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Physician Acceptance of Pharmacist Recommendations about Medication Prescribing Errors in Iraqi Hospitals

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Abstract

*The **objectives** of this study were to measure the incidence and types of medication prescribing errors (MPEs) in Iraqi hospitals, to calculate for the first time the percentage of physician agreement with pharmacist medication regimen review (MRR) recommendations regarding MPEs, and to identify the factors influencing the physician agreement rate with these recommendations. **Methods:** Fourteen pharmacists (10 females and 4 males) reviewed each hand-written physician order for 1506 patients who were admitted to two public hospitals in Al-Najaf, Iraq during August 2015. The pharmacists identified medication prescribing errors using the Medscape WebMD, LCC phone application as a reference. The pharmacists contacted the physicians (2 females and 34 males) in-person to address MPEs that were identified. **Results:** The pharmacists identified 78 physician orders containing 99 MPEs with an incidence of 6.57 percent of all the physician orders reviewed. The patients with MPEs were taking 4.8 medications on average. The MPEs included drug-drug interactions (65.7%), incorrect doses (16.2%), unnecessary medications (8.1%), contra-indications (7.1%), incorrect drug duration (2%), and untreated conditions (1%). The physicians implemented 37 (37.4%) pharmacist recommendations. Three factors were significantly related to physician acceptance of pharmacist recommendations. These were physician specialty, pharmacist gender, and patient gender. Pediatricians were less likely (OR= 0.1) to accept pharmacist recommendations compared to internal medicine physicians. Male pharmacists received more positive responses from physicians (OR=7.11) than female pharmacists. Lastly, the recommendations were significantly more likely to be accepted (OR= 3.72) when the patients were females. **Conclusions:** The incidence of MPEs is higher in Iraqi hospitalized patients than in the U.S. and U.K, but lower than in Brazil, Ethiopia, India, and Croatia. Drug-drug interactions were the most common type of MPEs in hospitals. Physician specialty and pharmacist gender and patient gender significantly influenced physician agreement with the pharmacist comments. Only one-third of the pharmacist recommendations were implemented. Phone drug applications would be helpful for daily hospital pharmacy practice. More pharmacist-physician collaboration is needed to address MPEs. Pharmacist-led MRR can identify and address MPEs to improve patient safety.*

Keywords: Physician acceptance, pharmacist recommendations, prescribing errors, Iraq, hospitals

Introduction

Healthcare scholars classify medication errors into four categories: those physicians make during prescribing, those pharmacists make during dispensing, those nurses or patients make during administration, and those, which occur during monitoring. Prescribing error is "'a failure in the prescribing process that leads to, or has the potential to lead to, harm to the patient' (Aronson, 2009) [1]. Prescribing errors are preventable events which include incorrect dose, incorrect duration, unnecessary medications, contraindications or interactions [2-4].

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Patients with medication prescribing errors (MPEs) are at risk for significant medication-related problems (MRPs) which include adverse drug events (ADEs) and harmful drug interactions. Adverse drug events (ADEs) are injuries due to adverse drug reactions or medication errors [4]. Adverse drug reactions are considered non-preventable while medication errors are considered preventable ADEs. Drug interactions include drug-drug, drug-food and drug-disease interactions and all of these can increase or decrease a drug's activity or aggravate another disease.

Simonson and colleagues report that MRPs contribute to approximately 200,000 deaths in the U.S. annually [5]. A one-year study in a teaching hospital in New York, USA identified and addressed 2103 prescribing errors [6]. One study of a teaching hospital in the U.S. identified 1.9% prescribing errors. During the 6-month study, the pharmacist prevented 479 medication errors in two pediatric hospitals [7]. In a 4-week period study in a British hospital, pharmacists reported 651 MPEs [8]. Systematic reviews have showed polypharmacy—concurrent use of multiple medications— is directly related to drug-drug interaction, ADEs and hospitalization [2, 9]. Pharmacists are often the last line of defense against physician prescribing errors. Many pharmacists assume identifying physician prescribing errors is enough to prevent patient harm. Despite this important role, pharmacists have no authority to change medication regimens without prescriber (physician) permission. Thus, pharmacists need to work with physicians to address errors. This study investigated the factors influencing physician acceptance of pharmacist recommendations.

Pharmacist-led medication regimen review (MRR) is an evaluation of patient drug regimens to prevent, identify, report, and resolve any MRPs such as medication errors, drug-contraindications, interactions, and inappropriate polypharmacy (unnecessary multiple medications) [10]. The MRR has been shown to lower the rates of medication errors , MPEs and other ADEs [11, 12]. Three randomized controlled trials found that pharmacist-led MRR significantly lowered drug-related problems and the number of repeated prescriptions among elderly patients above 65 years of age [13-15]. Additionally, a recent systematic review and meta-analysis of twenty one studies concluded that pharmacist-led MRR significantly improved subjects' blood pressure and lipid levels (low density lipoprotein) [16]. Consequently, MRR enhances medication safety and reduces hospitalization.

Pharmacists are the most competent health care providers to conduct a MRR because they have knowledge and experience in pharmacology, pharmacokinetics, pharmacodynamics, and pharmacy systems [12]. Pharmacists can access various medical data sources such as laboratory reports and patient medical records in addition to communicating with other health care providers [12]. A pharmacist conducts MRR to ensure that dosage levels are appropriate (neither over- nor under-dose), that all medications are necessary (supported by appropriate diagnosis), the patients are not allergic to prescribed medications, and there are no significant drug-drug or drug-disease interactions [10].

Several factors may influence effectiveness of pharmacist-led MRR and the degree of prescriber acceptance of pharmacist recommendations including medical ward, the individual characteristics, specialty and years of experience of both pharmacist and prescriber (physicians).

In 2013, a systematic review of medication errors in Middle Eastern countries found no study investigating this critical topic in Iraq [17]. There was only one Iraqi study measuring medication errors by 2014 and this was an observational study (without interventions) which evaluated the types and medication classes of these errors [18]. Although several studies have investigated pharmacist interventions in prescribing errors around the world [6, 8, 19-25], almost all of these studies were limited to evaluations of the incidence rate, causes, clinical significance and types of prescribing errors. However, a little is known about physician acceptance rate of pharmacist recommendations and only a couple of studies have focused on implementation of recommendations [26, 27]. None of the previous prescribing error studies in hospitals (to our knowledge) investigated factors influencing physician agreement with pharmacist recommendations. Almost all the previous studies that investigated pharmacist interventions in prescribing errors have used conventional medication review to find the medication errors. In our study, hospital pharmacists identified medication prescribing errors using the Medscape WebMD, LCC phone application as a reference. Additionally, our study is the first to investigate pharmacist interventions to address prescribing errors in Iraq.

The objectives of this study were to measure the incidence and types of MPEs in Iraqi hospitals, to calculate the percentage of physician agreement with pharmacist medication regimen review recommendations regarding medication prescribing errors (MPEs), and to identify for the first time the factors influencing the physician agreement rate.

Methods

This study was an interventional prospective study. Fourteen pharmacists (10 females and 4 males) prospectively reviewed 1506 hand-written physician medication orders for inpatients in two public teaching hospitals in Al-Najaf Province, Iraq during August 2015. The pharmacists had a mean age of 26.86 (±2.54) years and mean time of practice of 1.5 (±1.3) years. Eight of the pharmacists (four males and four females) were hospital employees and had the authority to contact the prescribers (physicians).The other six female pharmacists were college of pharmacy affiliated pharmacists - who helped the hospital pharmacists in MRR. The physicians' mean age was 50.5 (± 9.69) years.

The sampling included physician orders for every patient admitted into three wards during the month of the study (census sampling). These three wards were distributed between two teaching hospitals: one had surgery and internal medicine wards (80 beds), and the other had four pediatric wards (160 beds). The internal medicine ward contained a cardiology section while the surgery ward included general-surgery, thoracic-surgery, neuro-surgery and orthopedic-surgery.

The pharmacists identified MPEs using the Medscape WebMD, LCC phone application as a reference[28]. The MPEs included inappropriate doses, inappropriate treatment duration, contraindications, significant drug-drug interactions, untreated conditions, and unnecessary medications. Because the physician order was updated on a daily basis, the pharmacists reviewed physician orders, which had no MPEs twice, on two consecutive days. However, no changes were made to physician orders and no MPEs were found on the second day of the reviewing. To confirm the error, any order with MPEs was reviewed by two pharmacists. After the pharmacists identified MPEs and reported the type of error, they contacted (face-to-face) the prescriber (physician) to address the problems. Pharmacists reported whether the physicians accepted their recommendations or not and whether the MPEs addressed or not. Physician and pharmacist characteristics were also reported such as age, gender, specialty, and years of practice. Additionally, the pharmacist recorded the medical wards and the demographic data of the patients with the MPEs including age, gender in addition to the names of current medications (with doses, frequency and duration), and the number of days in the hospital. The study received permission from the Iraqi Universities and an exemption from the University of Iowa Institutional Review Board.

Statistical Analyses

The analyses were conducted using Statistical Analysis System (SAS, version 9.3, SAS Inc., Cary, North Carolina, USA). Means, range, and standard deviation (SD), frequencies and percentages of participant characteristics, such as pharmacists and physicians' age, gender, practice years and specialty, were calculated. Patients' age, gender, number of hospitalization days, and medications were also recorded. A binary logistic regression analysis was conducted to measure the association between the independent variables (ward, physician, pharmacist and patient characteristics), and the binary outcome variable (physician implementation of pharmacist recommendations: Yes/NO). The logistic regression analysis was conducted for the 78 independent medication orders with MPEs because the physicians who agreed with pharmacist recommendations about 21 orders addressed all 37 errors in these records at once. Bivariate regression analyses were conducted to reduce the number of independent variables included in the multivariate model and only those which were significant at 0.20 or better (p-value ≤ 0.20) such as ward, physician-experience year, pharmacist-gender, and patient-gender were included in the final regression model. Severity and types of the MPEs were also calculated. The figures were plotted using GraphPad Prism 6 software (San Diego California USA, www.graphpad.com).

Results

The pharmacists identified 78 physician orders with at least one prescribing error for a total of 99 errors and an incidence of 6.57 percent. The eight hospital pharmacists informed 36 physicians (2 females and 34 males) in-person about MPEs and nine of them were contacted more than once. The female pharmacists contacted physicians about 63 physician orders while the male pharmacists informed the physicians about 15 erroneous orders. The physician orders with MPEs had 4.80 (±2.1) medications on average not including intravenous fluids (glucose saline, Ringer's solution and normal saline) and oxygen. When the intravenous fluids were included, the patients with MPEs had an average of 5.06 (±2.1) medications. The 99 MPEs were found for 78 different patients (41 male and 37 female) with a mean age of 27.82 (±27.4) years (table-1). The pediatric, internal medicine and surgery wards had 43 (43.4%), 29 (29.3%), and 27 (27.3%) MPEs respectively. More than half the patients (51.3%) with MPEs were less than 18 years old (Table 1).

The pharmacists identified six different types of the MPEs (figure 1). Drug-drug interactions were the most common type (65.7%) while untreated conditions were the least common type (1.0%) of MPE (Figure 1). Drug contraindications included prescribing tramadol (opioid derivative) for patients less than 16 years old and mefenamic acid (non-steroidal anti-inflammatory drug, NSAID) for patients less than 14 years old. Incorrect doses included prescribing full regular doses for patients with renal or hepatic failure when the doses needed to be reduced (Table 2). Narrow therapeutic index drugs were found 37 times with MPEs including vancomycin (n= 9), amikacin (7), aminophylline (n=6), phenobarbital (n=6), phenytoin (n=3), digoxin (n=2), gentamycin (n=2) and valproate (n=1), and carbamazepine (n=1). Systemic antibiotics (28.3%) and cardiovascular medications (17.2%) were the most common medication categories involved in the MPEs (Figure 2). The majority of the MPEs were clinically significant (72.7%) and 19 (19.2%) of them were serious errors (Table 2).

The physicians implemented only 37 (37.4%) pharmacist recommendations (19 for male pharmacists and 18 for female pharmacists) to address these MPEs. The logistic analysis results showed that three factors were significantly associated with the outcome variable (physician implementation of pharmacist recommendations). Pediatricians were less likely (Odds Ratio (OR)= 0.10; 95% Confidence Interval (CI)= 0.01-0.73) to accept pharmacist recommendations compared to internal medicine physicians. The physicians were seven times more likely (OR=7.1; 95% CI=1.1-45.4) to respond positively to male pharmacists than female. Lastly, physicians had significantly more positive (OR=

3.7; 95% CI= 1.07-12.95) responses when the patients were female (Table-2).

Male pharmacists had no recommendations about minor errors while 11.27% of female pharmacists' recommendations were about minor errors. On the other hand, 25 % of male pharmacists' recommendations were about serious/fatal errors and 75% about significant errors whereas 16.9% and 71.83% of female pharmacists' recommendations were about serious and significant errors respectively.

Discussion

The pharmacists were younger and they had spent fewer years in practice than the physicians (Table 1). This may explain the low response rate of physicians to pharmacist recommendations. Half of the patients with MPEs were children because one of the two hospitals was a pediatric hospital. Two thirds of the MPEs were drug-drug interactions, which the physicians may not consider significant errors although some of them had potential serious consequences (Table 2). Only six (9.7%) of the rejected recommendations were about non-significant (minor) errors while 14 (22.6%) of them were about potentially serious errors. Taking multiple concurrent medications was probably reason for higher interaction errors.

Although the Iraqi physicians had about 10 times as many years of experience as the pharmacists, they committed relatively high prescribing error rates, which may be due to outdated pharmacotherapeutics knowledge. The lack of an electronic health record (EHR) in Iraqi hospitals may negatively influence prescribing practices because physicians may not have a full patient medical/ medication history in a paper chart, particularly if a patient has been admitted multiple times.

Our study found that the incidence of MPEs in the two Iraqi hospitals (6.6 %) was at least three times higher than in the U.S. (0.3-1.9%) and U.K (1.5%) [7, 8, 25]. A one-year study in a teaching hospital in NY, USA, found 0.399% prescribing errors[6]. A study of an internal medicine clinic in a university hospital in Zagreb, Croatia had higher incidence of MPEs (7.7%) than Iraqi hospitals [21]. Other countries had much higher MPE incidence rate. For example, Brazilian intensive care unit had 43.5 % MPEs, and Ethiopian, Saudi and Indian hospitals had 40 %, 56% and 34 % MPEs respectively [20, 22, 24, 29].

Two-third (65.7%) of the MPEs in this study were drug-drug interactions and 9.2%, 67.7% and 23.1% of them were minor, significant and serious interactions respectively. The number and types of medications used may have contributed to the high percentage of drug-drug interactions. In the pediatric hospital, 11 out of 43 children were treated for epilepsy or a febrile fit using phenytoin, phenobarbital, carbamazepine, valproate, and/ or clonazepam which are narrow therapeutic index medications and highly susceptible to drug-drug interactions particularly with antibiotics. Our study findings agree with an Indian study showing drug-drug interactions were the most common prescribing error in teaching hospitals (65.7% and 68.2% respectively) and antibiotics were the most frequent medication category associated with prescribing errors (28.3.3% and 29.4% respectively)[24]. Similarly, a study in Croatia found that drug-drug interactions were the most common error type and accounted for 14.7 percent of prescribing errors[21]. However, British, American and Saudi studies reported that incorrect dose was the most common prescribing error (54%, 39.7% and 22.1% respectively) [6, 8, 29]. Similarly, a 14-day study in teaching hospitals in Netherlands indicated the dosing errors (dose/duration) was the most common prescribing error type (63%) [19]. Therefore, among the reviewed studies in the literature, our study had the second highest percentage of drug-drug interaction errors.

This study identified systemic antibiotics as the most frequent therapeutic category were involved in all prescribing errors (28.3%). That suggests physicians chose antibiotic(s) without considering their interactions with chronic disease medications. Surgical and pediatric ward patients usually receive antibiotics either as post-operative prophylaxis or to treat systemic infections. The observational Iraqi study (in the Kurdistan region) also found that antibiotics were the most common therapeutic category associated with medication errors (32.4 %) in a pediatric hospital[18]. Likewise, the Brazilian (45.7%) and American (23.1%) studies found systemic antibiotics were the most frequent medication category involved in MPEs in neonates[22, 25]. In the Dutch study, central nervous system medications were the most commonly involved in prescribing errors[19]. Thus, this study confirmed the findings of studies from around the world that antibiotics are the most common medication category involved in prescribing errors [22, 24, 25].

The low physician acceptance of pharmacist recommendations suggests that physicians may underestimate the risk of drug-drug interactions. In fact, some of these interactions were categorized as serious errors. For instance, interactions of ceftriaxone with heparin, warfarin or ringer solution can have serious or even fatal risks for patients (Table 2). There were no hospital regulations requiring physicians' response to pharmacist recommendations. The difference between the physicians' and pharmacists' experience may also have contributed to the low physicians' acceptance rate of pharmacist recommendations. Physicians may consider the benefits of certain medications outweigh their risks. In contrast, a study in a pediatric and obstetric hospital in Spain found that the physician acceptance of pharmacist recommendations was three times (92.2%) higher than in Iraq [27].

In this study, the physicians who agreed with the pharmacist implemented the recommendations. Hence, the pharmacists helped to avert 37 MPEs. The pediatricians were less likely to agree with pharmacist recommendations because they may have a smaller available list of medications compared to internal medicine physicians. Thus, the pediatricians may not believe they need pharmacist recommendations. The physicians were more likely to implement the recommendations of male pharmacists which may be due to the fact that male physicians (96.8%) have stronger collaborative relationships with male pharmacists than females because of the strong gender barrier in this conservative city. A Canadian study found a gender bias among orthopedic surgeons when they referred and recommended total joint arthroplasty [30]. Hence, gender bias behavior cannot be excluded. Finally, because male pharmacists focused only on significant and serious MPEs, this may play a role to receive three times higher recommendation-acceptance rate from physician compared to female pharmacists.

The patients with MPEs had not been informed about the errors to avoid any patient-physician conflicts. The results showed the physicians significantly more accepted pharmacist recommendations when the patients were female. This result has no clear explanation because the patients were not involved in the pharmacist-physician communications.

There are two types of pharmacists working in Iraqi hospitals: General pharmacists who work in a main pharmacy to supply medications and maintain stock and clinical pharmacists who work in clinical wards [31]. The hospital pharmacists who participated in the study were clinical pharmacists and those passed a credential exam in clinical fields after their graduation. The duties of clinical pharmacists include reviewing medication regimens to minimize inappropriate prescribed medications, distributing medications to inpatients and counseling inpatients, caregivers and/or nurses about medication administrations [31]. However, there is no official quality auditing on pharmacist-led MRR and it is totally up to pharmacist to conduct a thorough or suboptimal reviewing because physicians are usually responsible for any prescribing errors. Thus, hospitals need to impose incentives and regulations encouraging pharmacists to review physician orders effectively to minimize prescribing errors. Furthermore, Iraqi Ministry of Health should issue regulations urging physicians to address pharmacists' recommendations. Iraqi hospital pharmacists and physicians should have the same medication error checking references to avoid disagreement about the safety of prescribed medications. Hospitals can hold workshops and seminars to increase awareness of prescriber error incidence and negative consequences. Healthcare providers should also exert more efforts to enhance their collaboration to eliminate the incidence of MPEs.

Limitations
This study was conducted for one month in one province. However, it involved three different medical wards in standard Iraqi governmental hospitals with a typical degree of pharmacist-physician collaboration. The study included public hospitals only because private hospitals have no hospital pharmacists.

Conclusions and Recommendations
Iraqi hospitalized patients with multiple medications experience a greater number of MPEs than patients in the U.K and U.S., but fewer than patients in Brazil, Saudi Arabia, Ethiopia and Croatia. Drug-drug interactions were the most common MPEs found in this study. Antibiotics and cardiovascular medications were the most frequent therapeutic categories associated with prescribing errors. Only one-third of the physicians complied with the pharmacist recommendations. Medical ward, pharmacist gender, and patient gender significantly influence physician implementation of pharmacist recommendations. Implementing EHR can enhance medication prescribing appropriateness. Phone drug applications would be helpful for daily hospital pharmacy practice. Pharmacist-led MRR can identify and address MPEs to improve patient safety. Fostering pharmacist-physician collaboration may increase physician acceptance rate of pharmacist recommendations. Pharmacists should review every single medication regimen before dispensing medications to minimize prescribing errors and patient harm and enhance patient health outcome.

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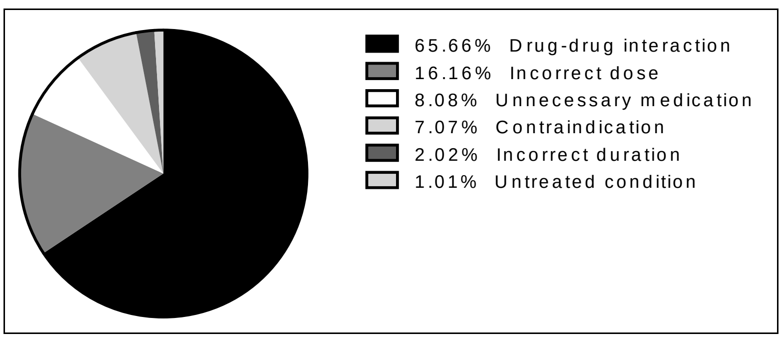
Table 1: Physician, pharmacist and patient with prescribing error characteristics

Characteristic	Mean	ST.DV	Minimum	Maximum
Physician age (years)	50.5	9.7	33	78
Physician practice years	16.9	8.6	1.0	40
Patient hospital days of stay	4.0	3.7	1.0	20
Child-Patient (N=40) age (years)	4.47	4.27	0.3	14
Adult-patient (N=38) age (years)	52.4	18.32	20	80
Number of patient Medications	4.8	2.1	1.0	10
Pharmacist age (years)	26.9	2.5	25	34
Pharmacist practice years	1.5	1.3	0.3	5.0

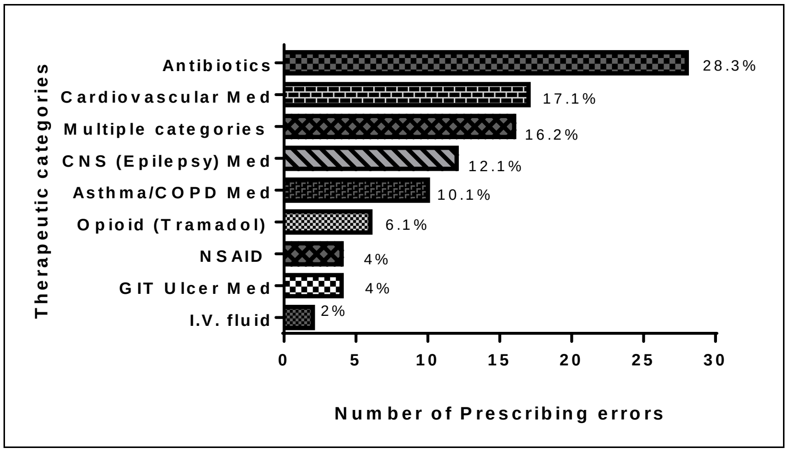
* ST.DV= standard deviation, number of physicians=36, number of pharmacists=14 and number of patients with medication prescribing errors=78.

Figure 1: Percentages and frequencies of medication prescribing error types



Contraindication means drug should not be used for patient because it is harmful such as prescribe mefenamic acid for patients with less than 14 years old. Incorrect duration means using treatment for longer or shorter period than that mentioned in the reference.

Figure 2: The frequencies of therapeutic categories involved in the prescribing errors



*Multiple drug-categories' interactions include: 6 systemic antibiotics with cardiovascular (CVD) medications, 6 systemic antibiotics with central nervous system (CNS) medications, 1 systemic antibiotic with respiratory medications, 1 CNS with respiratory medication. COPD= Chronic Obstructive Pulmonary Diseases (Chronic bronchitis or Emphysema) medications include systemic bronchodilators (salbutamol and aminophylline), and corticosteroids (hydrocortisone and dexamethasone) ; NSAID=Non-Steroidal Anti-inflammatory Drug (Mefenamic acid); GIT (Gatro-Intestinal Tract) Ulcer = H2-blocker (Ranitidin) or Proton Pump Inhibitor (Omeprazole); I.V. fluid = Intravenous fluid (Glucose Saline) is given to patient with uncontrolled Diabetes Mellitus.

Table 2: Frequency and examples about three levels of prescribing error severity

Prescribing error severity degree	N (%)	Example
Minor [1]	8 (8.1)	• Prescribing ranitidine and opemrazole concurrently to patients without GIT ulcer. • Interaction between Phenobarbital- phenytoin [4]
Significant [2]	72 (72.7)	• Prescribing tramadol to patients less than 16 year- old [5] • Prescribing mefenamic acid to patients less than 14 year-old. • No meropenem dose adjustment in patients with renal impairment (Creatinine Clearance=14 ml/min). • No metronidazole dose adjustment in patients with hepatic impairment. • Prescribing overdoses of oral salbutamol for children.
Serious [3]	19 (19.2)	• Interaction between ceftriaxone- warfarin [6]. • Interaction between ceftriaxone- heparin. • Prescribing Glucose Saline fluid to a diabetic child with Random Blood Glucose= 654mg/dl. • Interaction between ceftriaxone and ringer intravenous solution (Calcium gluconate)[7].

[1] Minor error has non-significant/potential inconvenient for patients. [2] Significant error has potential significant risk/ injury for patients. [3] Serious error has potential serious/fatal risk for patients.[4] "Phenobarbital decreases levels of phenytoin by increasing metabolism. Minor or non-significant interaction". [5] Severe respiratory depression reported with off-label use of tramadol in children. [6] "ceftriaxone increases effects of warfarin by anticoagulation. Possible serious or life-threatening interaction. Monitor closely". [7] "Do not use any calcium-containing solutions (including Ringer's) in combination with IV ceftriaxone; risk of potentially fatal particulate precipitation in lungs, kidneys. Separate by at least 48 hrs"[28].

Table-3: Logistic regression results: Factor influencing physician response to pharmacistdrug recommendations

Independent Variable	*Odds Ratio Estimate (OR)*	*95% Wald Confidence Limits*		*P-value*
Ward / Pediatrics vs Internal Medicine	0.10	0.01	0.73	0.02*
Ward / Surgery vs Internal Medicine	2.89	0.67	12.41	0.15
Physician-experience years	1.06	0.98	1.15	0.13
Pharmacist-gender/ male vs female	7.11	1.11	45.44	0.04*
Patient-gender/ female vs male	3.72	1.07	12.95	0.04*

*statistically significant (P≤ 0.05); Outcome variable (physician implementation of pharmacist recommendations): Yes vs NO. Number of orders had MPEs (N)=78.