# ASSESSMENT OF DRUG-DRUG INTERACTIONS IN SURGICAL INTENSIVE CARE UNIT

**Abstract number:** 5PSQ-126          **ATC code :** -

[1]A Koddouss, [1]L Zarayby, [2]R Cherkab , [2]L Barrou, [1]S Derfoufi

[1]CHU Ibn Rochd, Ibn Rochd Hospital, Pharmacy, Casablanca, Morocco [2]CHU Ibn Rochd, Ibn Rochd Hospital, Surgical Intensive Care Unit, Casablanca, Morocco

## Introduction

The pharmaceutical analysis of prescriptions is the first step of the dispensing act defined by Article R. 4235-48 of the Public Health Code and by the decree of April 6, 2011.

Drug–drug interaction is defined as a pharmacological or clinical response to the administration of two or more drugs that is different from the response they initiate when individually administered.

The clinical relevance of drug-drug interactions (DDIs) is clear: DDIs can increase the frequency and severity of adverse events (AEs) or increase the likelihood of treatment failure [1]

Hospitalized intensive care patients need more attention regarding drug–drug interactions due to complexity of their supported. Polypharmacy and their longer stay also influence the incidence rate of Potentiel Drug Drug Interactions (PDDIs).

The prevention of adverse events caused by potential interactions and their management :
- Are activities of the most importance in the practice of clinical pharmacy in Intensive Care Units;
- Being seen as one of the first actions to be developed in the clinical pharmacy services [2].

## Objectives

In the present study, our goal was to advance this research and quality improvement agenda by assessing the prevalence and characteristics of PDDIs exposure of patients hospitalized in adult Intensive Care Unit (ICU) of Ibn Rochd hospital.

## Patients & Methods

This is an observational study with a prospective data compilation (September 2016 – March 2017).

This research was carried out in a general adult ICU, with 12 beds.

This is a general ICU, tending for potentially critical patients or patients with an unbalance of one or more organic systems due to high-complexity surgeries, serious infections and other clinical situations that demand intensive life support.

Patients' personal information and drug treatments gathered are below :
- Number of patients hospitalized;
- The epidemiological parameters;
- Average length of stay for in-patients;
- Number of drug interactions;
- Drug class according to anatomical chemical therapeutic (ATC) classification .

The levels of identified drug interactions are based on "Guideline on the Investigation of Drug Interactions" edited by French National Agency for the Safety of Medicines and Health Products (ANSM) : warnings, precautions, possible adverse, contraindications.

Prescriptions are searched and analyzed by: THERIAQUE®, Thesaurus ANSM 2016, ScienceDirect and Pubmed.

The identified interactions are classified into pharmacokinetic and pharmacodynamics as it is described in literature. Factors related to patient and medicines are supposed to be taken into consideration upstream when assessing drug interactions.

Averages and percentages were calculated using Microsoft Excel 2007.

## Results

Were analyzed prescription orders of 131 patients, mean age of 50.21 ± 17.21. 47% were female and 53% were male.

Average of hospitalization in adult ICU = 8.18 ± 14.79 days. The 131 lines of prescriptions analyzed averaged 11.31 ± 3 drugs (range: 3-20).

A total of 102 unique generic drugs were administered :
**F**igure 1 shows the distribution of the drugs observed in this study according to the Anatomical Therapeutic Chemical (ATC) Classification.

**Table 1** lists the most drug exposures by ATC classification.

A total of 81 drug interactions was detected 28% (n=23) pharmacokinetic and 72% (n=58) pharmacodynamic **(Figure 2).**

ANSM classifies the drug interactions into 4 levels :
A contraindicated PDDIs exposure occurred in 5% (n=4) of all hospitalizations, a PDDI with possible adverse exposure in 43% (n=35), precautions in 42% (n=34), and warnings in 10% (n=8) **(Figure 3).**

Certain classes of drugs were commonly implicated in PDDIs, including opioids, antiinfective agents, neurologic agents, gastrointestinal agents, and cardiovascular agents **(Table 2).**
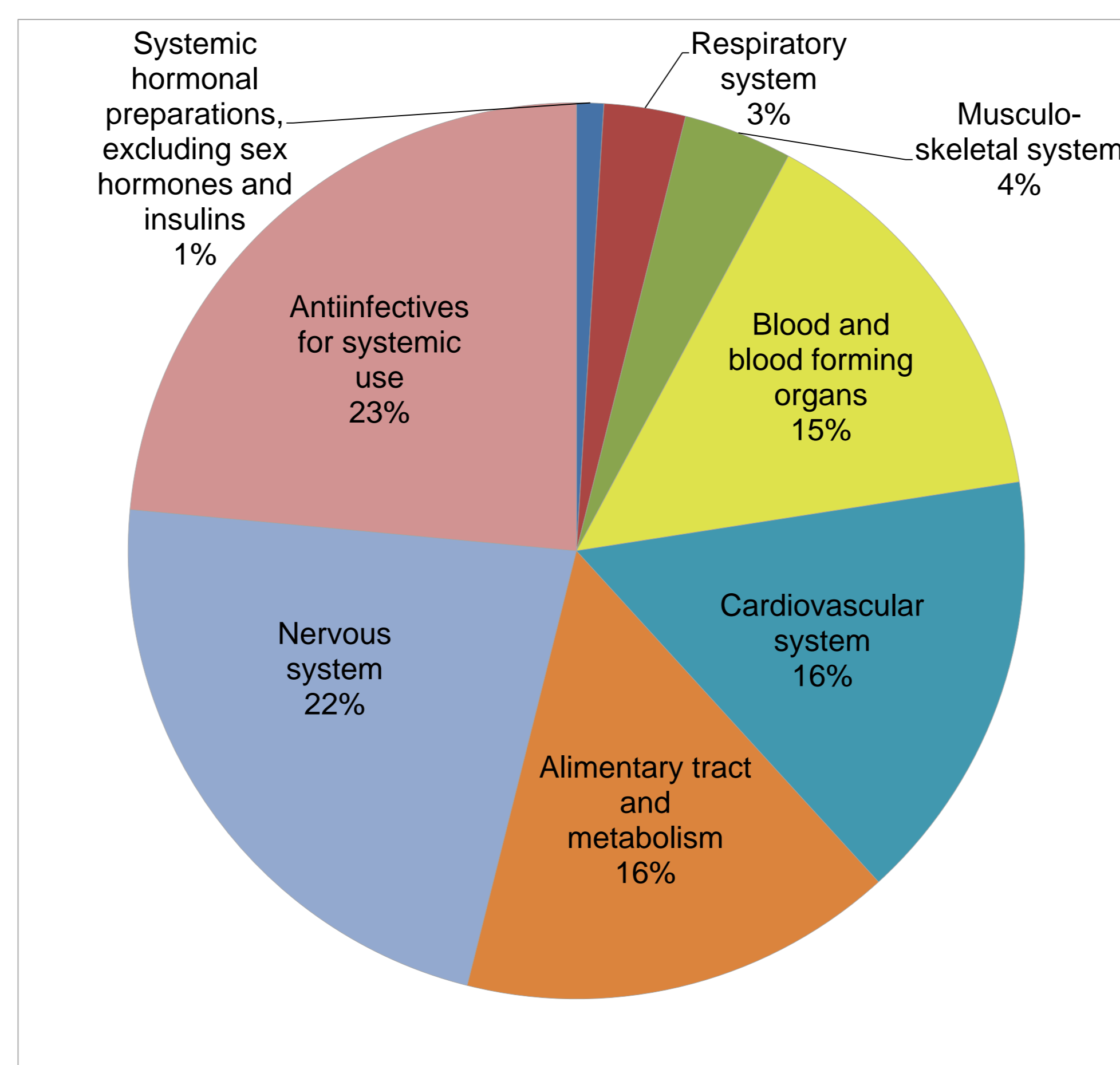


**Figure 1.** Frequency of medicines in UCI by ATC classification

**Table 1.** ATC classes and DCI most found in drug-drug interactions

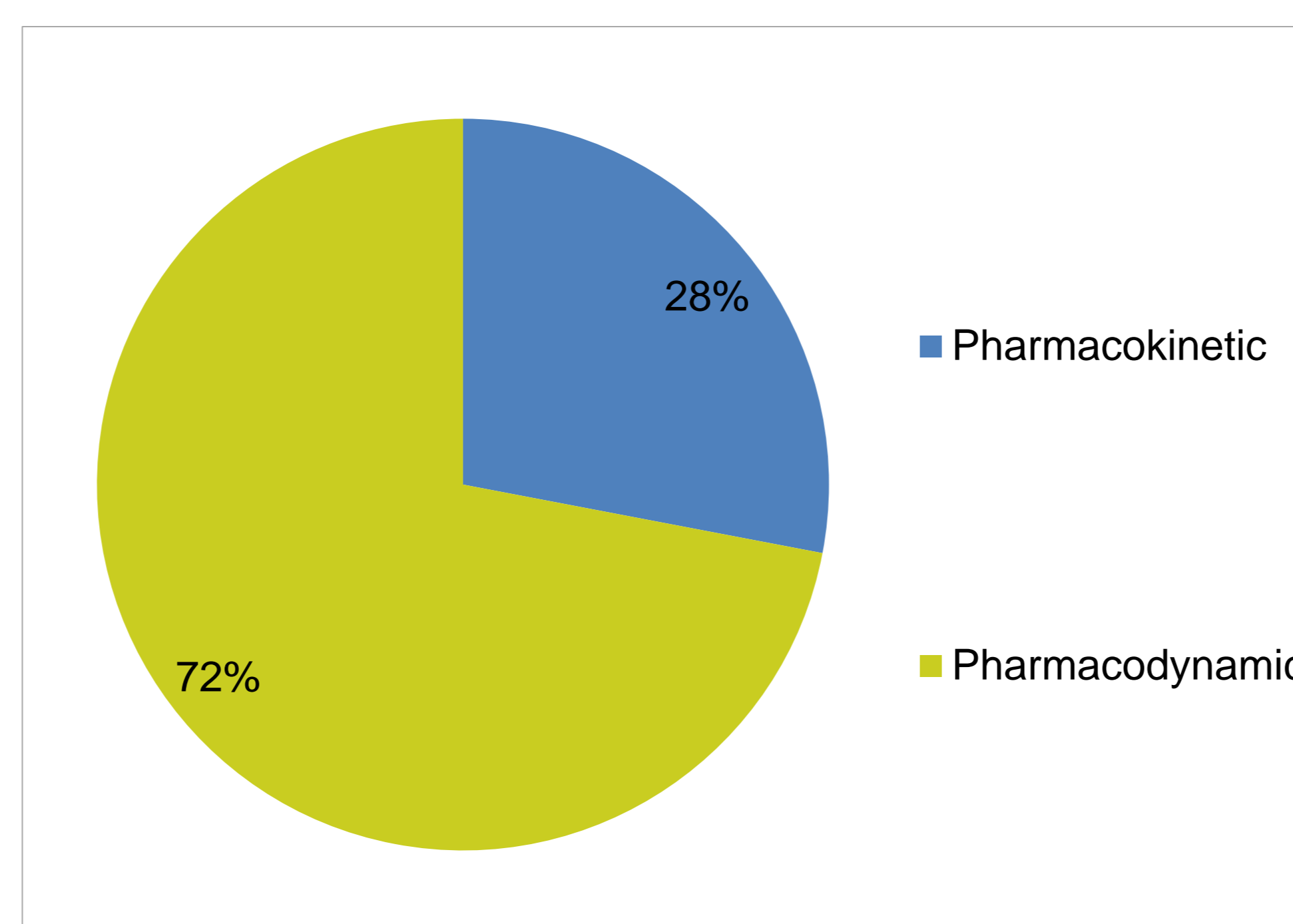| ATC classes | International Nonproprietary Name |
|---|---|
| Antiinfectives for systemic use | Colistin |
| | Amikacin |
| | Imipenem |
| | Vancomycin |
| | Metronidazole |
| | Ceftazidime |
| | Ceftriaxone |
| Nervous system | Fentanyl |
| | Midazolam |
| | Nefopam |
| | Morphine |
| | Paracetamol |
| | Carbamazepine |
| | Valproic acid |
| Alimentary tract and metabolism | Omeprazole |
| Cardiovascular system | Amiodarone |
| | Furosémide |
| Blood and blood forming organs | Enoxaparin |



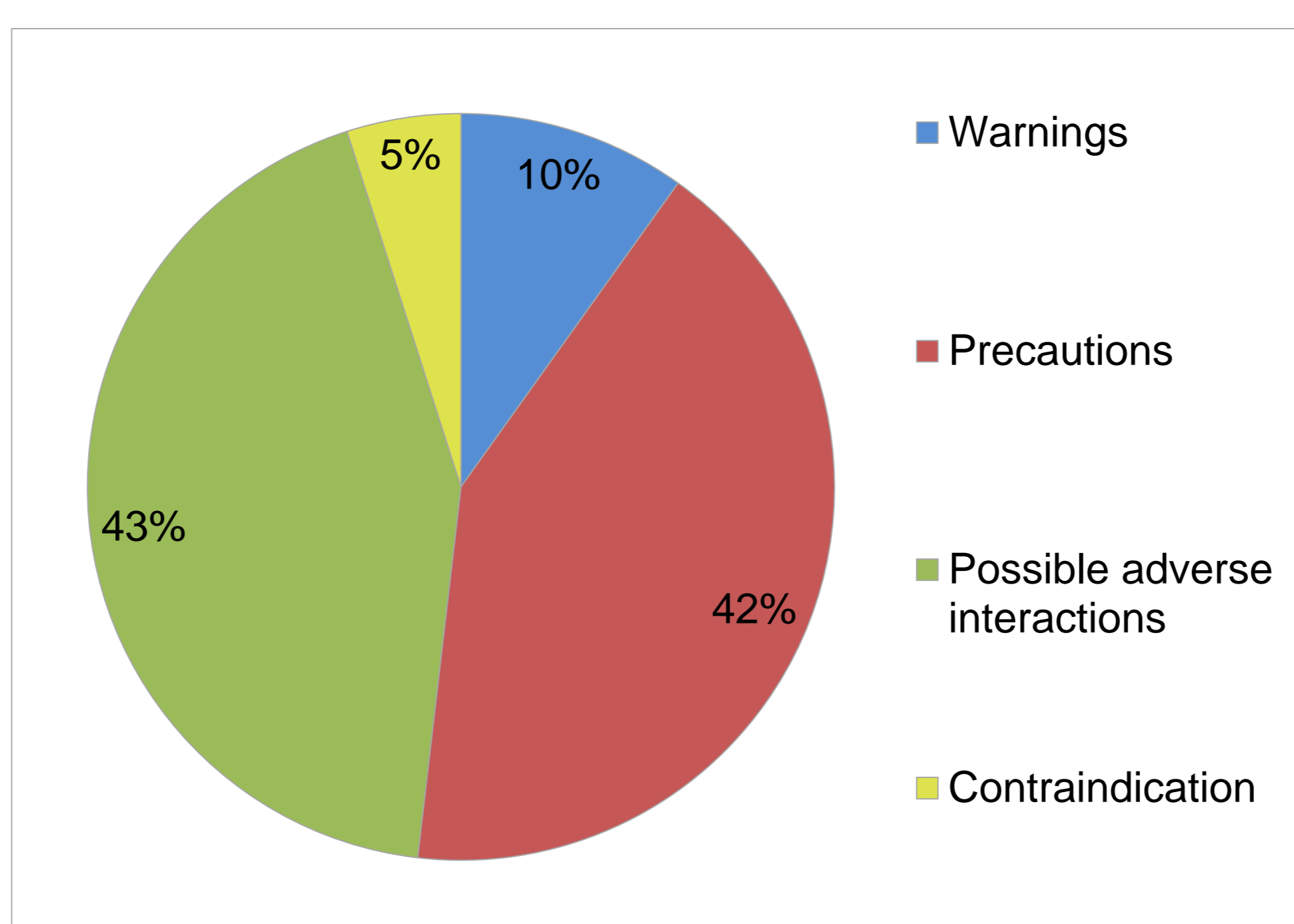**Figure 2.** Frequency of potential pharmacokinetic and pharmacodynamic interactions



**Figure 3.** Frequency of PDDIs by levels

**Table 2.** Examples of PDDIs Stratified by levels

| Drug-Drug Combination | Potential Adverse Drug Event (ADE) |
|---|---|
| **Contraindicated** | |
| Amiodarone and escitalopram | Meaningful QTc prolongation |
| Digoxin and gluconate calcium | Increase digoxin toxicity |
| Tigecycline and vitamin A | The risk of intracranial hypertension |
| Spironolacone and potassium chloride | Increased the risk of hyperkalaemia |
| **Possible adverse reaction** | |
| Imipenem and valproic acid | Decreased the serum concentration of valproic acid |
| Levomépromazine and haloperidol | Increased the depressive action |
| Aspirin and clopidogrel | Thrombocytopenia |
| **Precautions** | |
| Isoniazide and pyrazinamide | Addition of hepatotoxic effects: elevated transaminases |
| Amikacin and vancomycine | Increased ototoxicity |
| Digoxin and omeprazole | increased digoxinemia |
| **Warnings** | |
| Fentanyl and midazolam | Increased the depressive action |
| Morphine and nefopam | |
| Colistin and amikacin | Increased nephrotoxicity |
| Enoxaparin and potassium chloride | Increased the risk of hyperkalaemia |

## Discussion

Limitation of this study is its duration which is just for six months with little educational intervention aimed at improving retention of DDI knowledge of health care professionals.

Potential drug–drugs interactions (PDDIs) are observed to be one of the most frequently appearing challenge that may alter the pharmacokinetic and pharmacodynamics of the drugs thus alter the overall therapeutic response [3].

The knowledge of the pharmacological characteristics of the drug interactions assists in their clinical management.

The pDDIs present in prescription orders analyzed in this study that are considered clinically relevant have different types of mechanism of action. The most prevalent are the ones with additive pharmacological effects (n= 58) that potentially lead to an exacerbation of the therapeutic function or of the undesired adverse effects.

A study developed by Plaza et al. (2010) in Chile pointed out in its results that 23% of clinically significant adverse events observed in the studied (ICU) during the research were related to drug interactions [4].

It was also demonstrated the need for continuous education actions linked to the presence of interactions and the use of computerized systems for their detection, which can result in satisfactory diminishing of prescription orders with potential interactions [5].

Even though the whole clinical decision is individualized and requires a judicious evaluation on a case by case basis, it is evident the need for the critical evaluation of the clinical relevancy of the prevalent pDDIs in ICU outlining their risk profile and collecting [6].

## Conclusion

Our study concluded that the overall incidence of pDDIs was very high for hospitalized patients in intensive care. It shows the importance of the development of such data base in hospitals may help for the surveillance of pDDIs , and also the importance to implement pharmacovigilance system in order to avoid them .

## References

**[1]** Rekić, Dinko, Kellie S. Reynolds, Ping Zhao, Lei Zhang, Kenta Yoshida, Madhav Sachar, Micheline Piquette Miller, Shiew-Mei Huang, et Issam Zineh. « Clinical Drug–Drug Interaction Evaluations to Inform Drug Use and Enable Drug Access ». *Journal of Pharmaceutical Sciences* 106, nº 9 (septembre 2017): 2214-18. 7
**[2]** Chisholm-Burns, M., Lee, J., Spivey, C., Slack, M., Herrier, R., Hall-Lipsy, E., et al, 2010. US pharmacists' effect as team members on Patient care systematic review and meta-analyses. Medical Care 48,923–933
**[3]** Baxter, K., Preston, C.L.. « Stockley's Drug Interactions. Pharmaceutical Press London», 2010.
**[3]**Gagne, J., Maio, V., Rabinowitz, C., 2008. Prevalence and predictors of potential drug–drug interactions in Regione Emilia-Romagna,Italy. J. Clin. Pharm. Ther. 33 (2), 141–151.
**[4]** Plaza, J., Alamo, M., Torres, P., Fuentes, A., Lopez, F., 2010. Drug interactions and adverse events induced by drugs used in an intensive care unit. Revista Med. De Chile 138, 452–460.
**[5]** Paterno, M.D., Maviglia, S.M., Gorman, P.N., Seger, D.L., Yoshida,E., Seger, A.C., et al, 2009. Tiering drug–drug interaction alerts by severity increases compliance rates. J. Am. Med. Inform. Assoc. 16,40–46.
**[6]** Smithburger, P.L., Kane-Gill, S.L., Benedict, N.J., Falcione, B.A.,Seybert, A.L., 2010a. Grading the severity of drug–drug interactions in the intensive care unit: a comparison between clinician assessment and proprietary database severity rankings. Ann.Pharmacotherap. 44, 1718–1724.