International Journal of Clinical Pharmacy (2020) 42:979–994
https://doi.org/10.1007/s11096-020-01034-z

REVIEW ARTICLE

Impact of pharmacist interventions on medication errors in hospitalized pediatric patients: a systematic review and meta-analysis

Lina Mohammad Naseralallah[1] · Tarteel Ali Hussain[1] · Myriam Jaam[2] · Shane Ashley Pawluk[3,4]

Received: 24 February 2020 / Accepted: 10 April 2020 / Published online: 24 April 2020

Abstract

Background Medication errors are avoidable events that may occur at any stage of the medication use process. Implementing a clinical pharmacist is one strategy that is believed to reduce the number of medication errors. Pediatric patients, who are more vulnerable to medication errors due to several contributing factors, may benefit from the interventions of a pharmacist. *Aim of the review* To qualitatively and quantitatively evaluate the impact of clinical pharmacist interventions on medication error rates for hospitalized pediatric patients. *Methods* PubMed, EMBASE, Cochrane Controlled Trials Register and Google Scholar search engines were searched from database inception to February 2020. Study selection, data extraction and quality assessment was conducted by two independent reviewers. Observational and interventional studies were included. Data extraction was done manually and the Crowe Critical Appraisal Tool was used to critically appraise eligible articles. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using a random-effects model for rates of medication errors. *Results* 19 studies were systematically reviewed and 6 studies (29,291 patients) were included in the meta-analysis. Pharmacist interventions involved delivering educational sessions, reviewing prescriptions, attending rounds and implementing a unit-based clinical pharmacist. The systematic review indicated that the most common trigger for pharmacist interventions was inappropriate dosing. Pharmacist involvement was associated with significant reductions in the overall rate of medication errors occurrence (OR 0.27; 95% CI 0.15 to 0.49). *Conclusion* Pharmacist interventions are effective for reducing medication error rates in hospitalized pediatric patients.

Keywords Clinical pharmacist · Medication error · Pediatrics · Litterature Review

Impacts on practice

- A clinical pharmacist caring for pediatric patients can reduce the rates of medication errors.
- Direct pharmacist involvement in education, direct patient care, therapeutic drug monitoring, drug distribution oversight and quality improvement have been demonstrated to reduce the rates of medication errors in pediatric patients.
- Dosing errors are the most common medication errors occurring in hospitalized pediatric patients.

✉ Shane Ashley Pawluk
shane.pawluk@cw.bc.ca

[1] College of Pharmacy, QU Health, Qatar University, Doha, Qatar

[2] Clinical Pharmacy and Practice Department, College of Pharmacy, QU Health, Qatar University, Doha, Qatar

[3] Department of Pharmacy, Clinical Pharmacy, Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada

[4] Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

Introduction

Patient safety is one of the core goals in all healthcare systems and is a key step to ensure the provision of a high-quality care to patients [1]. Medication errors (ME) and preventable adverse drug events (ADEs) can take place in any healthcare system and can lead to patient harm [2]. Medication errors encompasses all events that could occur at any stage of the medication use process including

prescribing, transcribing, dispensing, administering and monitoring a medication. On the other hand, preventable ADEs are injuries resulting from medication use and may sometimes be a result of medication errors [3].

Pediatric patients are more prone to experience a medication error in a health care setting, and when such events occur, these errors have three times the potential to cause direct patient harm as compared to adult patients [4, 5]. Factors such as complex dosing, varying growth and development processes, availability and accuracy of dosage forms, the use of off-label formulations, limited physiologic reserves to buffer potential overdose errors, and variable communication capabilities all contribute to additional risks for medication errors in this population[4, 6–8]. These factors highlight the need for pediatric-specific prevention strategies for reducing medication errors and preventable ADEs.

Several strategies have been investigated to reduce the occurrence of these events in health care settings. One such strategy is the implementation of a clinical pharmacist within the ward. The clinical pharmacist's role has been evolving over the past decades as a healthcare practitioner who has expertise in appropriate safe and effective medication use [9]. Several systematic reviews and meta-analyses have indicated that a clinical pharmacists' interventions may reduce medication errors and preventable ADEs in hospitalized patients, including events that could lead to actual harm before reaching the patients. In addition, these interventions improved the quality of care provided to patients and reduced the overall cost of health which enhanced the efficiency of healthcare [10–15]. However, the majority of these studies focus on having a clinical pharmacist intervening with adult patients. Therefore, it is essential to study the effect of a clinical pharmacist caring for pediatric patients, given that they are more vulnerable to medication errors.

Aim of the review

The aim of this systematic review and meta-analysis is to evaluate the impact of clinical pharmacist interventions on reducing medication errors and preventable ADEs for pediatric patients in hospital settings and evaluate the overall quality of the available evidence.

Method

This systematic review and meta-analysis follows the recommendations by the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines and the Cochrane Handbook guidelines, to ensure inclusion of relevant information. The protocol of the study is registered with the International Prospective Register of Systematic Reviews (PROSPERO)—CRD42019126541[16].

Scope and search strategy

A Systematic review of published works was conducted to evaluate the role of pharmacist intervention on medication errors for inpatient pediatric patients. The following electronic databases were searched from inception until February 2020 to identify eligible articles: Ovid MEDLINE®, EMBASE, The Cochrane Database of Systematic Reviews, and Google Scholar. In addition, reference lists of the resulted systematic review articles were manually searched to locate additional relevant articles that were not identified through the database search.

The following Medical Subject Headings [MeSH] and keywords were incorporated using 'OR': 'pediatric(s), 'child', 'children', 'neonate', 'infant(s)', 'adolescent(s)'. These were combined with the following using 'AND': 'pharmacist(s)', 'Pharm* intervention'. The results from this search were combined with the following using 'AND': 'medication errors', 'prescribing error', 'preventable adverse drug reaction', 'medication discrepancy', 'inappropriate prescribing', 'safe prescribing', 'mistake'. The result of this search was limited further to 'English language' and 'Human species'.

Study selection and eligibility criteria

Studies were considered for inclusion if the primary focus was the assessment of medication errors as expressed as a rate or percentage. Appropriate study settings included hospital environments with a clear designation of including pediatric patients. A clear intervention directly involving a clinical pharmacist was necessary for inclusion. Only articles published in English were included. Editorials, commentaries or case-studies were excluded.

Study selection

Potential articles were first screened by title and abstract. EndNote X8® (2019 Clarivate) was used to remove duplicates and organize the reference list. Those that were of potential relevance were read independently by 2 authors to determine whether they met the inclusion criteria. Discrepancies were reviewed by study authors.

Data extraction

Two authors independently extracted study data using a standardized form which included the study authors and year, country, study design, hospital unit, study population

characteristics, pharmacist intervention, and outcomes obtained for medication errors. Discrepancies were reviewed by study authors.

Quality assessment

Quality of the included articles was assessed using Crowe Critical Appraisal Tool (CCAT) version 1.4 [17, 18]. This tool was selected as it was anticipated from other systematic reviews that studies included would have significantly different methodologies. The CCAT is divided into 8 categories and 22 items. Each item has multiple descriptors for ease of appraisal with each category receiving its own score on a 6 point scale (0–5). An overall score for each study can be expressed out of a total score of 40 points. Two independent raters assessed each study. Discrepancies were resolved after discussion between authors. Intraclass correlation coefficient (ICC) was calculated using IBM SPSS® statistical software version 22 to measure the consistency between the two raters in order to insure reliability.

Statistical analysis

Studies that reported a similar primary outcome measure with a numerical difference between medication errors for pre- and post-intervention were included in the meta-analysis. Meta-analysis was conducted using Cochrane Review Manager Software (RevMan 5.3; Nordic Cochrane Centre, Copenhagen, Denmark). A random-effects model was used to estimate the pooled odds ratios (ORs) for the primary analyses as heterogeneity is expected owing to the different settings (departments within the hospital) and different types of pharmacist intervention. Together with 95% confidence intervals (CIs), ORs and weighted mean differences were derived for dichotomous variables. Statistical heterogeneity among studies was evaluated using I^2 and P values.

Results

Identification and selection of studies

The electronic search yielded 598 citations and 8 additional records were identified from reference lists of included studies. After removal of duplicates, a total of 559 title and abstracts were screened for inclusion. A total of 67 full articles were screened of which 19 were included in this review. (Figure 1).

Characteristics of included studies

Major characteristics of the included studies are presented in Tables 1 and 2 for studies that showed numerical difference and studies that reported types of errors respectively. Of the 19 studies included, 11 were retrospective or prospective cohort studies [8, 19–28], 6 before-after studies [4, 29–33] and two cross–sectional observational studies [9, 34]. Most of the studies were conducted in the USA (n = 5) [8, 19, 21, 22, 24] followed by Spain (n = 3) [9, 23, 30], Netherlands (n = 2) [27, 31], Egypt (n = 2) [4, 33], one multicenter study across Europe [28] and one each from Canada[26], Brazil [34], Malaysia [32], India [25], Pakistan[29] and Saudi Arabia [20]. Only four studies were confined to multicenter [8, 23, 24, 28]. The majority of studies involved various hospital departments (n = 8) [8, 19, 21, 22, 24, 26–28] and three each from a neonatal intensive care unit (NICU) [25, 30, 31] and general medical ward [20, 29, 32]. Only two studies were conducted in the pediatric intensive care unit (PICU) [4, 34] and one in the pediatric surgery department [33], while the remaining two did not specify the hospital ward or unit [9, 23]. The two main pharmacist interventions were educational sessions (n = 5) [29–33] and review/validation of medication orders (n = 5) [9, 21, 23, 26, 27]. There were three studies for implementing a unit-based clinical pharmacist [19, 24, 28] and applying multiple interventions, such as combining monitoring medication orders and attending rounds [4, 8, 34], two studies for attending rounds [22, 25] and one study for implementing medication safety program designed and filled by pharmacist [20].

Quality of included studies

Two raters appraised each of the 19 studies, which resulted in 38 independent CCAT evaluations, the total score ranged from 16 to 35.5 out of 40. ICC showed a range of 0.948–0.997 for all studies which indicates high similarity between raters, thus excellent reliability (Table 3) [35]. The overall assessment mean for all studies was 27.87 out of 40 points with standard deviation of 6.04. Within the CCAT the sections the highest scores were for preliminary (4.18/5) and introduction (4.11/5), while the lowest were for ethics (2.89/5) and sampling (2.58/5). The mean scores by study and domain are summarized in Table 3.

Types of medication errors that prompted pharmacist interventions

Nineteen studies were included in this analysis. Of this, 13 studies had wrong dose as one of the three most common reasons for intervention [4, 9, 20, 21, 23–28, 30, 33, 34], reported as inappropriate dosing including overdosing or

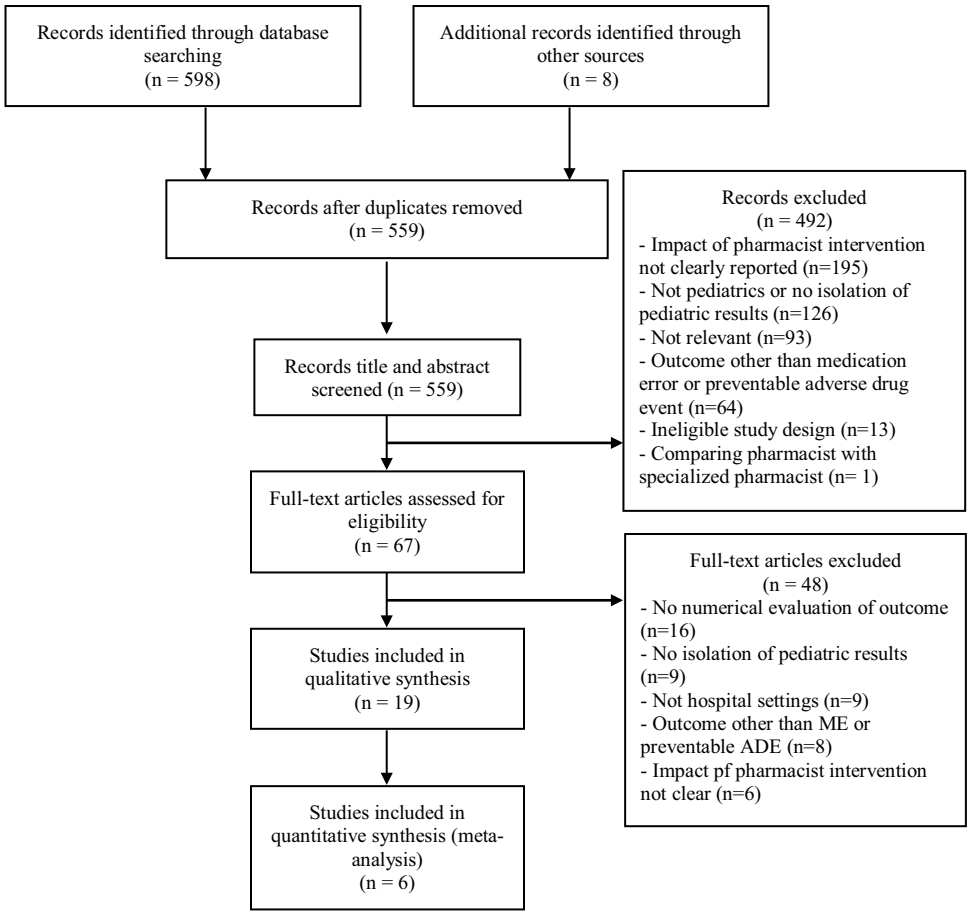

Fig. 1 PRISMA flow diagram of the study selection process

underdosing. Wrong drug was one of the top three causes for intervention in four articles which resulted in recommending an alternative therapy [22–24, 26]. Another type of error that also led to modification of therapy was for drug interaction and was among the three top reasons for pharmacist involvement in two studies [20, 25]. Three studies reported missing information (e.g. weight or date of birth) [9, 21, 22], inappropriate formulation [23, 26, 27], and wrong frequency [4, 29, 31] among the most common three triggers for intervention. Six studies rated the severity of pharmacist interventions: three showed that most interventions were moderate [4, 25, 31], and two were severe [9, 23]. One study revealed that out of 616 preventable errors, only 120 were harmful [8]. Five studies reported the acceptance rate of pharmacist interventions, of this, four studies showed an acceptance rate more than 55% [9, 23, 25, 27]. The remaining study showed acceptance rate of 83% without changing regimen [28].

Studies reporting quantitative outcomes of pharmacist interventions

Seven studies were included in this analysis. Six before-after studies were included in this analysis as they reported the number of medication errors pre and post intervention [4, 29–33]. One cohort study was excluded because it reported the results in error per patient-days [19]. Of the six studies included in the meta-analysis, five implemented an educational sessions designed and delivered by pharmacist to nurses and physicians [29, 30, 32, 33]. Five of six studies showed significant reduction ($P < 0.0001$) in the incidence of medication errors [4, 29–32]. The pooled OR (n = 29 291 patients) across all studies was 0.27 (95% CI 0.15 to 0.49). However, the results of these studies are substantially heterogeneous (Fig. 2). The impact of the unit-based pharmacist implemented in the cohort study, which measured the total serious medication errors (SMEs) and SMEs/1000 patient-days, was significant for the SMEs/1000 patient-days from the intensive care unit (ICU) ($P < 0.01$). However, there was no significant difference for the total SMEs in the ICU and for the total SMEs and SMEs/1000 patient-days in the surgical and medical wards [19].

Discussion

This systematic review and meta-analysis investigated the impact of clinical pharmacist interventions on medication error rates in hospitalized pediatric patients. It provides a

Table 1 Studies reporting quantitative outcomes of pharmacist interventions

Author (year of publication)	Country	Study design	Site and hospital department	Population characteristics	Pharmacist intervention	Key finding
Ahmed et al. [29]	Pakistan	Pre-post study	50-bed children ward	Not reported	Educate nurses about ME (1 month) Train nurses on Pediatric Medication Administration Record Sheet (PMARS)	Preintervention: n = 8179 orders, 82.13% showed errors, 98.34% of them were omission errors Postintervention: n = 7995 orders, 39.19% showed errors, 99.62% of them were omission errors Significant reduction in omission errors, incorrect dose, incorrect dosage form, incorrect frequency, incorrect time and unauthorized medicine ($P = 0.01$)
Alagha et al. [4]	Egypt	Pre-post study	12-bed PICU	Preintervention: n = 139, age (median): 10 years, weight (median): 7 kg, orders per patient (median): 9 Postintervention: n = 101, age (median): 9 years, weight (median): 7 kg, orders per patient (median): 10 No statistical difference between groups	Four interventions designed and implemented by clinical pharmacist: Point-of-care drug use assist Structured combined order and administration chart Orientation for new residents Residents feedback	Preintervention: n = 1417 orders 78.1% showed errors, 39.8% of them were moderate and 29.7% severe Postintervention: n = 1097 orders 35.6% showed errors, 24.1% of them were moderate and 7% severe Significant reduction in prescribing errors, severe, moderate, minor errors and in IV, oral and inhalation administration routes ($P \leq 0.05$). However, it was not significant for other routes Types of errors showed significant reduction are wrong dose, administration rate, concentration, frequency, selection, instruction ($P < 0.001$) and incomplete order ($P = 0.03$). However, it was not significant for unclear order

Table 1 (continued)

Author (year of publication)	Country	Study design	Site and hospital department	Population characteristics	Pharmacist intervention	Key finding
Campino et al. [30]	Spain	Pre-post study	42-bed NICU (level III), 12 of them of maximal care	N/A	15 informative sessions by a hospital pharmacist for all health professionals about MEs, a non-punitive culture on patient safety and about the study's aims	Preintervention: n = 4182 registers, 20.7% prescription error rate, 19.2% registers with one or more incidence Postintervention: n = 1512 registers, 3% prescription error rate, 2.9% registers with one or more incidence Significant reduction in prescription error rate and registers with one or more incidence ($P \leq 0.001$) The types of errors that showed significant reduction are incorrect dose, route not registered ($P < 0.001$), units not registered ($P < 0.05$) and incorrect units ($P = 0.029$). However, it was not significant for dose not registered, interval not registered, incorrect interval and incorrect route
Chedoe et al. [31]	Netherlands	Pre-post study	14-bed NICU	Preintervention: n = 20 (14 male), postconceptional age: 10 patients in 30–35 weeks, weight: 13 patients weighted 1–2 kg Postintervention: n = 22 (14 male) postconceptional age: 14 patients in 25–30 weeks, weight: 11 patients weighted 1–2 kg No significant difference between groups	An educational program developed and implemented by a clinical pharmacist, consists of five theoretical sessions to nurses. One individual practical teaching session for each nurse covering preparation and administration of all high demand medications on the ward	Preintervention: n = 311 doses, 159 errors occurred, 49% error rate Postintervention: n = 284 doses, 104 errors occurred, 31% error rate Significant reduction in error rate, preparation errors and administration errors ($P < 0.001$)
Chua et al. [32]	Malaysia	Pre-post study	Two pediatric general medical wards (18-bed and 19-bed)	Preintervention: n = 217, age (median): 8 months Postintervention: n = 208, age (median): 6 months	Sharing the findings of pre-intervention by the pharmacist with the ward staff and bring awareness about administration errors. Another five sessions of presentation were carried out	Preintervention: n = 1284 doses,44.3% error rate, 852 errors in total Postintervention: n = 1401 doses, 28.6% error rate, 496 errors in total Significant reduction in error rate ($P < 0.001$)

Table 1 (continued)

Author (year of publication)	Country	Study design	Site and hospital department	Population characteristics	Pharmacist intervention	Key finding
Fawaz et al. [33]	Egypt	Pre-post study	Pediatric surgery department	Preintervention: n = 110, 80 males, age (mean): 41.11 months, weight (mean): 13.86 kg Postintervention: n = 112, 81 males, age (mean): 43.72 months, weight (mean): 14.89 kg No statistical difference between groups	Educational session to physicians (pediatric surgery and anesthesia residents) about MEs detection and prevention. The session covered the following items: definition of MEs, medication use process, difference between MEs and ADEs, barriers to reporting MEs, categories of MEs, MEs reporting program, prevention strategies and the role of clinical pharmacist in the operating room	Preintervention: n = 936 orders, 33.33% showed errors Postintervention: n = 693 orders, 32.32% showed errors Significant reduction in category B ($P = 0.00006$) and C errors ($P = 0.005$) but not A and D Significant reduction in prescribing errors ($P = 0.04$) but not for transcribing and administration errors The types of errors that showed significant reduction are low dose, high dose, wrong concentration ($P < 0.05$). However, wrong route, wrong interval, duration not mentioned, wrong drug for age, dose not recorded and total errors were not significant

Table 1 (continued)

Author (year of publication)	Country	Study design	Site and hospital department	Population characteristics	Pharmacist intervention	Key finding
Kaushal et al. [19]	USA	Prospective cohort study	2 general medical units, 2 general surgical units, PICU and cardiac ICU	Preintervention: n = 401 (45% female), age: 52% above 6 years Postintervention: n = 359 (47% female) age: 34% above 6 years	Implement unit-based clinical pharmacists, their roles were: 1-Provide physicians with timely information and recommendations. 2-Facilitate communication between the healthcare team and the pharmacy 3-Assist nurses with drug preparation by providing information 4-Help monitor transcription and medication preparation, storage, and distribution systems 5-Part of the unit-based continuous quality improvement team.	In the ICU: Number of patient-days for intervention n = 835 compared to n = 759 for control. Out of these 5 serious medication errors (SMEs) occurred in intervention compared to 23 in control (not significant). Number of SMEs/1000 patient-days showed significant reduction ($P < 0.01$) In the general medical unit: Number of patient-days for intervention n = 1136 compared to n = 1319 for control. Results were not significant for both total SMEs and SMEs/1000 patient-days In the surgical medical unit: Number of patient-days for intervention n = 1109 compared to n = 1253 for control. Results were not significant for both total SMEs and SMEs/1000 patients-days

ME medication error, *ADE* adverse drug event, *SME* serious medication error

Table 2 Types of medication errors that prompted pharmacist interventions

Author (year of publication)	Country	Study design	Site and hospital department	Population characteristics	Pharmacist intervention	Key finding
Abuelsoud et al. [20]	Saudi Arabia	Prospective evaluation with descriptive analysis	Pediatric ward	n = 201 patients, age: < 12 years	Implement medication safety reporting system by clinical pharmacist during rounds. Developed through pharmacist round, pharmacy and therapeutic committee, medication safety committee and pharmacy improvement projects	The main reasons for intervention were drug–drug interaction (31%), wrong dose (28%) and no dose adjustment based on kidney function (9%)
Christiansen et al. [21]	USA	Prospective study	120-bed general pediatric ward and PICU	n = 24 patients, 50% male, age (median): 6.1 years, weight (median): 31.2 kg	Pediatric clinical pharmacist reviews prescriptions	n = 24 patients with 74 orders, 101 prescribing errors The main reasons for intervention were missing date of birth (48%), missing patient's weight (17%) and inappropriate weight-based dosing (17%)
Cunningham et al. [22]	USA	Prospective study	87-bed NICU, PICU and general pediatric ward	Not Reported	Pediatric clinical pharmacist attends rounds	n = 7408 orders with 1315 interventions The main reasons for intervention were drug therapy recommendation (46%), error in order (24.5%) and drug information request (8.9%)
Fernández-Llamazares et al. [9]	Spain	Cross-sectional epidemiological study	180 pediatric beds	Not Reported	Clinical pharmacist validates electronic prescription	n = 14 713 patients with 61 458 orders, pharmacist detected 1475 interventions The main reasons for intervention were wrong dose (47.5%) and missing information (8%) Significance grade: 64.4% significant Intervention outcome: 94.3% accepted with modification

Table 2 (continued)

Author (year of publication)	Country	Study design	Site and hospital department	Population characteristics	Pharmacist intervention	Key finding
Fernández-Llamazares et al. [23]	Spain	Multicenter prospective, descriptive, epidemiological study	1565-beds at eight pediatric hospitals	Age (median): 5 years	Clinical pharmacist validates orders	The main reasons for intervention were wrong dose (49.3%), inappropriate dosage form (15.1%) and wrong drug (10.7%) Significance grade: 51.9% significant Intervention outcome: 95.4% accepted with modification
Folli et al. [24]	USA	Multicenter prospective cohort study	Hospital A: 145-bed PICU, NICU and non-ICU ward Hospital B: 100-bed PICU, NICU and non-ICU ward	Age: 37.2% of patients were 1 month–2 years, 27.1% were < 1 month, the rest were older than 2 years	Pharmacists specialized in pediatric pharmacotherapy provide 24-hour unit dose services and complete clinical pharmacy services	Hospital A: n = 57,394 orders, pharmacist detected 281 errors, frequency of errors 4.9 per 1000 orders Hospital B: n = 43,628 orders, pharmacist detected 198 errors, frequency of errors 4.5 per 1000 orders The main reasons for intervention were overdose (55.1%), under-dose (26.9%) and wrong drug (5.6%)
Fortescue et al. [8]	USA	Multicenter prospective cohort study	Hospital A: 2 general medical wards, 1 general surgical ward, 1 short-stay medical ward and PICU Hospital B: general medical/surgical wards, PICU, and NICU	Not Reported	The study included 10 different interventions. One of them is pharmacist intervention through: 1-Implementing a clinical pharmacist on physician rounds 2-Monitoring medication ordering, transcribing and delivery Pharmacist impact was isolated	Total preventable errors: n = 616, pharmacist prevented 81.3%; out of this 58.3% were monitoring errors Harmful preventable errors: n = 120, the pharmacist prevented 88.3%; out of this 71.7% were monitoring errors Nonharmful preventable errors: n = 496, the pharmacist prevented 79.6%; out of this 55% are monitoring errors

Table 2 (continued)

Author (year of publication)	Country	Study design	Site and hospital department	Population characteristics	Pharmacist intervention	Key finding
Khan et al. [25]	India	Prospective, non-experimental and interventional study	1200-bed NICU	n = 150 patients, 86 male, gestational age (mean): 35.55 weeks, weight (mean): 2.316 kg	Clinical pharmacist attending rounds and monitoring patient's drug therapy	The main reasons for intervention were inappropriate dose/frequency (40.22%), drug interaction (17.24%) and transcription error (13.8%) Significance grade: 55.7% moderate Intervention outcome: 68.97% accepted with modification
Koren et al. [26]	Canada	First part of the study was retrospective and the second part was prospective	700-bed various wards at a tertiary children's hospital	Not reported	Clinical pharmacist reviews physicians' orders	Prospective: 390 interventions The main reasons for intervention were dose change (35%), formulation or administration change (20%) and recommending an alternate therapy (13%) or frequency change (13%) Retrospective: 516 interventions The main reasons for intervention were formulation or administration change (31%), dose change (27.4%) and change to a formulary agent (13%)
Maat et al. [27]	Netherlands	Prospective cohort with nested case–control study	220-bed medical and surgical wards	Not reported	Clinical pharmacist reviews computerized physician order entry (CPOE)	n = 9992 patients with 138 449 orders The main reasons for intervention were correction (81.1%) and completion (18.9%). The most common causes for correction were wrong dose (45.4%) and wrong drug formulation (9.4%) Intervention outcome: 57.7% accepted with modification

Table 2 (continued)

Author (year of publication)	Country	Study design	Site and hospital department	Population characteristics	Pharmacist intervention	Key finding
Prot-Labarthe et al. [28]	France, Quebec, Switzerland and Belgium	Multicenter prospective cohort study	60-bed PICU and pediatric cardiology units in four teaching hospitals	n = 270 patient, 53% male, age (median): 1.7 year, weight (median): 10.7 kg	Ward-based clinical pharmacist (variable hours of presence)	n = 270 patients with 5171 prescriptions, pharmacist identified 996 DRPs The main reasons for intervention were improper administration (29%), untreated indication (26%) and overdose (11%) Intervention outcome: 83% accepted without modification
Okumura et al. [34]	Brazil	Cross-sectional study	12-bed PICU	n = 53 patients, 63% male, age (mean): 1.5 year	Part-time clinical pharmacy services: 1-clinical rounds, 2-elaborate on institutional protocols, 3-antiepileptic therapeutic drug monitoring, 4-review prescriptions	Only 35 patients included as they showed DRP, n = 141 DRPs The main reasons for intervention were preventing incompatible intravenous solutions (21%) and wrong dose (17%)

ICC intraclass correlation coefficient, *CI* confidence interval

Table 3 Cumulative quality assessment results

Study	Preliminary	Intro	Design	Sampling	Data analysis	Ethics	Results	Discussion	Overall	ICC (CI)
Studies reporting quantitative outcomes of pharmacists interventions										
Ahmed et al. [29]	3	3	3	1.5	3.5	3	3	2.5	22.5	0.992 (0.967–0.998)
Alagha et al. [4]	4.5	5	4.5	2.5	3	0	3.5	5	28	0.994 (0.974–0.999)
Campino et al. [30]	5	3.5	4.5	4.5	4.5	0.5	3.5	3.5	29.5	0.997 (0.988–0.999)
Chedoe et al. [31]	5	5	4	4	5	4.5	4	4.5	36	0.992 (0.966–0.998)
Chua et al. [32]	4.5	4.5	3	1.5	3	4.5	4	4	29	0.977 (0.893–0.995)
Fawaz et al. [33]	4	2	3.5	2.5	3.5	1.5	3.5	3	25.5	0.983 (0.910–0.996)
Kaushal et al. [19]	5	4.5	4.5	3.5	4.5	5	4	4.5	35.5	0.996 (0.982–0.999)
Studies reporting types of medication errors that prompted pharmacist interventions										
Abuelsoud et al. [20]	5	3	4	2.5	4.5	1	3.5	2.5	26	0.991 (0.961–0.998)
Christiansen et al. [21]	3.5	5	2	1	2.5	3	2	2	21	0.981 (0.912–0.996)
Cunningham et al. [22]	4	4.5	3	2.5	4	2	3	4	27	0.996 (0.981–0.999)
Fernández et al. [9]	5	4.5	5	3	3.5	3	3	3	30	0.992 (0.958–0.998)
Fernández et al. [23]	4.5	4.5	4.5	4	4.5	5	3.5	4	34.5	0.996 (0.981–0.999)
Folli et al. [24]	4	4	4	2	3.5	3.5	3.5	3.5	28	0.990 (0.959–0.998)
Fortescue et al. [8]	4.5	5	3.5	4	4.5	4.5	3.5	4.5	34	0.987 (0.927–0.997)
Khan et al. [25]	3	2	2.5	1.5	2.5	1	2.5	2	17	0.973 (0.870–0.994)
Koren et al. [26]	1.5	3	3	1	3	0	2.5	2	16	0.978 (0.910–0.995)
Maat et al. [27]	5	4.5	4.5	3	2.5	4	3	4.5	31	0.992 (0.959–0.998)
Okumura et al. [34]	4.5	4.5	4.5	3	3.5	4.5	3.5	4	32	0.984 (0.917–0.997)
Prot-Labarthe et al. [28]	4	4	3	1.5	3	4.5	2.5	4.5	27	0.948 (0.710–0.989)
Overall (SD)	4.18 (0.98)	4.11 (0.98)	3.71 (1.04)	2.58 (1.48)	3.61 (1.03)	2.89 (1.80)	3.24 (0.71)	3.55 (1.08)	27.87 (6.04)	–

comprehensive overview and analysis of the most common types of errors that lead to pharmacist interventions and their significance grade (mild, moderate, severe) as well as the rate of acceptance of the pharmacists' recommendations. Previous studies and reviews demonstrated the importance of clinical pharmacists with pediatric patients' management. Benefits highlighted included: identifying drug related problems, recommending suitable medications, improve medication use and reduce medication related costs as well as reduce medication errors [36, 37]. Similar benefits were also observed with interventions targeted at adult population medication error prevention [10–15]. Such findings highlight that pharmacist's involvement is essential to reduce medication errors regardless of the population involved.

Despite the heterogeneity of studies included in this meta-analysis the overall aggregate effect of pharmacist's interventions demonstrated a significant beneficial outcome in reducing the odds of medication errors by 73%. Interventions that showed most benefit include correcting prescribing errors (dosing errors, units of measurement, route, and frequency) [29, 30]. Previous studies highlight that most medication errors occur during the prescribing process [36, 38]. Therefore, it is very important to include pharmacists in clinical ward rounds with prescribers. This gives the pharmacists the opportunity to prevent prescribing errors in the first place and therefore reduce the delays which happen when trying to correct these errors later.

The focus of this review was the hospital setting, since medication errors are more likely to occur within a tertiary healthcare setting compared to primary settings. Moreover, the role of pharmacists in preventing medication errors in hospital settings can have a far more benefit as compared to clinics and community settings due to the nature of complex patients received in hospitals as compared to other settings [39–41]. Nonetheless, it is important to investigate the role of pharmacists in preventing medication errors in other settings separately and highlight whether the same magnitude of benefit can be observed.

The main pharmacist intervention found in our study was educational sessions done by pharmacists to other healthcare providers, mainly nurses and physicians. In addition, reviewing or validating orders and implementing a unit-based clinical pharmacist were among the most common interventions in this systematic review. A previous systematic review that focused on ICU patients showed that the most common intervention was implementing a pharmacist within the medical team which is one of the top interventions in our study [10].

The main strength in this meta-analysis is that up to our knowledge this is the first review to numerically assess the impact of pharmacist interventions on medication error rates for pediatric patients in hospital settings. In addition, the systematic review included studies from different countries in various parts of the world which could enhance the generalizability of outcomes. The use of the CCAT offered further insight into the studies included in this analysis as the general quality of data between studies could be compared. The CCAT was selected in this analysis as it has been found to be more reliable than an informal appraisal of various research studies. The uniform manner of appraisal offered through the CCAT has been found to almost eliminate the rater effect with no substantial subject matter knowledge effect [42].

This study has some limitations that should be addressed. First, the overall quality of all components was 27.87 out of 40 which is considered moderate. This was mainly due to poor reporting of sampling and ethics approval as those two domains had the lowest overall ranking within the CCAT. Although sampling is essential to minimize the risk of selection bias, ethics disclosure does not introduce any particular type of bias to the study, thus do not affect the internal validity of the review. Moreover, the included studies were published in peer reviewed journals, a majority of which require ethical disclosure prior to publication. Second, some of the studies included a combination of pharmacist interventions, thus it cannot be guaranteed which intervention caused the reduction in medication errors. Significant heterogeneity in the studies included in the meta-analysis was identified which might be due to many reasons including, the variation in the implemented pharmacist interventions in addition to the method of detecting medication errors and the definition of medication discrepancy varied from one study to another. Moreover, some studies have reported results as medication errors and others as preventable ADRs. Lastly, this systematic review identified studies published between 1987 and 2018. With this wide range of dates, it is likely that clinical pharmacist practice and understanding of medication errors has changed over this time frame. As such, the outcomes from earlier conducted studies may report different outcomes compared to more recent studies due to practice changes and changes to the context of general healthcare.

Future studies should focus on evaluating the role of pharmacist interventions on medication errors in outpatient settings. This will allow for a better insight to the pharmacist impact in society and will enable the healthcare system to identify the areas or settings in which more attention and improvements are required. Furthermore, subgroup analysis of the outcomes of the current study might be required in order to examine the impact of a pharmacist on particular types of errors such as prescribing errors or administration errors; it will be beneficial to overcome this heterogeneity.

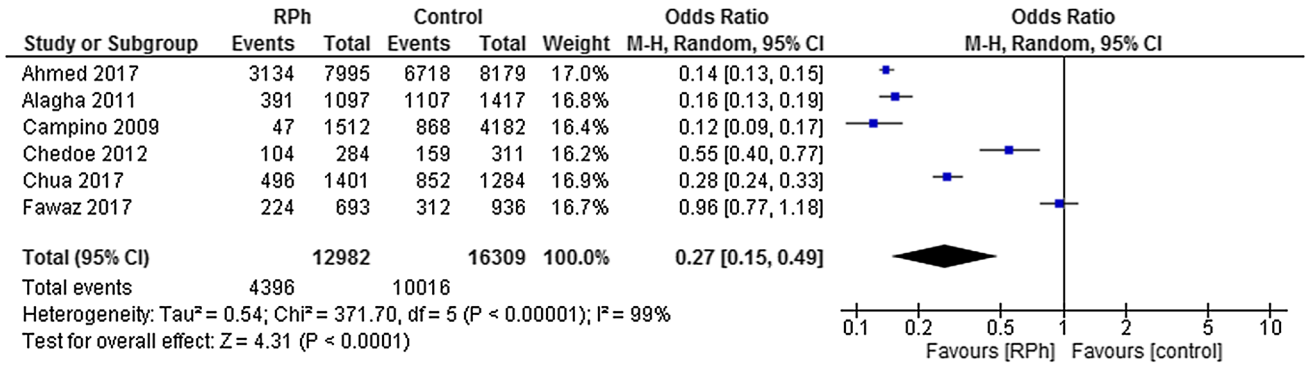

Fig. 2 Forest plot of registered pharmacist (RPh) effect on medication errors

Conclusion

Medication errors remain to be of great concern especially when it comes to the pediatric population. Prescribing errors including inappropriate dosing and selecting inappropriate medications were the main medication errors reported within the included articles. Pharmacist interventions play an important role in reducing medication errors in the pediatric population. These interventions include educational sessions, review/validation of medication orders, and implementing a ward-based pharmacist or a medication safety program involving a pharmacist [20]. Overall, the findings from this review support the implementation of a clinical pharmacist in order to reduce the occurrence of medication errors in pediatric patients.

Acknowledgements None

Funding No funding was received for this project.

Conflicts of interest The authors declare that they have no conflict of interest.

References

1. Campino A, Lopez-de-Heredia MC, Lopez-Heredia I, Valls ISA. Medication errors in a neonatal intensive care unit. Influence of observation on the error rate. Acta Paediatr. 2008;97(11):1591–4.
2. New England Quality Innovation Network-Quality Improvement Organization. Adverse drug events—What do we really mean? United States: Centers for Medicare & Medicaid Services. [cited 2020 Apr 7]. Available from: http://doh.hpc.go.th/data/HA2018/ADR_ADE.pdf.
3. Morimoto T, Gandhi TK, Seger AC, Hsieh TC, Bates DW. Adverse drug events and medication errors: detection and classification methods. Qual Saf Health Care. 2004;13(4):306–14.
4. Alagha HZ, Badary OA, Ibrahim HM, Sabri NA. Reducing prescribing errors in the paediatric intensive care unit: an experience from Egypt. Acta Paediatr. 2011;100(10):e169–74.
5. Costello JL, Torowicz DL, Yeh TS. Effects of a pharmacist-led pediatrics medication safety team on medication-error reporting. Am J Health-Syst Pharm. 2007;64(13):1422–6.
6. Poole RL, Carleton BC. Medication errors: neonates, infants and children are the most vulnerable. JPPT. 2008;13(2):65–7.
7. Doherty C, Mc Donnell C. Tenfold medication errors: 5 years' experience at a university-affiliated pediatric hospital. Pediatrics. 2012;129(5):916–24.
8. Fortescue EB, Kaushal R, Landrigan CP, McKenna KJ, Clapp MD, Federico F, et al. Prioritizing strategies for preventing medication errors and adverse drug events in pediatric inpatients. Pediatrics. 2003;111:722–9.
9. 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):564–8.
10. Wang T, Benedict N, Olsen KM, Luan R, Zhu X, Zhou N, et al. Effect of critical care pharmacist's intervention on medication errors: a systematic review and meta-analysis of observational studies. J Crit Care. 2015;30(5):1101–6.
11. Manias E, Williams A, Liew D. Interventions to reduce medication errors in adult intensive care: a systematic review. Br J Clin Pharmacol. 2012;74(3):411–23.
12. Cohen V, Jellinek SP, Hatch A, Motov S. Effect of clinical pharmacists on care in the emergency department: a systematic review. Am J Health-Syst Pharm. 2009;66(15):1353–61.
13. Maidment ID, Lelliott P, Paton C. Medication errors in mental healthcare: a systematic review. Qual Saf Health Care. 2006;15(6):409–13.
14. Noormandi A, Karimzadeh I, Mirjalili M, Khalili H. Clinical and economic impacts of clinical pharmacists' interventions in Iran: a systematic review. Daru. 2019;27(1):361–78.
15. Keers RN, Williams SD, Cooke J, Walsh T, Ashcroft DM. Impact of interventions designed to reduce medication administration errors in hospitals: a systematic review. Drug Saf. 2014;37(5):317–32.
16. Pawluk S, Hussain T, Naseralallah L. The effect of clinical pharmacist interventions on reducing medication errors in pediatric patients: a systematic review. PROSPERO 2019; CRD42019126541. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019126541.
17. M C. Crowe Critical Appraisal Tool (v1.4): Conchra; 2011 [cited 2020 Apr 7]. Available from: https://conchra.com.au/2015/12/08/crowe-critical-appraisal-tool-v1-4/.
18. Crowe M, Sheppard L. A general critical appraisal tool: an evaluation of construct validity. Int J Nurs Stud. 2011;48(12):1505–16.

19. Kaushal R, Bates DW, Abramson EL, Soukup JR, Goldmann DA. Unit-based clinical pharmacists' prevention of serious medication errors in pediatric inpatients. Am J Health-Syst Pharm. 2008;65(13):1254–60.
20. Abuelsoud NN. Improving medication safety through implementation of medication error reporting systems in different medical specialities. J Pharm Pract Res. 2018;48(6):537–42.
21. Christiansen SR, Morgan JA, Hilmas E, Shepardson A. Impact of a prescription review program on the accuracy and safety of discharge prescriptions in a pediatric hospital setting. JPPT. 2008;13(4):226–32.
22. Cunningham KJ. Analysis of clinical interventions and the impact of pediatric pharmacists on medication error prevention in a teaching hospital. JPPT. 2012;17(4):365–73.
23. Fernandez-Llamazares CM, Pozas M, Feal B, Cabanas MJ, Villaronga M, Hernandez-Gago Y, et al. Profile of prescribing errors detected by clinical pharmacists in paediatric hospitals in Spain. Int J Clin Pharm. 2013;35(4):638–46.
24. Folli HL, Poole RL, Benitz WE, Russo JC. Medication error prevention by clinical pharmacists in two children's hospitals. Pediatrics. 1987;79(5):718–22.
25. Khan SN, Joseph S, Sasidharan P, Faap A. A study of clinical pharmacist initiated interventions for the optimal use of medications in a neonatal intensive care unit (NICU) of a tertiary care hospital in South India. Int J Pharm Sci. 2015;8:1.
26. Koren G, Reich A, Hales B. Use of clinical pharmacists to prevent medication errors in children. J Pharm Technol. 1991;7(6):219–21.
27. Maat B, Au YS, Bollen CW, van Vught AJ, Egberts TCG, Rademaker CMA. Clinical pharmacy interventions in paediatric electronic prescriptions. Arch Dis Child. 2013;98(3):222–7.
28. Prot-Labarthe S, Di Paolo ER, Lavoie A, Quennery S, Bussieres JF, Brion F, et al. Pediatric drug-related problems: a multicenter study in four French-speaking countries. Int J Clin Pharm. 2013;35(2):251–9.
29. Ahmed T, Haq N, Rehman M, Nasim A. The impact of pharmacist intervention on medication errors in a teaching hospital Quetta, Pakistan. Value Health. 2016;19(7):A630.
30. Campino A, Lopez-Herrera MC, Lopez-de-Heredia I, Valls-i-Soler A. Educational strategy to reduce medication errors in a neonatal intensive care unit. Acta Paediatr. 2009;98(5):782–5.
31. Chedoe I, Molendijk H, Hospes W, Van den Heuvel ER, Taxis K. The effect of a multifaceted educational intervention on medication preparation and administration errors in neonatal intensive care. Arch Dis Child Fetal Neonatal Ed. 2012;97(6):F449–55.
32. Chua S-S, Choo S-M, Sulaiman CZ, Omar A, Thong M-K. Effects of sharing information on drug administration errors in pediatric wards: a pre-post intervention study. Ther Clin Risk Manag. 2017;13:345–53.
33. Fawaz MG, Sabri NA, Albaghdady AA, Malek FAA. Detection and prevention of medication errors in the operating rooms of a pediatric surgery department in Egypt. Int J Pharm Sci Rev Res. 2017;42(2):100–6.
34. Okumura LM, da Silva DM, Comarella L. Relation between safe use of medicines and clinical pharmacy services at pediatric intensive care units. Rev Paul Pediatr. 2016;34:397–402.
35. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016;15(2):155–63.
36. Drovandi A, Robertson K, Tucker M, Robinson N, Perks S, Kairuz T. A systematic review of clinical pharmacist interventions in paediatric hospital patients. Eur J Pediatr. 2018;177(8):1139–48.
37. Sanghera N, Chan P-Y, Khaki ZF, Planner C, Lee KKC, Cranswick NE, et al. Interventions of hospital pharmacists in improving drug therapy in children: a systematic literature review. Drug Saf. 2006;29(11):1031–47.
38. Ghaleb MA, Barber N, Franklin BD, Yeung VW, Khaki ZF, Wong IC. Systematic review of medication errors in pediatric patients. Ann Pharmacother. 2006;40(10):1766–76.
39. Smith M, Giuliano MR, Starkowski MP. In Connecticut: improving patient medication management in primary care. Health Aff (Millwood). 2011;30(4):646–54.
40. Simpson SH. The roles we have as hospital pharmacists. Can J Hosp Pharm. 2017;70(1):3–4.
41. Mossialos E, Naci H, Courtin E. Expanding the role of community pharmacists: policymaking in the absence of policy-relevant evidence? Health Policy. 2013;111(2):135–48.
42. Crowe M, Sheppard L, Campbell A. Camparison of the effects of using the crowe critical appraisal tool versus informal appraisal in assessing health research: a randomised trial. Int J Evid Based Healthcare. 2011;9(4):444–9.