Medication error in pediatric patients: an updated systematic review (2015-2021)

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ABSTRACT

Medication errors (MEs) are defined broadly as medication prescription, distribution, or administration errors. MEs are considered as the most common type of medical error in hospitalized patients, with pediatric patients having a ME rate up to three times that of adult patients. MEs resulting in extended hospitalization, readmission, impairments, and other complications in hospitalized children are frequently documented. To assess the MEs in pediatric patients by reviewing previous studies (from 2015 to 2021) that reported MEs in pediatric patients. Studies related to our subject were explored using PubMed and Google scholar databases. The keywords included were “MEs, prescribing errors, administration errors, adverse drug events, Dosing errors, hospitalized children, pediatric patients” were used in various combinations. The inclusion criteria were original studies that reported MEs in pediatric patients and full text-articles. A total of 456 articles were obtained; only six articles were eligible for the inclusion criteria. The included studies were conducted on a total number of 8,860 MEs. The six included studies were divided into; two studies were prospective observational studies, two retrospective studies, one cross-sectional study, and one study based on a national mandatory reporting system. Our analysis found high rates of MEs among pediatric patients. The most common MEs were prescribing errors, dosing errors, followed by incorrect administration time. The medication groups with the highest ratio of MEs were anti-hypertensives, antimycotics, and drugs for nasal preparation, followed by anti-asthmatic drugs, antibiotics, and analgesics. Additionally, morphine, paracetamol, and gentamicin were also associated with MEs in pediatric patients. More research is needed to evaluate the need for and viability of pharmacy services in pediatric settings.

Keywords: Medication errors, prescribing errors, administration errors, adverse drug events, hospitalized children, pediatric patients.

Introduction

Medication errors (MEs) are generally defined as errors in the prescription, distribution, or administration of a medicine. MEs are the most significant avoidable source of patient death. The term “medication administration error” refers to “any variation between what the patient got or was meant to get and what the prescriber intended in the original prescription” [1].

Medical errors are considered as a primary cause of morbidity and death in the United States. MEs are the most prevalent kind of medical errors in hospitalized patients. The ME rate in pediatric patients is up to three times that of adult patients. Because many prescription mistakes and adverse drug events (ADEs) are avoided, initiatives to enhance medication safety are a crucial key component of a comprehensive strategy to delivering quality care to children [2].

Children are more vulnerable to MEs and the risk of harm since the pharmaceutical dosage is dependent on weight or surface area. The lack of acceptable formulations for

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children demands drug modification in order to provide the proper dosage. [3]

MEs that result in extended hospitalization, readmission, impairments, and other complications are often documented in hospitalized children. According to studies, 2.3% to 6% of pediatric patients may be harmed by MEs and adverse medication responses. Dosing errors are the most commonly reported errors, followed by inaccurate timing, inappropriate medicine preparation, and omission errors. Medicines for intravenous administration are the most often linked to MEs in children [4,5].

Owing to several factors, including lack of standard pediatric drug dosing and formulations, weight-based dosing, verbal orders, a hectic environment with frequent interruptions, a lack of clinical pharmacists on the emergency department (ED) care team, the pediatric emergency care setting is recognized as a high-risk environment for MEs. The majority of pediatric patients seeking care in EDs are not seen in pediatric hospitals but rather in community hospitals, which may treat a few pediatric patients. This, in turn, results in many pediatric MEs, owing to several factors as the absence of a specialized pediatric clinical pharmacist [6].

The current study reviews the prevalence of MEs among pediatric patients, predicts MEs, and analyzes MEs in pediatric critical care services.

Method and Search strategy

The current systematic review is an updated systematic review of the articles discussing the MEs in pediatric patients since 2015. This systematic analysis follows the PRISMA checklist guidance for systematic review and meta-analysis [7]. Two databases were used for searching purpose: PubMed and Google scholar databases. The two databases were used to search for studies conducted on our main subject, “MEs in pediatric patients.” The studies were published between 2015 and 2021.

The searching process involved using various keywords, including “MEs, prescribing errors, administration errors, ADEs, dosing errors, hospitalized children, and pediatric patients.” The involved keywords were used in several combinations to obtain all possible articles. All the titles produced from this primary exploration were revised.

Eligibility criteria

After reviewing the titles of the obtained articles, only articles focused on MEs in pediatric patients were included, whereas articles conducted on MEs before 2015 were excluded. Also, articles conducted on MEs in adult patients were excluded. The second step included reviewing the abstract of the remaining articles on MEs in pediatric patients to select only articles written in English and original articles. In contrast, review articles, letters to editors, case series, and cases reports were excluded.

The final stage included original articles written in English and reported MEs, prescribing errors, pediatric patients; these articles were further explored to exclude non-available full-text articles, duplicate articles, and articles with unsatisfying content, such as articles with overlapped or incomplete data. The full description of the search strategy is shown in Figure 1.

Data reviewing and collection

Articles were reviewed for abstracts and the full text to extract the data of interest and transfer data into a pre-designed excel sheet. The selected data were then revised through the excel sheet, and then the data was transferred to one table to summarize the chosen data to facilitate the analysis of data.

Results

This systematic review included six articles that met the eligible criteria [8,9,4,10,11,12] (Table 1). The included studies were published in 2015 [8], 2016 [9], 2017 [4], 2020 [10,11], and 2021 [12]. Two studies were prospective observational studies [8,9], two studies were retrospective [4,12], one cross-sectional study [11], and one study was based on a national mandatory reporting system [10].

The included studies involved a total of 8,860 medication orders. The study population was pediatric patients; and, one study was conducted on neonates [10]. One study included 1,129 medication orders in critically ill children in a pediatric intensive care unit (PICU) [8]. One study reviewed 1,115 medication orders from 233 hospitalized children in the pediatric ward of Nekemte Referral hospital in West Ethiopia [9]. A study was conducted on 2071 MEs, including 487 harmful MEs reports from public hospitals on patients aged 0-17 years in Europe [4]. A study included 1,522 pediatric MEs reported from secondary care [10], and one study included 2,347 prescriptions from 301 patients in a Mexican secondary-tertiary level public hospital [11]. Another study included 676 children (6 to 18 years) with psychiatric complaints [12].

In one study [8], the rate of prescribing errors was reported to be 14%. The ME rate was found to be more than 50% in all pediatric critical care settings, and pediatric critical care units had the highest ME/patient index (13.1) in another study [11]. Three studies discussed the medication classes associated with MEs. In one of them [8], the medication groups with the highest proportion of MPEs were anti-hypertensives, antimycotics, and nasal, with error rates of 50% each, followed by anti-asthmatic drugs (25%), antibiotics (15%), and analgesics (14%). In another study, MEs were most commonly noted in antidepressant and antipsychotic classes [12]. In a third study, common medicines associated with MEs included morphine, paracetamol, and gentamicin [4].

Ten errors (70%) were classified as MPEs, requiring interventions and causing patient harm, accounting for 9% of all medication orders. 45 MPEs (30%) did not
cause patient harm [8]. Another study found that 75.1% of patients experienced MEs, 513 (46.0%) experienced MEs, 75 (6.7%) experienced potential ADEs, and 17 (1.5%) experienced actual ADEs. The most common MEs (118; 23.0%) were dosing errors, followed by the wrong drug (109; 21.2%) and the wrong time of administration (79; 15.4%) [9]. Three studies discussed the types of errors involved in MEs. According to one study [4], most MEs occurred during prescribing (40.8%), followed by dispensing (38.7%). Harmful MEs primarily occurred during dispensing (40.3%). Dosing errors were the most prevalent type of error, accounting for 47.7% of all MEs and 45.4% of harmful MEs. Another study found that the most implicated errors were dosing errors (32%) and omissions (21%) [10]. Omission errors were found in 376 patients (76.6%), commission errors in 44 patients (9.0%), and both in 71 patients (14.4%). There were 8 (18.1%) serious commission errors and 8 (18.1%) significant commission errors. One-third of patients (30.5%) had one ME, (23.9%) had two, (11.7%) had three, and 5% had four in the third study [12]. MEs caused no harm (74.9%), mild harm (11.7%), moderate harm (10.5%), or severe harm (1.3%), but none were lethal [4]. Another study showed a total of 1,252 potential MEs (72%), with 379 of these considered clinically relevant due to their potential harm. The area with the most significant number of MEs (n = 867) was PICU. The most common MEs were the use of abbreviations (50.9%) and the incorrect speed of administration (11.4%). Only 11.7% of drugs were considered ideal medication orders [11]. Being on three or more anti-psychiatric medications was significantly associated with a prescription error [12].

**Discussion**

In hospitalized patients, MEs are common and are a top priority in healthcare systems worldwide. MEs, which are defined as any errors that occur during the medication-use process, can occur during the prescribing, dispensing, transcribing, administering, and monitoring of medications. These errors are frequently preventable, resulting in increased patient morbidity and mortality, healthcare costs, and unnecessary hospitalization [13]. According to the World Health Organization, few studies compare MEs across different patient populations, particularly pediatric patients. Each hospitalized patient population has different pharmaco-therapeutic needs, and it is critical to determine whether each group has
**Table 1. Details of included articles**

<table>
<thead>
<tr>
<th>Author and Publication year</th>
<th>Study design</th>
<th>Population, sample size and characterization</th>
<th>Main points</th>
<th>Results and main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Glanzmann et al. (2015) [8]</td>
<td>Prospective observational study</td>
<td>Critically ill children in a PICU.</td>
<td>To determine the number and type of medication prescribing errors in critically ill children in a PICU.</td>
<td>A total of 1,129 medication orders were analysed. There were 151 prescribing errors, giving an overall error rate of 14%. The medication groups with the highest proportion of MPEs were antihypertensives, antimycotics and drugs for nasal preparation with error rates of each 50%, followed by antiasthmatic drugs (25%), antibiotics (15%) and analgesics (14%). One hundred four errors (70%) were classified as MPEs which required interventions and/or resulted in patient harm equivalent to 9% of all medication orders. Forty-five MPEs (30%) did not result in patient harm.</td>
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<tr>
<td>2. Dedefo et al. (2016) [9]</td>
<td>A prospective observational study</td>
<td>233 hospitalized children in the pediatric ward of Nekemte Referral hospital in West Ethiopia.</td>
<td>To identify the independent predictors of MEs and ADEs</td>
<td>75.1% of patients were exposed to MEs. From the 1,115 medication orders reviewed, 513 (46.0%) MEs, 75 (6.7%) potential ADEs and 17 (1.5%) actual ADEs were identified. Most MEs were dosing errors (118; 23.0%), followed by wrong drug (109; 21.2%) and wrong time of administration (79; 15.4%). On multivariable logistic regression analysis, length of hospital stay of ≥ 5 days, and number of medication of 4-6 and number of medication of ≥7 were independent predictors of MEs; and length of hospital stay of ≥ 5 days and number of disease conditions ≥2 were independent predictors of ADEs.</td>
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<td>3. Rishoej et al. (2017) [4]</td>
<td>Study based on a national mandatory reporting system</td>
<td>Reports from public hospitals on patients aged 0-17 years in Europe.</td>
<td>To describe MEs in hospitalized children reported to the national mandatory reporting and learning system, the Danish Patient Safety Database</td>
<td>A total of 2,071 MEs including 487 harmful MEs were identified. Most MEs occurred during prescribing (40.8%), followed by dispensing (38.7%). Harmful MEs occurred mainly during prescribing (40.3%). Dosing errors were the most reported type of error. 47.7% of all MEs and 45.4% of harmful MEs. Antibiotics and analgesics were the most frequently reported medication classes. Common medicines associated with MEs included morphine, paracetamol, and gentamicin. MEs caused no harm (74.9%), mild (11.7%), moderate (10.5%), or severe harm (1.3%), but none were lethal.</td>
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<tr>
<td>4. Conn et al. (2020) [10]</td>
<td>A retrospective study</td>
<td>1,522 pediatric MEs reported from secondary care between 2011 and 2015, including all hospitals and community pediatric settings in Northern Ireland.</td>
<td>To evaluate the types, characteristics, and areas of risk within reported MEs in pediatric patients</td>
<td>Neonates, particularly in intensive care, were implicated in 19% of all errors. The medications most represented in risk were antimicrobials, paracetamol, vaccines, and intravenous fluids. The error types most implicated were dosing errors (32%) and omissions (21%).</td>
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<td>5. Brennan et al. (2020) [11]</td>
<td>A cross-sectional study</td>
<td>301 patients in a Mexican secondary-tertiary level public hospital</td>
<td>To describe and analyze MEs in the pediatric critical care services during the prescription stage.</td>
<td>In 2,347 prescriptions from 301 patients from all critical care services, a total of 1,252 potential MEs (72%) were identified, and of these 379 were considered as clinically relevant due to their potential harm. The area with the highest number of MEs was PICU (n = 867). The ME rate was &gt;50% in all pediatric critical care services and PICU had the highest ME/patient index (13.1). The most frequent MEs were use of abbreviations (50.9%) and wrong speed rate of administration (11.4%), and only 11.7% of the total drugs were considered as ideal medication orders.</td>
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<td>6. Sethuraman et al. (2021) [12]</td>
<td>A retrospective study</td>
<td>676 Children (6 to 18 years) with psychiatric complaints and a length of stay of more than 6 hours.</td>
<td>To describe MEs in children with mental health illness who were boarded in a PED for more than 6 hours.</td>
<td>A total of 676 patients (53.1% males) with a median age of 14 years were included. The median length of stay was 11.7 hours. A total of 974 MEs occurred in 491 (72.7%) patients. Omission errors were noted in 376 patients (76.6%), commission in 44 patients (9.0%), and both in 71 patients (14.4%). Among commission errors, 8 (18.1%) were serious and 8 (18.1%) were significant. One third of patients (30.5%) had 1 ME, 23.9% had 2, 11.7% had 3, and 5% had 4. MEs were most commonly noted in antidepressant and antipsychotic classes. One third (35.8%) of errors involved two medication classes. Being on 3 or 4 or more anti-psychiatric medications was significantly associated with a prescription error.</td>
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206 different MEs. As a result, the inability of healthcare systems to develop targeted strategies to reduce the incidence of error is hampered [14].

209 In our analysis, five out of the six included studies were conducted on pediatric patients [8,9,4,11,12]. In addition, one study was conducted on neonates [10]. Our analysis’s frequency of MEs ranged from 14% [8] to more than 50% [11]. It was reported that MEs are the most common type of error in PICUs. Furthermore, the ME rate in pediatric patients is thought to be three times higher than in adults. Children, including neonates and premature infants, are more vulnerable to MEs in these settings due to the high-stakes situations associated with critically ill children, particularly weight-based dosing errors and medication administration delays [15].

211 The PICU is a setting in which critically ill children; necessitate the administration of multiple medications. The possibility that greater care may also cause harm is unexpected and has received little attention in the past. Patients in intensive care units receive twice as many drugs as patients in general care units, making them at a greater risk of an ADE or an adverse drug reaction [16]. According to the study [8], in our analysis, 70% of MEs in pediatrics required intervention and resulted in patient harm; however, 30% did not need medical intervention.

215 There is limited published data on the frequency and nature of harms caused by MEs (preventable ADEs) in PICUs and NICUs, and it is mainly limited to one country, which represents a significant area for future research because this type of harm contributes to an extended length of hospital stay and additional healthcare costs [17]. Preventable ADEs are estimated to cost the National Health Service an additional £14.8 million per year in the United Kingdom [18]. Understanding avoidable harm is more important for identifying key challenges to improving patient care. This would allow for the development of effective remedial interventions to reduce harmful MEs and associated costs, ultimately supporting the current World Health Organization’s global safety campaign to improve patient safety [19].

228 In a study that assessed predictors of MEs and ADEs [9], most MEs were dosing errors (23.0%), followed by wrong drug selection (21.2%) and wrong time of administration (15.4%). It was reported that dispensing errors occur when the medication dispensed/delivered by the pharmacy does not correspond to the order written in the doctor’s prescription [1]. In this context, one of the studies included in our analysis [4] found that the frequency of dispensing errors is (38.7%). In 2015, Ashcroft et al. [20] had defined the prescribing error as any error in the prescription process that causes (or has the potential to cause) patient harm. In our analysis, prescribing errors were revealed to be 40.8% of MEs, and dosing errors were the most reported type of errors with a percentage of 47.7% [4].

229 Stevens et al. [21] reported that medication dosing errors are still common and can have life-threatening consequences, especially in pediatric patients, where dosing often requires weight-based calculations. This agreed with our analysis, as dosing errors were the most implicated errors in neonates (32%) [10].

233 Our analysis revealed that the medication groups with the highest proportion of MPEs were anti-hypertensives, drugs, antimycotics, with error rates of each 50%, followed by anti-asthmatic drugs (25%), antibiotics (15%), and analgesics (14%). In agreement with our analysis, Engum et al. [22] found a higher error rate associated with antibiotic prescribing. Additionally, Nori et al. [23] found that antibiotics are the class of drugs most commonly responsible for MEs in pediatric patients. Furthermore, Ghaleb et al. [24] reported that...
antibiotics and sedatives were the most common drugs associated with MEs among children patients.

**Conclusion**

Our analysis found high rates of MEs among pediatric patients. The most common MEs were prescribing errors, dosing errors, followed by incorrect administration time. The medication groups with the highest ratio of MEs were anti-hypertensives, antimycotics, and drugs for nasal preparation, followed by anti-asthmatic drugs, antibiotics, and analgesics. Additionally, morphine, paracetamol, and gentamicin were also associated with MEs in pediatric patients. Maintaining safe pharmacotherapeutic practices should be a top priority for all health professionals, but clinical pharmacists have the potential to reduce MEs significantly. However, more research is needed to develop targeted strategies that integrate critical pharmacy services into wards, quality-control tools, and health indicators to prevent MEs. In addition, additional research is required to determine the need for pharmacy services in the pediatric care setting and their viability.

**List of Abbreviations**

ME: Medication Error

**Conflict of interest**

The authors declare that there is no conflict of interest regarding the publication of this article.

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