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RESEARCH ARTICLE

# Evaluation of potential drug-drug interaction in indoor patients of pediatric department of tertiary care hospital

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## ABSTRACT

**Background:** Pediatric population is having high chances of drug-drug interactions (DDIs) because off-label use of drugs, weight-based dose adjustments, and pharmacokinetically, they are different from adult population. Hospitalized pediatric population is more vulnerable to face adverse consequences reserve physiology, medication dosing errors and polypharmacy. Thus, chances are more of potential DDIs (pDDIs) in pediatric patients. There has been focus mainly on adult population, less studies regarding DDIs or pDDIs in pediatric population have been documented. **Aims and Objectives:** The primary objective of the study is to identify pDDIs in pediatric patients. Determining prevalence, types of pDDIs, and factors associated with pDDIs are secondary objective. **Materials and Methods:** A prospective, observational study was conducted in pediatric ward of tertiary care hospital during April 2018–August 2018. The principal investigator collected the data from hospital case papers and recorded in pre-tested case record form. Drugs prescribed in each patient were assessed using Lexicomp software (version 4.4.0), which is internet-based free software used to predict pDDIs. DDIs were categorized in minor, moderate, and major according to their severity assessed by software. If necessary, the investigator also interviewed patients or caretaker to gather information. **Results:** A total of 300 patients were included during the study period. Among them, 157 (52.3%) were boys and 143 (48%) were girls. A total number of pDDIs were 235 (78%), of which 227 (97%) were minor and 3 (1.2%) were major DDIs. The most common DDI was between ondansetron and paracetamol (224). A potential major DDIs were observed between ondansetron and dextromethorphan (2) and ondansetron and phenytoin (1). **Conclusion:** The most common DDIs occurred with ondansetron and paracetamol, which were minor in severity. There were no clinical DDIs. Not all patients with major or moderate DDIs were suffered clinically but better to take due precautions to avoid adverse consequences.

**KEY WORDS:** Potential Drug Interactions; Pediatrics; Factors; Prevalence

## INTRODUCTION

As the usage of drug is having two sides, one beneficial and one undesirable, it requires updated vision for the best use out of it. Drug use has been a long way practice and that has faced many alarming disasters but that have helped to improve in awareness and methods of drug safety monitoring. In case of drugs' undesirable effects, adverse drug events (ADEs), adverse drug reactions (ADRs), and medication errors can be noted which require monitoring of treatment process. Interactions with concomitantly or simultaneously administered drugs or with food can also lead to adverse reactions to the patient. Based on the current data, there have been increased incidences of polypharmacy.[1,2] Lacking in updated evidence-based medicines is mainly associated with multimorbidity and

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associated polypharmacy that can increase chances of drug interactions.

In clinical practice, two or more drugs are combined in such a way that the potency or efficiency of one drug is significantly modified by the presence of another.[3] When two drugs administered concomitantly and could have theoretical drug interactions, can be known as potential drug-drug interactions (pDDIs).[4] pDDIs are predictable and preventable cause of drug-related adverse events.[5] Out of all ADEs, DDIs account 19%[6] while 3–26% DDIs ended in hospital admissions. The Boston Collaborative Drug Surveillance Program found 3600 ADRs, of which 6.5% due to drug interactions in 83,200 drug exposures in almost 10,000 patients.[7] These DDIs can lead to increase in economic burden on health-care system with risk to health of patient. Increase in hospital stay also increase bed occupancy in hospitals and can increase morbidity and mortality among patient population. This suggests that DDIs endanger the patient safety aspect.[8] The Institute of Medicine has focused medication safety in children with recognition and prevention of ADEs, for effective health care.[9] Pediatric population is having high chances of DDIs because off-label use of drugs, weight-based dose adjustments, and pharmacokinetically, they are different from adult population. Hospitalized pediatric population is more vulnerable to face adverse consequences reserve physiology, medication dosing errors and polypharmacy. Thus, chances are more of pDDIs in pediatric patients.[10] There has been focus mainly on adult population, less studies regarding DDIs or pDDIs in pediatric population have been documented.[8]

Hence, the present study was carried out with the objectives of to determine the demography about DDIs, to know the severity of DDIs, and to focus on factors associated with DDIs.

## MATERIALS AND METHODS

An observational, prospective, cross-sectional study was conducted in a pediatric department at a tertiary care hospital, from April 2018 to August 2018. The study was approved by the Institutional Ethics Committee (approval number - 20/13). Patients whose guardian gave consent, who were given systemic therapy, all patients admitted to pediatric ward and patients of both genders were included in the study while patients whose guardian did not give consent, who were given topical treatment were excluded from the study. In this study, chart review method was used. The investigator checked the case paper of admitted patient on the 1st day of admission. If necessary, investigator also interviewed patients or caretaker to gather information. The collected data were entered in pre-validated case record form. Demographic data were analyzed using Microsoft Excel 2007. DDIs were assessed by Lexicomp software (version – 4.4.0). Validation of software was previously done in different studies.[11] According to software, DDIs were classified as "minor" those do not require monitoring of patient, "moderate" in which monitoring is required, and "major" in which modification in therapy should be carried out.

## RESULTS

A total number of patients enrolled during the study period were 300, among them, 157 (52.3%) were boys and 143 (48%) were girls. Mean score of age was 3.5 months. Patients <1 year of age (109) were more in number followed by age group 1 year–5 years (106). In 224 (75%) case papers, final diagnosis was mentioned while 22 (7.3%) had differential diagnosis in the form of symptoms. The most common cause for indoor admission was gastrointestinal (GI) and liver infections such as acute gastroenteritis, dysentery, viral hepatitis, and enteric fever in 126 (42%) patients followed by respiratory tract infection such as post-measles pneumonia, bronchiolitis, and reactive airway disease who were in 29 (10%) patients [Table 1]. In 300 patients, a total of 1043 drugs were prescribed including IV fluids. Majority of patients 115 (38.3%) were prescribed two drugs while 87 (29%) were having three drugs [Table 2]. Among prescribed drugs, GI drugs were commonly prescribed (476, 46%) followed by analgesics (249, 24%) and antimicrobials 122 (12%) [Figure 1].

A total number of pDDIs were 235 (78%) in 300 patients. Of which, 227 (97%) were minor and 3 (1.2%) were major DDIs

**Table 1:** Demographic details

| Age group | *n* (300) |
|---|---|
| <1 | 109 |
| 1–5 | 106 |
| 6–10 | 78 |
| >10 | 7 |
| Gender | |
| Male | 157 |
| Female | 143 |
| Diagnosis | |
| Final diagnosis | 224 |
| Symptoms | 33 |
| No diagnosis | 43 |

**Table 2:** Number of prescribed drugs

| Number of drugs per prescription | Number of patients |
|---|---|
| 0 | 17 |
| 1 | 19 |
| 2 | 115 |
| 3 | 87 |
| 4 | 37 |
| 5 | 15 |
| 6 | 2 |
| 7 | 8 |

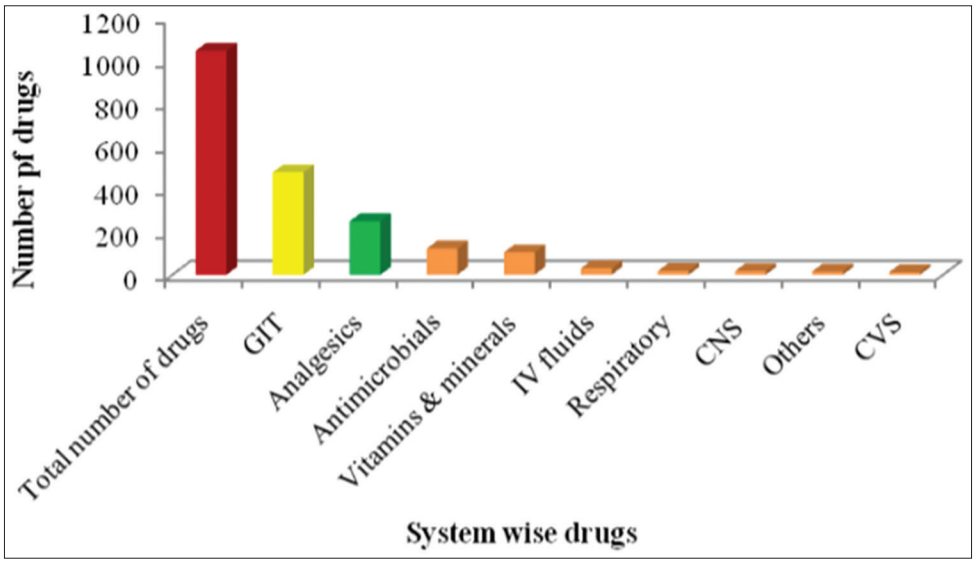


**Figure 1:** Types and numbers of drugs prescribed

[Figure 2]. Age group of 1–5 years had highest number of DDIs 86 (37%) while <1 year of age had 83 (35.3%) DDIs [Table 3]. In potential minor DDIs, GI was most commonly involved (224). In GI drugs, ondansetron was the culprit drug which had maximum chances of drug interaction with paracetamol. Ondansetron was actually used in 41 cases; others had instruction to use when required. A total of three major DDIs were detected. Mostly, phenytoin was involved in potential major DDIs. However, fortunately, none of them were clinically observed. Moderate DDIs involve digoxin, propranolol, levosalbutamol, etc. [Table 4].

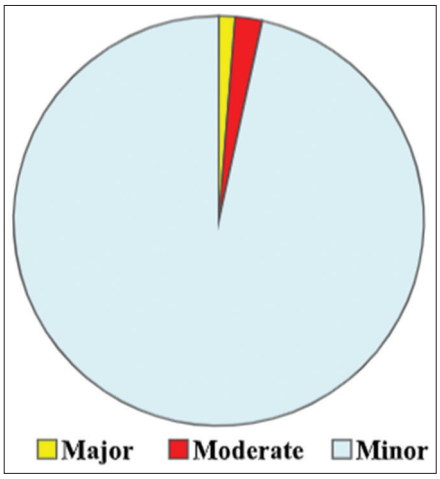


**Figure 2:** Types of drug-drug interactions

**Table 3:** Age wise drug-drug interactions distribution

| Age group (years) | Minor (*n*) | Moderate (*n*) | Major (*n*) | Total (*n*) |
|---|---|---|---|---|
| <1 | 81 | 2 | 0 | 83 |
| 1–5 | 86 | 0 | 0 | 86 |
| 6–10 | 53 | 3 | 3 | 59 |
| >10 | 7 | 0 | 0 | 07 |

**Table 4:** Major and moderate drug-drug interactions

| Major | Moderate |
|---|---|
| Ondansetron+dextromethorphan | Amikacin+ceftriaxone |
| Phenytoin+ondansetron | Phenytoin+ranitidine |
| | Phenytoin+paracetamol |
| | Adrenaline+levosalbutamol |
| | Digoxin+propranolol |

## DISCUSSION

In health-care system, purpose is not only the patient's successful treatment but also to provide quality of treatment, where patient safety plays a key role. According to To err is human, safety is a freedom from accidental injury.[12] In the current era, where health care workers are aware of ADRs and ADEs, they still should know about DDIs. A study by Glassman *et al*. reported that clinicians can correctly identify 44% (range 11–64%) of all DDI pairs and 54% of disease-contraindication pairs. That is the reason why we need clinicians' expertness to detect DDIs and thus will have a chance of reduction in the ADEs and we can take care of patients' safety. Furthermore, there will be prevention of medical and legal problems.[13] DDIs are usually a part of ADEs. Patient may present with an ADR and if it is scrutinized, it could have been due to combination of two or more drugs.[14,15]

We used data to be collected on the day of admission because studies reported 21.8% of DDIs in infants on the 1st day.[8] We found 35.3% pDDIs in patients <1 year of age. Chances of more number of DDIs in this age are due to underdeveloped anatomical and physiological systems. In our study, we found out DDIs at higher rate with at least one patient showed one interaction that supported by the result with the study by Morales-Ríos *et al.* and Feinstein *et al*., in which one half of the study population had DDIs.[8,16] A study by Mousavi and

Ghanbari also observed higher rate of DDIs with geriatric population.[17] Our study had high number of minor DDIs, which were not harmful to patient. Among them, GI drugs were mainly involved in pDDIs. High number of admitted patients with GI and liver infection could be one of the reasons for that. Particularly, ondansetron showed highest presence. In case of minor pDDs, out of 224, only 41 (18.3%) patients were administered ondansetron, while others had instruction to take when required. In our study, its mainly combined effect has been observed with paracetamol, the most commonly prescribed drug but same as ondansetron less administered in this study so that could have reduced the chances of DDIs. Reliability of this interaction was fair by Lexicomp software. Ondansetron was also present in major pDDIs with dextromethorphan and phenytoin. This shows that the use of ondansetron should be cautious. It should be used only when required plus should be watched out for the other drugs that can interact with it. In case of major or moderate pDDIs, patients were administered more than two drugs. Along with that, patients' clinical conditions were also compromised. This suggests that polypharmacy and complex clinical condition of patient may increase the chances of DDIs.[15,18]

Positive finding of this study is less use of antimicrobials, so interactions could have occurred due to them are very few. These are pDDIs, we could not infer the actual DDIs that can lead to ADEs. Studies have been reported that not every pDDI can lead to ADE.[8,19,20] Some drug combinations have beneficial effects require for better clinical outcome where monitoring the drug therapy or follow-up is necessary to avoid negative outcomes.[21] Main purpose of evaluating pDDIs is to have idea regarding proper management of adverse outcome due to DDIs.[22] However, disadvantage of such programs is that sometimes clinicians' or investigators may not double-check the interaction and not feel clinically relevant. This phenomenon is known as "alert fatigue." Their consequences can lead to major error in drug therapy.[23-25] Sometimes one can feel more alert to avoid all DDIs, but it can lower therapeutic benefit. Further research can be directed to corelate clinically present DDIs with mortality and morbidity.[14]

We could not assess clinical relevance of pDDIs that are the major limitation of our study. As we assessed only case papers, it is possible that prescribers might have upheld the treatment or withdrew the drug after adverse outcome. Prescriber's suggestions for DDIs can further help in evaluating high relevant DDIs.

## CONCLUSION

High rate of pDDIs was observed with minor in severity. Fortunately, there was the absence clinical DDIs. Cautious use of ondansetron should be done to avoid adverse effects due to the drug. However, this study has measured the pDDIs in pediatric population which calls for further detailed research focusing finding and clinical relevance of DDIs.

## REFERENCES


1. Tripathi KD, editor. Drug interactions. In: Essentials of Medical Pharmacology. 7th ed. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2013. p. 929.
2. Getachew H, Assen M, Dula F, Bhagavathula A. Potential drug drug interactions in pediatric wards of Gondar university hospital, Ethiopia: A cross sectional study. Asian Pac J Trop Biomed 2016;6:534-8.
3. Goldberg RM, Mabee J, Chan L, Wong S. Drug-drug and drug-disease interactions in the ED: Analysis of a high-risk population. Am J Emerg Med 1996;14:447-50.
4. Uijtendaal EV, van Harssel LL, Hugenholtz GW, Kuck EM, Zwart-van Rijkom JE, Cremer OL, *et al.* Analysis of potential drug-drug interactions in medical intensive care unit patients. Pharmacotherapy 2014;34:213-9.
5. Bertsche T, Pfaff J, Schiller P, Kaltschmidt J, Pruszydlo MG, Stremmel W, *et al.* Prevention of adverse drug reactions in intensive care patients by personal intervention based on an electronic clinical decision support system. Intensive Care Med 2010;36:665-72.
6. Kannan B, Nagella AB, Prabhu AS, Sasidharan GM, Ramesh AS, Madhugiri V, *et al.* Incidence of potential drug-drug interactions in a limited and stereotyped prescription setting comparison of two free online pharmacopoeias. Cureus 2016;8:e886.
7. Patel PS, Rana DA, Suthar JV, Malhotra SD, Patel VJ. A study of potential adverse drug-drug interactions among prescribed drugs in medicine outpatient department of a tertiary care teaching hospital. J Basic Clin Pharm 2014;5:44-8.
8. Feinstein J, Dingwei D, Zhong W, Freedman J, Feudtner C. Potential drug2drug interactions in infant, child, and adolescent patients in children's hospitals. Pediatrics 2015;135:e100-8.
9. Aspden P. US Committee on Identifying and Preventing Medication Errors. Washington, DC: National Academies Press; 2007.
10. Shah SS, Hall M, Goodman DM, Feuer P, Sharma V, Fargason C Jr., *et al.* Off-label drug use in hospitalized children. Arch Pediatr Adolesc Med 2007;161:282-90.
11. Kheshti R, Aalipour M, Namazi S. A comparison of five common drug-drug interaction software programs regarding accuracy and comprehensiveness. J Res Pharm Pract 2016;5:257-63.
12. Garrouste-Orgeas M, Philippart F, Bruel C, Max A, Lau N, Misset B, *et al.* Overview of medical errors and adverse events. Ann Intensive Care 2012;2:2.
13. Glassman PA, Simon B, Belperio P, Lanto A. Improving recognition of drug interactions: Benefits and barriers to using automated drug alerts. Med Care 2002;40:1161-71.
14. Mahmood M, Malone DC, Skrepnek GH, Abarca J, Armstrong EP, Murphy JE, *et al.* Potential drug-drug interactions within veterans affairs medical centers. Am J Health Syst Pharm 2007;64:1500-5.
15. Dai D, Feinstein JA, Morrison W, Zuppa AF, Feudtner C. Epidemiology of polypharmacy and potential drug-drug interactions among pediatric patients in ICUs of U.S. Children's hospitals. Pediatr Crit Care Med 2016;17:e218-28.

16. Morales-Ríos O, Jasso-Gutiérrez L, Reyes-López A, Garduño-Espinosa J, Muñoz-Hernández O. Potential drug-drug interactions and their risk factors in pediatric patients admitted to the emergency department of a tertiary care hospital in Mexico. PLoS One 2018;13:e0190882.
17. Mousavi S, Ghanbari G. Potential drug-drug interactions among hospitalized patients in a developing country. Caspian J Intern Med 2017;8:282-8.
18. Martinbiancho J, Zuckermann J, Dos Santos L, Silva MM. Profile of drug interactions in hospitalized children. Pharm Pract (Granada) 2007;5:157-61.
19. Dechanont S, Maphanta S, Butthum B, Kongkaew C. Hospital admissions/visits associated with drug-drug interactions: A systematic review and meta-analysis. Pharmacoepidemiol Drug Saf 2014;23:489-97.
20. Rashed AN, Wong IC, Cranswick N, Tomlin S, Rascher W, Neubert A, *et al.* Risk factors associated with adverse drug reactions in hospitalised children: International multicentre study. Eur J Clin Pharmacol 2012;68:801-10.
21. May JR, DiPiro JT, Sisley JF. Drug interactions in surgical patients. Am J Surg 1987;153:327-35.
22. Becker ML, Kallewaard M, Caspers PW, Schalekamp T, Stricker BH. Potential determinants of drug-drug interaction associated dispensing in community pharmacies. Drug Saf 2005;28:371-8.
23. Peterson JF, Bates DW. Preventable medication errors: Identifying and eliminating serious drug interactions. J Am Pharm Assoc (Wash) 2001;41:159-60.
24. Bates DW, Leape LL, Cullen DJ, Laird N, Petersen LA, Teich JM, *et al.* Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. JAMA 1998;280:1311-6.
25. Chen YF, Avery AJ, Neil KE, Johnson C, Dewey ME, Stockley IH, *et al.* Incidence and possible causes of prescribing potentially hazardous/contraindicated drug combinations in general practice. Drug Saf 2005;28:67-80.

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