# Assessment of drug-related problems in pediatric inpatients by clinical pharmacist-led medication review: An observational study

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**ABSTRACT**: It is well-known that problems related to pharmacotherapy affect pediatric patients' therapy outcomes. Evaluating pharmacotherapy by a clinical pharmacist in pediatric clinics could ameliorate drug-related problems (DRPs). This study aimed to identify and compare the prevalence and types of DRPs in pediatric patients in two study phases: the prospective phase while providing clinical pharmacist-led medication review service and the retrospective phase among subjects obtained by age-sex-diagnose–matching according to the prospective phase. This observational study consisted of two phases (the prospective part between June 2019 and February 2020 and the retrospective part between December 2018 and February 2019) and was conducted in a pediatric unit of a university hospital. Turkish version of Pharmaceutical Care Network Europe Foundation Classification V9.1 is used to identify DRPs. Lexicomp® and Micromedex® were the resources used to assess the potential drug-drug interactions. Medscape® and UpToDate® recommendations and evidence-based guidelines were applied in assessing compliance with approved pharmacotherapy of patients. Prevalence and types of DRPs and clinical pharmacist interventions were assessed. Among 174 patients, at least one DRP was seen in 78,16% of the patients, and 527 DRPs were identified. Some of the problems were related to drug-drug interaction (64,90%), therapeutic monitoring (11,39%), and dosing (11,01%). Anti-infectives, bronchodilators, and inhaled corticosteroids were the most frequently used drugs. There were significant differences in duration of hospitalization (*p*=0,025), number of drugs used (*p*=0,003), and total DRPs (*p*=0,019) between the study and control groups. The findings demonstrate the potential to detect DRPs through pharmacist involvement in direct patient care.

**KEYWORDS**: Clinical pharmacy; pediatrics; drug-related problems; pharmaceutical care.

## 1. INTRODUCTION

A worldwide change has been occurring about the professional role of pharmacists. This profession's transformation includes the actions related to co-responsibility in achieving therapeutic goals, cost-effectiveness in pharmacotherapy, and reducing the number of drug-induced re-hospitalization [1, 2]. With developmental differences that change from day to day, pediatric patients constitute a very different population from adults [3]. Pediatric Pharmacy ensures safe and effective drug use and optimal medication therapy outcomes in children up to 18 years of age [4].

Detecting drug-related problems (DRPs) is crucial in pharmaceutical care since they may interfere with optimal therapy outcomes, resulting in increased morbidity and mortality leading to more significant healthcare expenditures. The data on the impact of clinical pharmacist interventions on preventing DRPs in the pediatric unit is limited. There is evidence that clinical pharmacist interventions reduce adverse drug events and medication errors in pediatrics [5-10] and other healthcare settings [11]. Mentioning that pediatric patients are exposed to medication errors three times more than adults in their article, Özdemir *et al.* [12] have shown that the participation of clinical pharmacists in the multidisciplinary team is beneficial in the detection, prevention, and reduction of medication errors.

Complex pharmacotherapy regimens could be potentially harmful to patients if not managed correctly [13]. One of the common reasons for preparing dilutions and opening capsules in pediatric pharmacotherapy is the limited number of adapted oral pediatric drug formulations, creating a risk of weight-based dosing miscalculation [14, 15]. The challenges of carrying out a scientific study with children include; extensive developmental differences, being a more vulnerable population, and consent complexities leading to off-label use of drugs and extrapolation of safety and efficacy data from adult literature [16].

Drug-related problems are common and costly, resulting in significant harm or injury [17]. Some differences make infants and children more susceptible to medication errors and related injuries; one of these differences is limited buffering capacity, which can be specified as: A small dosing error in an adult may have minimal consequences or even go undetected; however, the same dosing error could be fatal in a neonate [15]. Pharmacists participate increasingly in clinical processes and perform tasks in patient care to prevent problems caused by drug therapy [18].

### 1.1. Aim of the study

This study aims to identify and compare the prevalence and types of DRPs in pediatric patients in two study phases: the prospective phase while providing clinical pharmacist-led medication review service and the retrospective phase among subjects obtained by age-sex-diagnose–matching according to the prospective phase.

### 1.2. Ethics approval

Ethical approval of the study was obtained from the Istanbul Haydarpasa Numune Training and Research Hospital, Clinical Research Ethics Committee on 25.02.2019 with the decision number HNEAH-KAEK 2019/25-748. All procedures performed in this study involving human participants followed the Declaration of Helsinki (as revised in 2013). The study was conducted with pediatric patients, and their legal guardians signed a freely given, informed consent form. All legal guardians received oral and written information before giving their written consent.

### 2. RESULTS

Relatives of 90 patients were informed to participate in the study, and three refused to participate. In the prospective part, data of the 87 patients admitted to the clinic mentioned above between June 2019 and February 2020 were evaluated. The retrospective control group of the study consisted of 87 patients who were match-selected in line with the prospective part inside the pool of 728 patients admitted to the same clinic between December 2018 and February 2019 and discharged from the same clinic.

Among 174 patients, 59.77% were male (study group n=53, control group n=51) and 70 were female (study group n=34, control group n=36). The median age of all patients was 19 (Interquartile range [IQR] 4-86) months. The other medians were calculated as height 76,50 (IQR 60-125) cm, weight 10 (IQR 6,40-21,00) kg, body mass index 16,67 (IQR 14,24-19,36) kg/m², number of drugs used n=5 (IQR 3,00-6,25), and duration of hospitalization 5 (IQR 4-7) days. 68,4% of all patients were 60 months or younger. Co-morbidities have been identified in 24,1% of patients. Existing drug allergy information has been obtained through patient medical history in 2,9% of patients. Among the total of 174 patients, 527 DRPs (an average of 3,03 DRP per patient) have been detected. Of all patients, 78,16% had at least one DRP, and 58,62% of all patients had at least one drug-drug interaction (DDI). There was no significant difference between the study and control groups in age, sex, height, weight, BMI, DDIs, and the use of the most frequent drug classes ($p$>0,05). However, there were significant differences in duration of hospitalization ($p$=0,025), number of drugs used ($p$=0,003), and total DRPs ($p$=0,019) between groups. Two of the most frequently encountered International Statistical Classification of Diseases and Related Health Problems groups and their percentages within the groups are as follows: diseases of the respiratory system, control group 63,8% and study group 62,5%; diseases of the genitourinary system, control group 9,5% and study group 8,9%. The characteristics of the pediatric patients are shown in Table 1. Within the 39 pharmacological categories encountered during the study, the last three lines in Table 1 show the most frequently used three pharmacological categories and the total number of drugs used in these categories.

In the prospective part, 96,55% patients had polypharmacy, which was 88,51% patients for the control group. Additionally, 58,62% patients for the study group and 43,68% patients for the control group had at least five different drugs in their treatment.

In this study, the most common drug-related problem codes were "treatment effectiveness" and "treatment safety," which accounted for over 94% (496 of 527 DRPs). The most prominent problem was

"Adverse drug event (possibly) occurring," which accounted for approximately 79% of the problems (414 of 527 DRPs).

**Table 1.** Characteristics of pediatric patients (n=174)

| Variables | Study Group (n=87) | Control Group (n=87) | *p*-value |
|---|---|---|---|
| Age (months) median<br>IQR 25-75 | 19<br>3-92 | 19<br>5-79 | NS |
| 60 months or younger n (% within the group) | 59 (67.8%) | 60 (69.0%) | NS |
| Sex<br>  Female (% within the group)<br>  Male (% within the group) | <br>39.1<br>60.9 | <br>41.4<br>58.6 | NS |
| Weight (kg) median<br>IQR 25-75<br>Missing data | 10<br>6.45-28.75<br>2 | 10<br>6.15-18<br>49 | NS |
| Height (cm) median<br>IQR 25-75<br>Missing data | 76<br>60-126.5<br>2 | 83<br>60-110<br>56 | NS |
| Body Mass Index (kg/m²) median<br>IQR 25-75<br>Missing data | 16.89<br>14.49-19.65<br>2 | 16.33<br>13.72-18.93<br>56 | NS |
| Duration of hospitalization (day) median<br>IQR 25-75 | 6<br>4-8 | 5<br>3-7 | 0,025 |
| Number of drugs used median<br>IQR 25-75 | 5<br>3-7 | 4<br>3-6 | 0,003 |
| Number of drug-related problems median<br>IQR 25-75 | 3<br>1-5 | 2<br>0-4 | 0,019 |
| Had at least one drug-drug interaction n (% within the group) | 54 (62.1%) | 48 (55.2%) | NS |
| Anti-infective for systemic use n (%) | 133 (88.5%) | 115 (79.3%) | NS |
| Beta-2 agonist n (%) | 52 (58.6%) | 50 (57.5%) | NS |
| Corticosteroid, inhaler n (%) | 51 (57.5%) | 48 (54.0%) | NS |

NS: Nonsignificant

Regarding the causes of DRPs, the most common primary cause domain was "drug selection" with over 77%, and "Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements" was the most common cause, accounting for approximately 65%.

DDIs have been separated into two groups according to the outcome: A possible adverse event (90,06%) and possible ineffectiveness (9,94%). A total of 208 and 121 DDIs were detected in the study and control groups, respectively. In the prospective study group, the most common interactions were methylprednisolone-salbutamol (Lexicomp, B) with 16,35% and budesonide-clarithromycin (Micromedex, Moderate) with 15,38%. In the retrospective control group, the most common interactions were methylprednisolone-salbutamol (Lexicomp, B) with 24,79% and budesonide-clarithromycin (Micromedex, Moderate) with 16,53%. Four interactions in the Lexicomp X category were found in the study group which were; acetazolamide-topiramate, pheniramine-ipratropium, ipratropium-oxybutynin, and ipratropium-cetirizine. No interactions have been found within the Lexicomp X category in the control group and no interactions have been found related to the Micromedex Contraindicated category in both of the groups.

Wrong dosage (dose too low and dose too high combined) accounted for 11,01% of all DRPs. Figure 1 shows the comparison of DRP Problem Codes, and Figure 2 shows the comparison of DRP Cause Codes. The distribution of the DRPs is shown in Table 2.
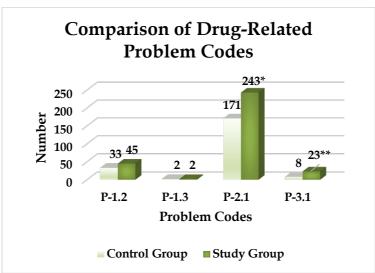
## Comparison of Drug-Related Problem Codes



**Figure 1.** Comparison of the number of DRPs according to PCNE Classification between control and study groups.
P-1.2: Effect of drug treatment not optimal; P-1.3: Untreated symptoms or indication; P-2.1: Adverse drug event (possibly) occurring; P-3.1: Unnecessary drug treatment; *$p<0,05$; **$p<0,01$.
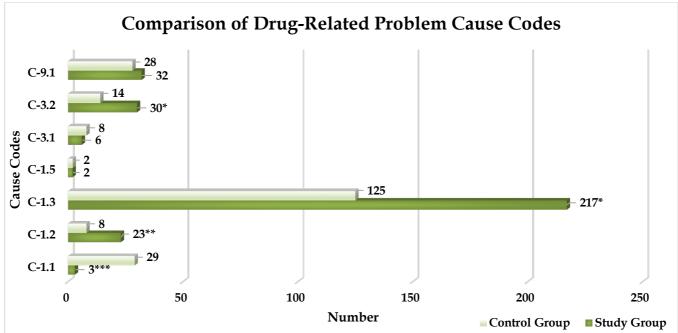
## Comparison of Drug-Related Problem Cause Codes



**Figure 2.** Comparison of the number of DRP causes according to PCNE Classification between control and study groups.
C-1.1: Inappropriate drug according to guidelines/formulary; C-1.2: No indication for drug; C-1.3: Inappropriate combination of drugs, or drugs and herbal medications, or drugs and dietary supplements; C-1.5: No or incomplete drug treatment in spite of existing indication; C-3.1: Drug dose too low; C-3.2: Drug dose of a single active ingredient too high; C-9.1: No or inappropriate outcome monitoring (incl. Therapeutic Drug Monitoring); *$p<0,05$; **$p<0,01$; ***$p<0,001$.

**Table 2.** Causes and numbers of drug-related problems

| Causes for DRPs | n |
|---|---|
| Inappropriate combination of a drug (possible adverse event) | 308 |
| No or inappropriate outcome monitoring (incl. Therapeutic Drug Monitoring) | 60 |
| Drug dose of a single active ingredient too high | 44 |
| Inappropriate combination of a drug (possible ineffectiveness) | 34 |
| Inappropriate drug according to guidelines/formulary | 32 |
| No indication for a drug | 31 |
| Drug dose too low | 14 |
| No or incomplete drug treatment in spite of existing indication | 4 |
| Total DRPs | 527 |

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Correlations have been found between the number of DRPs and duration of hospitalization (moderate, r=0,377; $p<0,001$), number of drugs used (strong, r=0,782; $p<0,001$), number of co-morbidities (weak, r=0,257; $p=0,001$). There were no significant correlations between the number of DRPs and age ($p>0.05$).

Table 3 shows the increased risk of having DRPs on related factors.

**Table 3.** Odds ratios of the factors related to the existence of DRPs

| | Having at least one DRP Odds Ratio | 95% Confidence Interval | | *p*-value |
|---|---|---|---|---|
| | | Lower | Upper | |
| **Antiinfective for Systemic Use** | 7,515 | 3,132 | 18,030 | <0,001 |
| **Beta-2 Agonist** | 5,662 | 2,530 | 12,672 | <0,001 |
| **Corticosteroid, Inhaler** | 7,101 | 3,016 | 16,718 | <0,001 |
| **Polypharmacy[a]** | 31,959 | 7,376 | 138,482 | <0,001 |
| **Being 60 months or younger** | 1,809 | 0,860 | 3,805 | NS |
| **Having at least one co-morbidities** | 2,467 | 0,895 | 6,797 | NS |

[a]Having at least two drugs in the treatment
NS: Nonsignificant

## 3. DISCUSSION

The literature shows that clinical pharmacy services are considered beneficial by physicians. In many studies, pharmacists' evaluations have contributed to the treatment; however, there are few studies in the pediatric clinic, especially in Turkey [19]. Our study is the first report on DRPs in a general pediatrics department using the PCNE Classification in Turkey to the best of our knowledge. This study aimed to identify and compare the prevalence and types of DRPs in pediatric patients in two study phases. Retrospective studies may not adequately demonstrate the potential of clinical pharmacists' role in detecting DRPs. A clinical pharmacist being present in the clinic could be more beneficial in detecting DRPs, because the problem may not have been noticed in the past cases, the noticed problem may not have been recorded or the record may have been lost. In our study with matched patients whose demographic characteristics were insignificant from each other, the reason for the high number of DRPs detected in the prospective phase compared to the retrospective phase was thought to be due to the presence of the clinical pharmacist in the clinic.

This study had limitations. It was limited to one hospital with a small sample size and a non-randomized retrospective control group. As the study had a retrospective evaluation, this evaluation was limited to previously documented, unstandardized data from various clinicians.

This study took place in general pediatrics, and therefore it was limited regarding the types of problems and causes encountered. Matching parameters have been applied to the subjects of this study's retrospective control group. However, it must be illuminated that the difference between the number of diagnoses is because some of the patients had more than one diagnosis. The study group's diagnoses having more numbers than the control group might be attributed to the distinction between investigating data within medical records and the digital environment (prospective phase) versus searching only the digital environment (retrospective phase). Medical records of the control group were archived, and the researcher could not reach and extract data from related files.

In Turkey, according to regulations, pharmacists do not have the authorization to change treatments. Therefore, during this study, the pharmacist could only offer physicians therapy-related comments on DRPs. Even the recommendations made to the physicians on the relevant subjects were considered reasonable at times; the pharmacist did not have the possibility of checking the status of the DRPs due to limited time spent in the clinic.

The most encountered pharmacological group related to DRPs was anti-infectives. Similarly, anti-infectives were the most common class of drugs involved in DRPs in Birarra *et al*.'s study [20]. Bizuneh *et al*. [21] found that the most common drug classes involved in DRPs were antibiotics (39.5%).

Ibrahim *et al*. [22] found that the chance of having a medication-related problem is 6% higher with every additional medication. We also found that polypharmacy increases DRP risk by approximately 32 times.

We observed a different approach to patient treatments between the groups, which was the increased inhaler use in the study group for acute bronchiolitis. It was observed that even though guidelines state the opposite, physicians tend to prescribe more inhaled products such as salbutamol and budesonide. In bronchiolitis, bronchodilators such as salbutamol do not improve oxygen saturation, reduce hospital admission after outpatient treatment, shorten the duration of hospitalization, and reduce the time to resolution of illness at home [23]. However, we found that salbutamol was preferred to treat respiratory diseases. Possible explanations for barriers to guideline adherence are unwillingness to discontinue therapy in a clinically improving child, perceived patient demand for drugs, lack of accountability or feedback about prescribing,

clinician dissatisfaction with not meeting patient expectations, diagnostic uncertainty, and defensive practice [24, 25].

Hsia *et al.* [26] conducted their study in 2019, and by using The World Health Organization Essential Medicines List Access, Watch, and Reserve (AWaRe) classification, they evaluated the patterns of hospital antibiotic use. They found substantial global variation in the proportion of AWaRe antibiotics used in hospitalized neonates and children and attracted attention to antimicrobial resistance as a rapidly emerging global public health crisis. In their study, regional patterns of AWaRe antibiotic prescribing to children by drug utilization 90% have been expressed. As can be seen in Africa (12,0%), Eastern Mediterranean (24,2%), Europe (10,1%), and South-East Asia (15,4%) in our study, ceftriaxone was the most preferred antibiotic. Almost one out of every four antibiotics was ceftriaxone in our study.

According to Fernández-Llamazares *et al.* [27], recommendations were considered to have been accepted if the physician implemented the change suggested by the pharmacist within 24 hours of the recommendation. Nevertheless, PCNE Classification, by detailing the possibilities, provides more options. Interventions could be shaped as only informing prescribers by PCNE Classification as applied in this study, and implementation could have been evaluated separately. Jafarian *et al.* [28] indicated that 98 interventions were proposed by the clinical pharmacist, of which 59,2% of them were accepted in their study. However, in our study, the researcher lacked the possibility of checking the status of the DRPs due to limited time spent in the clinic.

Further research could pioneer the development of educational programs among healthcare professionals' intercommunication both face-to-face and in a digital environment to imply efficient strategies to detect and solve DRPs. Simplified economic approaches could be added to research more frequently to see the role of clinical pharmacists more vividly.

## 4. CONCLUSION

The findings of this study show that drug-related problems are detectable by the pharmacist. According to two study phases between which the patients have no statistical difference related to their diagnosis, sex, and age, the pharmacist can detect more DRPs by making instant assessments in the clinic, compared to retrospective file evaluations. Although pharmacists do not have a long history in hospital clinics, it has been observed that other healthcare professionals can benefit from clinical pharmacist-led medication reviews.

## 5. MATERIALS AND METHODS

### 5.1. Study design

This observational study has been designed in two phases: the prospective phase during providing clinical pharmacist-led medication review service between June 2019 and February 2020 and the retrospective phase (as usual care without any clinical pharmacy service provided) among patients obtained by age-sex-diagnose–matching according to the prospective phase between December 2018 and February 2019. This study was conducted in a pediatric unit of a university hospital.

### 5.2. Study population

The pediatric patients (<18 years old) admitted to the unit have been included in the prospective part without any exclusion criteria during the study. The retrospective control group of the study was admitted to the same clinic between December 2018 and February 2019 and discharged from the same clinic. According to patient records of the prospective part, age-sex-diagnose–matched control subjects of the retrospective analyses have been randomly selected within the pool of 728 patients. The matching search was repeated when there was no match for age, sex, and diagnosis altogether. The second match search was done by changing the month/age by ±1, and when needed, a third match search was done by changing the sex. The sample size was not calculated due to including every eligible patient during the prospective period.

### 5.3. Clinical pharmacist-led medication review

Pharmaceutical Care Network Europe Foundation (PCNE) describes medication review as, "Medication review is a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug-related problems and recommending interventions." [29]. Clinical pharmacy practitioner have acted based on this definition during the whole study period.

A clinical pharmacist (Ph.D. candidate) was present in the pediatric clinic for two days every week throughout the prospective study. During the study period, the clinical pharmacist was present in the hospital to join the residents, specialists, and supervisor ward rounds on Tuesdays and Thursdays. In this way, the

clinical pharmacist could have been present during ward rounds with the multi-disciplinary team to carry out the study.

The data resulting from clinical pharmacist evaluation has been shared with the physicians in charge of the related treatment. Clinical pharmacist-led medication review using the translated Turkish version of PCNE Classification for drug-related problems V9.1 [30] was provided in pediatric patients admitted to the unit.

The patients' kidney function was evaluated using the "Schwartz" formula widely used in pediatric patients. Patient-specific dosing compliance (weight, kidney function, indication) and drug interactions were evaluated by Lexicomp®, Medscape®, Micromedex®, and UpToDate® information resources.

"Prescriber informed only" was the only recorded intervention for the study group, and "No Intervention" was a mandatory option for the medication review during the retrospective phase of the study. The patients' problems related to drug treatment were presented to the physicians verbally. For each provided information, interventions have been proposed to prescribers; however, acceptance and implementation status remained unknown due to the obligatory interval of days of the researcher's presence in the clinic. There was no transmission of information from clinical pharmacist to patients or their legal guardians following the study design through the study. The outcome of interventions resulted in "Problem status unknown" for the study group and "No need or possibility to solve the problem" for the control group according to PCNE Classification V9.1.

### 5.4. Data Collection

The patient medical data were obtained from reviewing medical charts or electronic records, and it was checked verbally by the patient's caregivers.

The following characteristics of the patients were documented: sex, age, height, weight, body mass index, current/past diseases, laboratory data, information about the drugs used (name of the drug, dose, frequency of drug use, drug formulation type, duration of use), allergy history. In the light of this information, concordant clinical pharmacy services were evaluated, and possible changes in their treatments were discussed. The patients' simultaneous use of two different drugs or more was considered polypharmacy [31]. All the measures were taken during the conduct of the study to reduce the potential for bias.

The pharmacist reviewed the collected data, recorded the identified DRPs according to The PCNE Classification V9.1, and formulated intervention proposals.

### 5.5. Data Analysis

Pearson's chi-square test was used to examine the relationships between categorical variables. A p-value<0,05 at the 95% confidence interval was considered statistically significant. For continuous data, whether the distribution is normal or not was analyzed with the Kolmogorov Smirnov test, and it was seen that the data did not comply with the normal distribution criteria. Therefore, the differences between the two groups were compared with the Mann-Whitney U test used for non-parametric data. The odds ratio determined whether different clinical conditions pose a risk for DRPs. Any missing data have been indicated within relevant table cells. The impact of the parameters that have missing data did not generate the need for sensitivity analysis.

## REFERENCES

[1] Dalton K, Byrne S. Role of the pharmacist in reducing healthcare costs: current insights. Integr Pharm Res Pract. 2017; 6: 37–46. [CrossRef]

[2] Messerli M, Blozik E, Vriends N, Hersberger KE. Impact of a community pharmacist-led medication review on medicines use in patients on polypharmacy--a prospective randomised controlled trial. BMC Health Serv Res. 2016; 16: 145. [CrossRef]

[3] Fernandez E, Perez R, Hernandez A, Tejada P, Arteta M, Ramos JT. Factors and mechanisms for pharmacokinetic differences between pediatric population and adults. Pharmaceutics. 2011;3(1):53-72. [CrossRef]

[4] The Board of Pharmacy Specialties, Pediatric Pharmacy. https://www.bpsweb.org/bps-specialties/pediatric-pharmacy/ (accessed on 29 April 2022)

[5] Hon MY, Chua XY, Premakumar CM, Mohamed Shah N. Drug-related problems in a general paediatric ward of a tertiary care hospital in Malaysia. Int J Clin Pharm. 2020; 42(3): 948-955. [CrossRef]

[6] Malfará M, Pernassi M, Aragon D, Carlotti A. Impact of the clinical pharmacist interventions on prevention of pharmacotherapy related problems in the paediatric intensive care unit. Int J Clin Pharm. 2018; 40(3): 513-519. [CrossRef]

[7] Nguyen TH, Le VTT, Quach DN, Diep HG, Nguyen NK, Lam AN, Pham ST, Taxis K, Nguyen T, Nguyen PM. Drug-Related Problems in Prescribing for Pediatric Outpatients in Vietnam. Healthcare (Basel). 2021; 9(3): 327. [CrossRef]

[8] Prot-Labarthe S, Di Paolo ER, Lavoie A, Quennery S, Bussières JF, Brion F, Bourdon O. Pediatric drug-related problems: a multicenter study in four French-speaking countries. Int J Clin Pharm. 2013; 35(2): 251-259. [CrossRef]

[9] Tripathi S, Crabtree HM, Fryer KR, Graner KK, Arteaga GM. Impact of clinical pharmacist on the pediatric ıntensive care practice: An 11-year tertiary center experience. J Pediatr Pharmacol Ther. 2015; 20(4): 290-298. [CrossRef]

[10] Yismaw MB, Adam H, Engidawork E. Identification and resolution of drug-related problems among childhood cancer patients in Ethiopia. J Oncol. 2020; 2020: 6785835. [CrossRef]

[11] Liu XX, Wang HX, Hu YY, Zhu XT, Tan X, Yang Y, Hang YF, Zhu JG. Drug-related problems identified by clinical pharmacists in nephrology department of a tertiary hospital in China-a single center study. Ann Palliat Med. 2021; 10(8): 8701-8708. [CrossRef]

[12] Özdemir N, Kara E, Büyükçam A, Aykaç K, Çeliker A, Demirkan K, Kara A. Evaluation of medication errors in pediatric patients using antibiotics. Turk J Pediatr. 2021; 63(6): 970-977. [CrossRef]

[13] Duerden M, Avery T, Payne R. Polypharmacy and medicines optimisation - Making it safe and sound. First ed., The King's Fund, UK, 2013.

[14] Batchelor HK, Marriott JF. Formulations for children: Problems and solutions. Br J Clin Pharmacol. 2015;79(3):405-418. [CrossRef]

[15] Kaufmann J, Laschat M, Wappler F. Medication errors in pediatric emergencies: a systematic analysis. Dtsch Arztebl Int. 2012;109(38):609-616. [CrossRef]

[16] Benavides S, Nahata MC, Pediatric Pharmacotherapy, first ed., American College of Clinical Pharmacy, Lenexa, Kansas, United States of America 2013, p: 48-52.

[17] Van den Bemt PM, Egberts TC, de Jong-van den Berg LT, Brouwers JR. Drug-related problems in hospitalised patients. Drug Saf. 2000 Apr;22(4):321-333. [CrossRef]

[18] Dalton K, Byrne S. Role of the pharmacist in reducing healthcare costs: current insights. Integr Pharm Res Pract. 2017;6:37-46. [CrossRef]

[19] Kara E, Kelleci Çakır B, Sancar M, Demirkan K. Impact of clinical pharmacist-led ınterventions in Turkey. Turk J Pharm Sci. 2021; 18(4): 517-526. [CrossRef]

[20] Birarra MK, Heye TB, Shibeshi W. Assessment of drug-related problems in pediatric ward of Zewditu Memorial Referral Hospital, Addis Ababa, Ethiopia. Int J Clin Pharm. 2017; 39(5): 1039-1046. [CrossRef]

[21] Bizuneh GK, Adamu BA, Bizuayehu GT, Adane SD. A prospective observational study of drug therapy problems in pediatric ward of a referral hospital, northeastern Ethiopia. Int J Pediatr. 2020; 2020: 4323189. [CrossRef]

[22] Ibrahim N, Wong IC, Tomlin S, Sinha MD, Rees L, Jani Y. Epidemiology of medication-related problems in children with kidney disease. Pediatr Nephrol. 2015; 30(4): 623-633. [CrossRef]

[23] Gadomski AM, Scribani MB. Bronchodilators for bronchiolitis. Cochrane Database Syst Rev. 2014; 2014(6): CD001266. [CrossRef]

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[24] Dempsey PP, Businger AC, Whaley LE, Gagne JJ, Linder JA. Primary care clinicians' perceptions about antibiotic prescribing for acute bronchitis: A qualitative study. BMC Fam Pract. 2014; 15: 194. [CrossRef]

[25] Lugo RA, Salyer JW, Dean JM. Albuterol in acute bronchiolitis--continued therapy despite poor response? Pharmacotherapy. 1998; 18(1): 198-202.

[26] Hsia Y, Lee BR, Versporten A, Yang Y, Bielicki J, Jackson C, Newland J, Goossens H, Magrini N, Sharland M; GARPEC and Global-PPS networks. Use of the WHO Access, Watch, and Reserve classification to define patterns of hospital antibiotic use (AWaRe): An analysis of paediatric survey data from 56 countries. Lancet Glob Health. 2019; 7(7): e861-e871. Erratum in: Lancet Glob Health. 2021 Jun;9(6):e758. [CrossRef]

[27] Fernández-Llamazares CM, Calleja-Hernandez MA, Manrique-Rodriguez S, Pérez-Sanz C, Duran-García E, Sanjurjo-Saez M. Impact of clinical pharmacist interventions in reducing paediatric prescribing errors. Arch Dis Child. 2012; 97(6): 564-568. [CrossRef]

[28] Jafarian K, Allameh Z, Memarzadeh M, Saffaei A, Peymani P, Sabzghabaee AM. The responsibility of clinical pharmacists for the safety of medication use in hospitalized children: A middle eastern experience. J Res Pharm Pract. 2019; 8(2): 83-91. [CrossRef]

[29] Griese-Mammen N, Hersberger KE, Messerli M, Leikola S, Horvat N, van Mil JWF, Kos M. PCNE definition of medication review: reaching agreement. Int J Clin Pharm. 2018; 40(5): 1199-1208. [CrossRef]

[30] Pharmaceutical Care Network Europe. PCNE Classification V 9.1. 2020. https://www.pcne.org/working-groups/2/drug-related-problem-classification. (accessed on 06 December 2021).

[31] Bakaki PM, Horace A, Dawson N, Winterstein A, Waldron J, Staley J, Pestana Knight EM, Meropol SB, Liu R, Johnson H, Golchin N, Feinstein JA, Bolen SD, Kleinman LC. Defining pediatric polypharmacy: A scoping review. PLoS One. 2018; 13(11): e0208047. [CrossRef]