authors. No sensitive data or proprietary content was shared with the chatbot during the study. The use of AI was compliant with the ethical guidelines and privacy regulations of the journal and institution.

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Table 1: Comparing the baseline characteristics of studied cases between patients with and without drug therapy-related problems (DTRP) (N=310)

Variables	N (%)	DTRP		P	Variables	N (%)	DTRP		P
		Yes(n=231)	No(n=79)				Yes(n=231)	No(n=79)	
Gender					**Age (year)**				
Male	167(53.9)	129 (77.2)	38 (22.8)	NS	<2	27 (8.7)	12 (44.4)	15 (55.6)	0.04
Female	143(46.1)	102 (71.3)	41 (28.7)		3-12	36 (11.6)	27 (75.0)	09 (25.0)	
Region					13-18	10 (3.2)	10 (100)	00 (00.0)	
Emirati	53 (17.1)	42 (79.2)	11 (20.8)	NS	19-30	40 (12.9)	33 (82.5)	07 (17.5)	
Asian	96 (31.0)	71 (73.9)	25 (26.1)		31-40	98 (31.6)	71 (72.4)	27 (27.6)	
Arabs	95 (30.6)	69 (72.6)	26 (27.4)		41-50	44 (14.2)	28 (63.6)	16 (36.4)	
Southeast Asians	16 (5.2)	13 (81.2)	03 (18.8)		51-60	25 (8.1)	23 (92.0)	02 (08.0)	
Westerns	44 (14.2)	33 (75.0)	11 (25.0)		>60 30 (9.7)	23 (76.6)	07 (23.4)		
African	06 (1.9)	03 (50.0)	03 (50.0)		**Body mass index**				
Habits					<18.5	58 (19.0)	40 (68.9)	18 (31.1)	0.05
Smoking	109(35.2)	86 (78.9)	23 (21.1)	0.05	18.5-<25	70 (23.0)	56 (80.0)	14 (20.0)	
Alcohol	56 (18.1)	45 (80.3)	11 (29.7)	0.03	25-<30	107(34.0)	82 (76.6)	25 (23.4)	
Allergy					>30	75 (24.0)	53 (70.6)	22 (29.4)	
Medicine	13 (4.2)	10 (76.9)	03 (23.1)	0.05	**Family history of disease**				
Food	51 (16.5)	42 (82.3)	09 (19.7)	0.02	Yes	136(59.1)	94 (69.1)	42 (30.9)	0.02
Admitting ward					No	94 (40.9)	57 (60.6)	37 (39.4)	
Surgery	123(39.7)	94 (76.5)	29 (23.5)	0.01	**Comorbidity**				
ICU	34 (11.0)	32 (88.2)	02 (5.8)		Yes	161(51.9)	146 (90.6)	15(09.4)	0.01
IM	63 (20.3)	45 (71.4)	18 (28.6)		No	149(48.1)	85 (57.0))	64 (43.0)	
Pediatrics	55 (17.7)	37 (67.2)	18 (32.8)						
O&G	35 (11.3)	22 (62.8)	13 (37.2)						

O&G: Obstetrics &Gynecology; IM: internal medicine; ICU: intensive care unit; NS: not significant.
Chi Square test, P<0.05 was deemed significant.

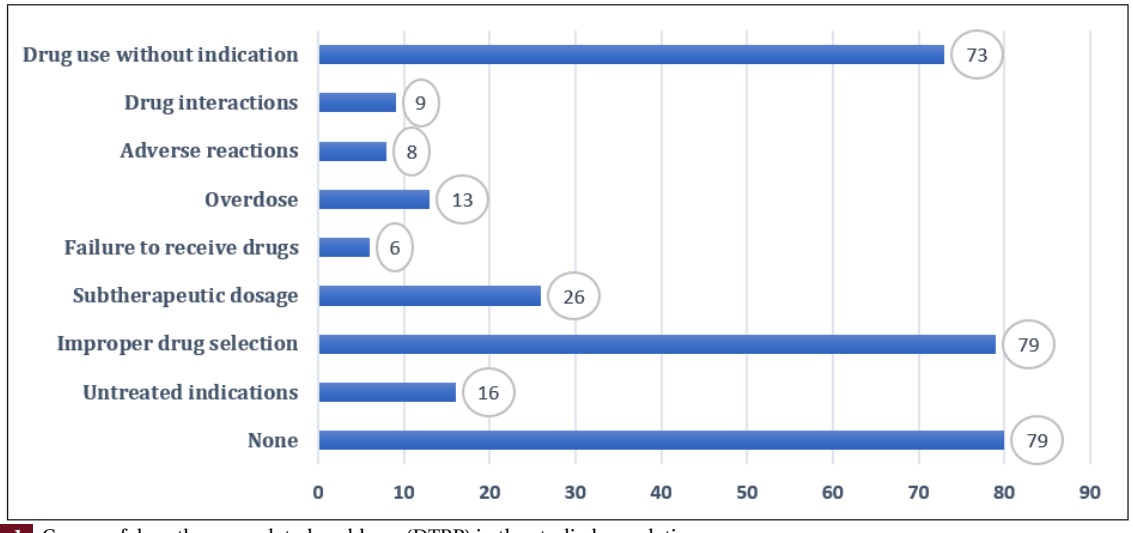

Figure 1: Causes of drug therapy-related problems (DTRP) in the studied population.

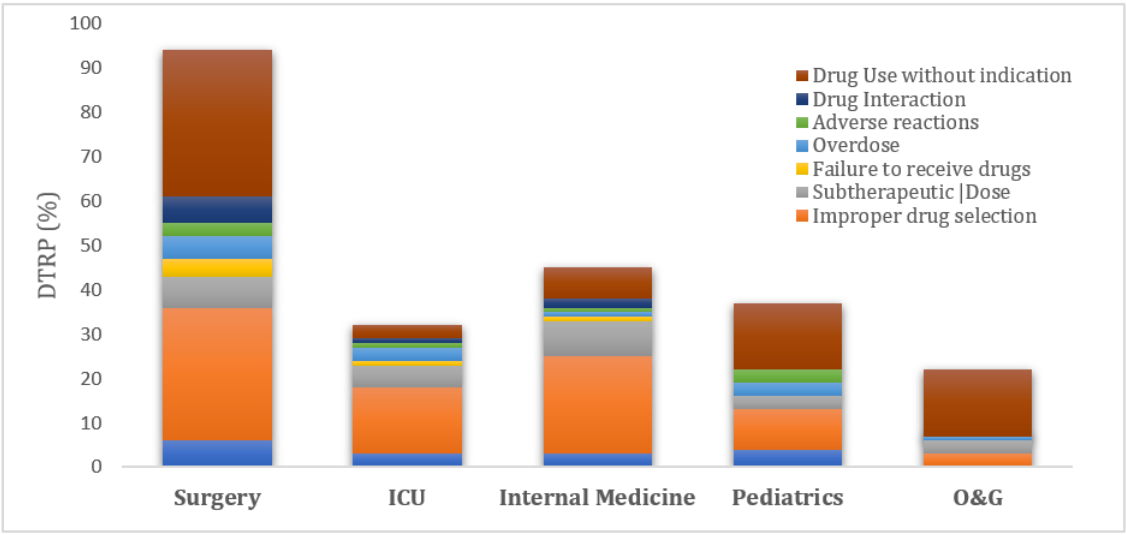

Figure 2: The distribution of different causes of drug therapy-related problems (DTRP) based on the hospital admission ward. O&G: obstetrics and gynecology; ICU: intensive care unit.

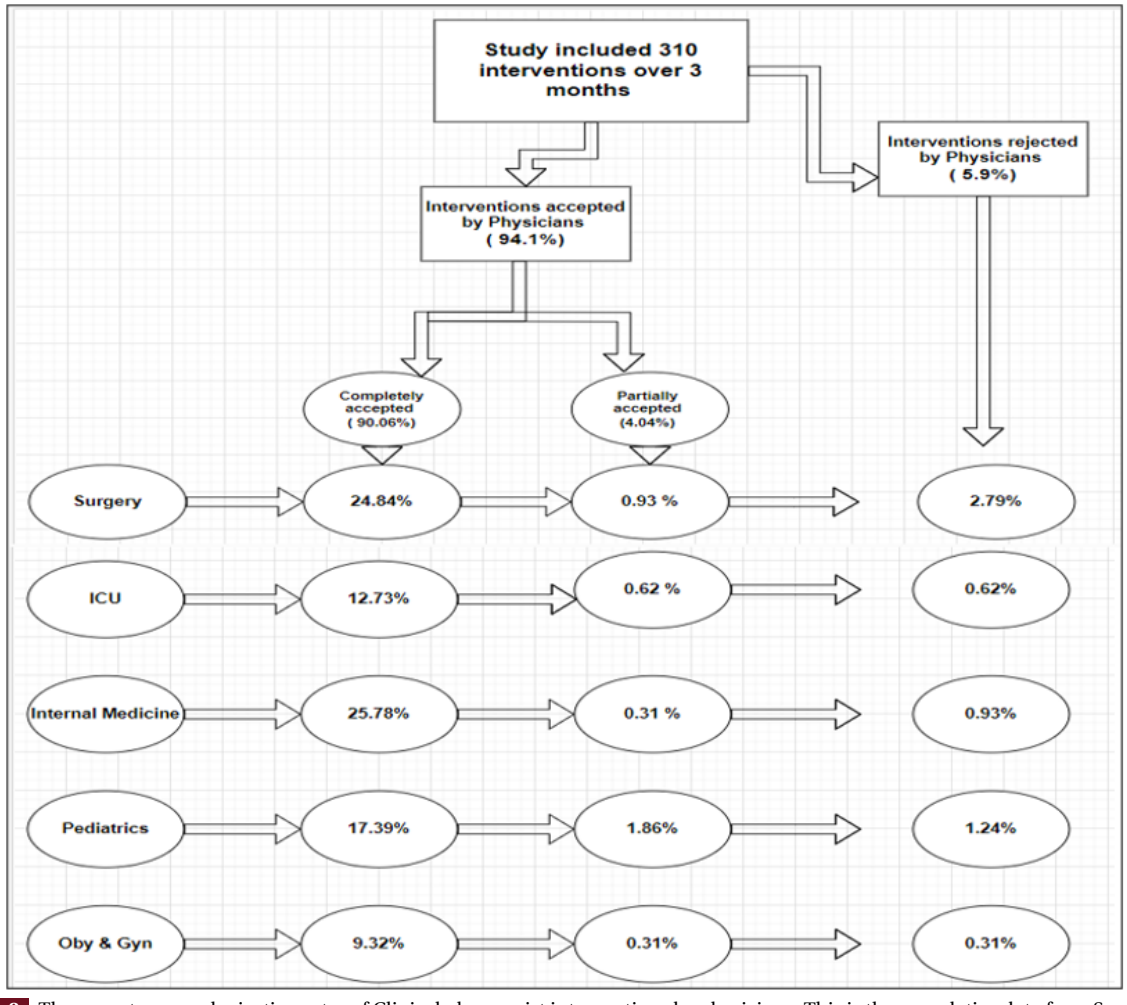

Figure 3: The acceptance and rejection rates of Clinical pharmacist interventions by physicians. This is the cumulative data from September 2022- December 2022, for a total of 310 interventions. Complete acceptance was defined as an immediate response to clinical pharmacist intervention; Partial acceptance was when intervention was accepted but immediate action was not taken; and Rejection was when clinical pharmacist intervention was refused due to certain reasons. ICU: intensive care unit; Oby &Gyn: obstetrics and gynecology.