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Prevalence of Medications Errors and Factors of Harmful Errors in Neonates and Paediatrics at Tertiary and Paediatric Hospitals: A Multicenter Study

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ABSTRACT

Medication errors (ME) are human mistakes that may occur during drug use, prescribing administration or monitoring. This study aimed to determine the Prevalence of MEs among pediatric patients receiving tertiary treatment in pediatric speciality hospitals and describe their patterns and causes. Three institutions participated in a multicenter retrospective analysis. Reports of all MEs involving paediatrics aged ≤13 years who were hospitalised or visited the Emergency Department or outpatient clinics were reviewed 1 January 2019 - 31 December 2019. The National Coordinating Council for Medication Error Reporting and Prevention classification was used to categorise MEs and to define PRME (category CI) and patient–harming MEs (category EI). A retrospective study was conducted with a total of 318 MEs reported, with an overall prevalence of 0.9 per 1,000 patients. The Prevalence was markedly lower in the CHT (0.35 / 1,000 patients) than in KAMC and KFSH&RC (1.73 and 3.5). The highest rate of MEs was observed in admitted wards (14.69 / 1,000 patients). Most commonly, MEs occurred at the prescribing stage (81.1%), were caused by a physician (83.3%), and were discovered by the pharmacist (85.5%). Improper medication dosage (34.0%), frequency (14.2%), and duration (10.4%) were the three most common forms of MEs. Paediatric inpatient treatment has a significant frequency of MEs, accounting for 24% of hospitalisations. The ME may not get to the patient if independent double-check prescriptions, accurate medication reconciliation of new prescriptions against the previously prescribed, and improved medicine labelling and packaging techniques are used.

INTRODUCTION

Medications are active substances used to treat, prevent, and diagnose diseases and constitute a valuable tool for modern medicine. However, improper use of medications can cause harmful consequences to the patient, leading to death (Hussain *et al.*, 2014). From the public health view, medications and pharmaceutical substances are authorised in local markets in perspective to help improve the population's health and reduce disease rates and related morbidity and mortality (Laatikainen *et al.*, 2022). From this point, medications' positive therapeutic and or preventive effect is only judged under optimal safety and effectiveness conditions of usage (Maaskant *et al.*, 2015). Medication errors "MEs" constitute a circumstance where Medication is administered outside the recognised safety and effectiveness usage conditions. They are defined as human mistakes occurring in hospitals and represent an issue of high priority in healthcare systems globally (Tajik, 2020). They may occur due to misunderstanding during handoffs as the healthcare providers may not be well affiliated across borders (Alqenae *et al.*, 2020). These errors may occur during the drug's use, prescribing, administration, or monitoring, thus involving all healthcare professionals (Abuelsoud, 2019). They may result in increased illness severity, other adverse effects, or death and are associated with unnecessary healthcare costs (Khaemba, 2014).

Medication errors account for 84.2% of all medical errors, estimated to cause 98,000 hospital deaths and more than one million injuries annually, costing up to $ 29 billion globally. Consequently, medical errors rank as one of the top causes of death in the United States besides car accidents, breast cancer, and acquired immunodeficiency syndrome (A Truter, 2017; Khaemba, 2014; Krzyzaniak & Bajorek, 2016). Medication errors involve errors due to human or system factors. A study indicates (Escrivá Gracia *et al.*, 2019) medication-related occurrences cause approximately 2 per 1000 hospital fatalities and 6-12% of hospital admissions, respectively. Human-related errors are a lack of performance and/or compliance with procedures or protocols. Many factors including misunderstanding, inaccurate copying, lack of knowledge, heavy workload, misjudgment, use of nonstandard abbreviations, lack of information about the patient, and insufficient or shortage of staff (Rodziewicz *et al.*, 2022; Thomas *et al.*, 2019). Besides health professional factors, patient-related factors may also underlie ME, such as patients' lack of understanding of their treatment and administration errors, related to prescription and incorrect dosages (Valencia Quintero *et al.*, 2021). The risk of human errors increases with an increased workload, stress, sleep deprivation, drugs with similar and complex names, and handling of medications by non-pharmacists, besides non-ergonomically designed

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information systems (Khayam, 2015). A review based in Iran revealed that ME was the most common type of medical error, with Prevalence ranging from (10-80%) (Vaziri *et al*., 2019).

Suppose MEs constitute a global concern for causing severe medical consequences. In that case, they should be more seriously considered for infants and children, especially in developing countries where this age category represents a large proportion of the population (Hmedat *et al*., 2017). MEs are prevalent in PICUs and NICUs, affecting medication orders and patient days (Alghamdi *et al*., 2019). While prescribing safety has become very clear in adults, the focus has been less on newborns, infants, children, and adolescents, as clinical trials are insufficient for children due to cost and liability problems and regulations that impede such studies (Al-Jeraisy *et al*., 2011). Moreover, the Prevalence of ME in pediatric patients is three times higher than in adults (Brennan-Bourdon *et al*., 2020). The available evidence suggests that MEs among pediatric patients represent a greater risk of death than adults, owing to additional factors that put children at higher risk from MEs, such as age and weight differences, in addition to other physiological features (Al-Jeraisy *et al*., 2011; Fernández-Llamazares *et al*., 2012; Impicciatore *et al*., 2001; Kaushal *et al*., 2001).

Further, MEs have been reported in various pediatric settings with an incidence rate of 1 in 6.4 medication orders (Dedefo *et al*., 2016). These involved multiple medications, and several risk factors have been identified in the literature (Antonucci & Porcella, 2014; Khayam, 2015). Such observations make the prevention of MEs a priority for health systems and a clinical necessity, integrated under the broad mission of protecting patients. Consequently, several efforts are undertaken to reduce drug error rates, using multiple human and technological tools, both at the healthcare provider's and patient's levels (Dedefo *et al*., 2016; Devine EB, 2005; Fernández-Llamazares *et al*., 2012; Hussain *et al*., 2014; Ross *et al*., 2000).

Among these strategic actions is monitoring MEs, which has become an essential tool to improve the safety and efficacy of medication dispensation systems by analysing the risk in case errors are reported. The use of Computerised provider order entry (CPOE) was shown to reduce the Prevalence of ME highly (Liu *et al*., 2023). Error reporting systems depend on the ability of physicians, pharmacists, and nurses to commit error detection and reporting protocols (Khaemba, 2014). As determined in one study, nurses were less likely to report ME as they feared the consequences that followed it. Physicians were more likely to report the Me. These considerations are of higher importance in the pediatric population. As such, we designed this study to provide insight into the extent and determinants of MEs among neonates and children in tertiary and pediatric hospitals in the Western region of Saudi Arabia. The following objectives were explored:

• To estimate the yearly Prevalence of MEs among pediatric and neonatal patients in different types of hospital settings.

• To compare the Prevalence of MEs between the different hospitals (tertiary and paediatrics) and different departments to determine the settings with the highest risk of MEs.

• To describe the pattern and categorisation of MEs based on the reported data;

• To investigate patient and healthcare Professional-related factors associated with MEs and to analyse the predictors of the Patient -Reaching MEs (PRME) and Patient-Harming MEs (PHME).

MATERIALS AND METHODS

Study Design

Three referral hospitals in the Western region of Saudi Arabia-King AbdulAziz, medical city National Guard (KAMCJED, a 751-bed hospital), Children's Hospital of Taif (CHT), and King Faisal specialist hospital and Research Centre Jeddah (KFSHRC, a 380-bed hospital-were the subjects of a multicenter retrospective study.

Data was gathered for this investigation from 1 January 2019 - 31 December 2019. There were no increased patient hazards or interventions in the research. Initially, the study involved all eight tertiary and pediatric hospitals in the Western region. Subsequently, a systematic sampling method was used to include all cases of MEs reporting over the study period from all participating centres. However, due to feasibility challenges, cluster sampling was used to select three centres depending on the authors' convenience and data accessibility.

Ethical Considerations

The protocol conformed with the Declaration of Helsinki's ethical guidelines for using human subjects' data and material in medical research. Institutional Review Board provided the Ethical Approval for KFSH with IRB study number 202068, KAIMARC with IRB study number RJ20/173/J, and an official approval letter from TAIF's Director of health affairs.

Eligibility Criteria

The Inclusion Criteria for this study were as follows: A) The study included all MEs reports declared in the participating centres from 1 January 2019 - 31 December 2019. B) Only ME reports concerning neonates and pediatric patients under 13 years admitted or visited the outpatient clinics or emergency were included.

The Exclusion Criteria were:

A) Patients over 13 years were excluded from the study.

B) Oncology and haematology neonates and paediatrics units were excluded.

C) Patients with incomplete data were excluded from the study.

Data Collection

A structured, precoded Excel form was used to collect all relevant data from both sources, i.e., the ME report and patient file. The form was designed by authors based on

the crucial ME report content and the literature review of relevant studies. The Excel form collected the following data:

1. ME-related data including date, location (hospital, department), a person who reported the ME, stage of error (prescribing, transcription, dispensing, administration, monitoring), type of MEs (incorrect dose, incorrect Medication, incorrect route, expired Medication, missed Medication, and incorrect time), and medicines in the cause (name, indication, dose, route, higher alert [yes/no], dosage form). Further, the severity of MEs was classified using the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) categorisation (MERP, 1998)

2. Patient-related factors, including age, gender, weight, medical history, chronic disease, mental illness (yes/no), consciousness status on the day of the ME (conscious/unconscious), number of medications prescribed on the day of the ME, length of hospital stay, presence of a caregiver and relation to the child (mother, father)

3. Data relating to the healthcare professional in the cause of the ME, including speciality (pharmacist, physician, nurse), grade (senior, junior), position (temporary, contract worker, permanent).

4. There is a predefined list of 8 contributing factors: missing clinical information, lack of double-checking, and lack of staff education and training.

Besides, data regarding the number of admissions by participating centres and units were collected on a separate sheet and used as a denominator in calculating ME Prevalence, as indicated later.

Procedure

The researchers conducted the data collection onsite. ME reports, including electronic and handwritten reports, were retrieved from the participating centres' ME reporting system. The corresponding patients' files were reviewed to extract further relevant data not available in the information. Data were entered directly using the predesigned Excel form, which resulted in 3 separate databases, one for each centre. The principal investigator and coauthors reviewed the three partial databases for accuracy and completeness and then merged them into one final database. The final database was coded to respect the patient's confidentiality before being shared for statistical analysis.

Study Outcomes

The study defined one primary outcome and two secondary outcomes. The primary outcome consisted of the Prevalence of MEs, which 1,000 patients computed regarding the total number of admissions and/or visits in each centre over the study period. The secondary outcomes consisted of Patient-Reaching ME (PRME), defined as a ME of NCC MERP category CI. Further, Patient-Harming ME (PHME) was also a secondary outcome, expressed as a ME of NCC MERP category EI.

Statistical Methods

The database was edited and imported to SPSS version 21 for statistical analysis. The results of the descriptive statistics that were carried out to present the patterns of MEs and associated factors were presented as frequency and percentage. Using cross-tabulations, Chi-Square and Fisher's Exact Tests were used to analyse PatientReaching MEs (PRME). On the contrary, the independent risk factors of PRME were analysed by a technique known as Multivariate Binary Logistic Regression. With a Confidence Interval (CI) of 95%, results were presented as Odds Ratio (OD). A P-value < 0.05 is considered statistically significant for the study.

RESULTS AND DISCUSSIONS

Prevalence of Neonates and Pediatric Medication Errors by Department and Centre

The three participating centres reported 318 MEs in total,

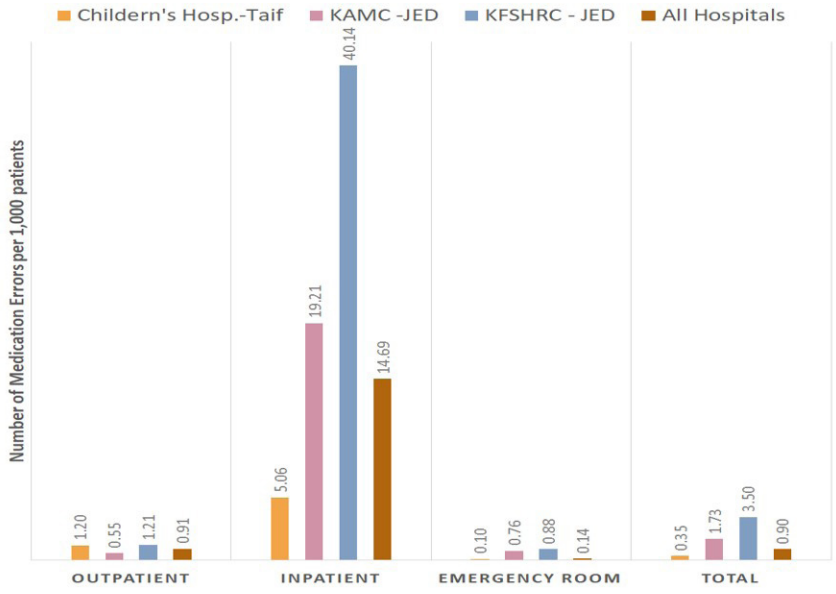

Figure 1: Prevalence of Medication Errors by Department and Centres in Three Tertiary Care Hospitals of Western Saudi Arabia, 2019

including 135 (KFSH), 93 (CHT), and 90 (KAMC), and an overall prevalence of 0.9 per 1,000 patients. Compared to the two tertiary care hospitals, KAMC and KFSH, the rate was lower at the Children's Hospital (0.35 per 1,000 patients) than at both facilities (Figure 1). The Prevalence of MEs varied significantly amongst hospitals. At the departmental level, inpatient wards had the most significant rates of MEs (14.69 per 1,000 patients), whereas emergency departments had the lowest rates (0.14).

Patient-Related Factors of ME

Table 1 illustrates the demographic and clinical features of individuals with MEs. The age distribution of the 318 patients revealed two main age groups: 1 month-2 years (37.7%) and 6-12 years (35.5%), with 57.2% of the patients being male. 60.4% of the patients in the study had comorbidities, and 7.2% had mental disabilities. The patient was unconscious in 13.8% of the instances, was taking four or more prescriptions in 48.1% of the cases, and had no carer present in 30.2% of the cases when the medication mistakes happened.

Table 1: Patient-Related Factors of Medication Errors

Parameter	Category	Frequency	Percentage
Center	CHAT	93	29.2
	KAMC	90	28.3
	KFSH	135	42.5
Patient's age *	0-30 days	9	2.8
	31 days – 2 years	120	37.7
	2-6 years	72	22.6
	6-12 years	113	35.5
Gender *	Male	182	57.2
	Female	132	41.5
Weight *	<5 kg	1	.3
	510 kg	132	41.5
	1120 kg	101	31.8
	>20 kg	79	24.8
Comorbidity‡	Any	192	60.4
	Cancer	39	12.3
	Hematological disease	35	11.0
	Mental disability	23	7.2
	Other chronic condition	184	57.9
Consciousness state *	Conscious	270	84.9
	Unconscious	44	13.8
Number of medications	13	86	27.0
	46	153	48.1
	7+	73	23.0
	Data not available	6	1.9
Presence of caregiver	No	96	30.2
	Yes	215	67.6
	Data not available	1	2.2

** Because of missing data, not all values sum up to the total*

‡ A patient may have more than one comorbidity

Patterns and Characteristics of MEs

Most commonly, MEs occurred at the prescribing stage (81.1%), were caused by a physician (83.3%), and were discovered by the pharmacist (85.5%). Premature medicine dose (34.0%), incorrect frequency (14.2%), and duration (10.4%) were the most common types of MEs, and cumulative mistakes (two or more errors in the same report) were discovered in 5.0% of instances (Table 2). The most common medication classes involved in MEs were antibiotics (25.5%), followed by supplements (9.4%) and corticosteroids (7.2%). High-alert medications were involved in 17.3% of the cases. The most common routes of administration were oral (49.7%) and IV (40.3%). Other medication characteristics are depicted in Table 3. Of the total MEs, 47 (14.8%) reached the patient (PRMEs rate=14.8%, NCC MERP class CF), among which only 2 (0.6%) were harmful and required intervention (PHMEs rate=0.6%, NCC MERP class EF) (Table 4).

Table 2: Characterising Patterns of Medication Errors

Error Characteristic	Category	Frequency	Percentage
Location	General Ward	139	43.7
	Outpatient clinics	89	28.0
	ED	34	10.7
	Pediatric ICU	31	9.7
	Neonatal ICU	23	7.2
	Nursery	2	0.6
Stage	Prescribing	258	81.1
	Transcription	3	0.9
	Dispensing	33	10.4
	Administration	20	6.3
	Monitoring	4	1.3
Type	Improper dose	108	34.0
	Wrong frequency	45	14.2
	Wrong duration	33	10.4
	Wrong strength	24	7.5
	Wrong Medication	23	7.2
	Wrong rate of infusion	20	6.3
	Wrong route	15	4.7
	Duplication	15	4.7
	Wrong dosage form	9	2.8
	ContraindicationKnown allergy	7	2.2
	Delayed dispensation	5	1.6
	Expired Medication	4	1.3
	Monitoring error	3	0.9
	Wrong patient	1	0.3
	Other §	6	1.9
Cumulative error	No (only one medication error)	302	95.0
	Yes (2 or more)	16	5.0
Days from prescription	Same day	305	95.9
	One day or more later	13	4.1
Person who discovered the error	Pharmacist	272	85.5
	Physician	2	0.6
	Nurse	43	13.5
	Patient	1	0.3
Professional in cause	Nurse	11	3.5
	Pharmacist	35	11.0
	Physician	265	83.3
	Data missing	7	2.2
Position	Junior	74	23.3
	Senior	56	17.6
	Data not available	188	59.1

§ Include damaged Medication (3), wrong instruction (2 cases), and trade name in prescription (1)

Table 3: Characteristics of the involved Medication

Parameter	Category	Frequency	Percentage
Class	Antibiotic	81	25.5
	Supplements (vitamins, minerals, etc.)	30	9.4
	Corticosteroids	23	7.2
	Antihypertensive	20	6.3
	Electrolyte	18	5.7
	Analgesic	15	4.7
	Anticonvulsant Antiepileptic	13	4.1
	Laxative	10	3.1
	Anti vomiting	8	2.5
	Psychotropics	8	2.5
	Other §	92	28.9
Route of administration	Oral	158	49.7
	IV	128	40.3
	IM	7	2.2
	Subcutaneous	9	2.8
	Topical / Local	16	5.0
	Other	7	2.2
Offlabel use	No	307	96.5
	Yes	11	3.5
Offlabel dose	No	313	98.4
	Yes	5	1.6
Offlabel route	No	317	99.7
	Yes	1	0.3
High alert	No	263	82.7
	Yes	55	17.3

§ Include 29 other medication classes involving 1 (0.3%) and 7 (2.2%) cases

Table 4: Distribution of Medication Errors According to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) classification

NCC MERP category	N	%
The error did not reach a patient	271	85.2
A: Circumstances or events that have the capacity to cause the error.	42	13.2
B: An error occurred, but the error did not reach the patient	229	72.0
Error reached the patient	47	14.8
C: An error occurred that reached the patient but did not cause harm.	35	11.0
D: An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm.	10	3.1
E: An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention.	1	0.3
F: An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalisation.	1	0.3

Factors Contributing to MEs

A lack of staff education and training regarding ME was identified in most cases (90.2%). The next three most frequently identified factors included an absence of double-checking (66.8%), missing clinical information of the patient (48.1%), and missing drug information (32.0%) (Figure 2).

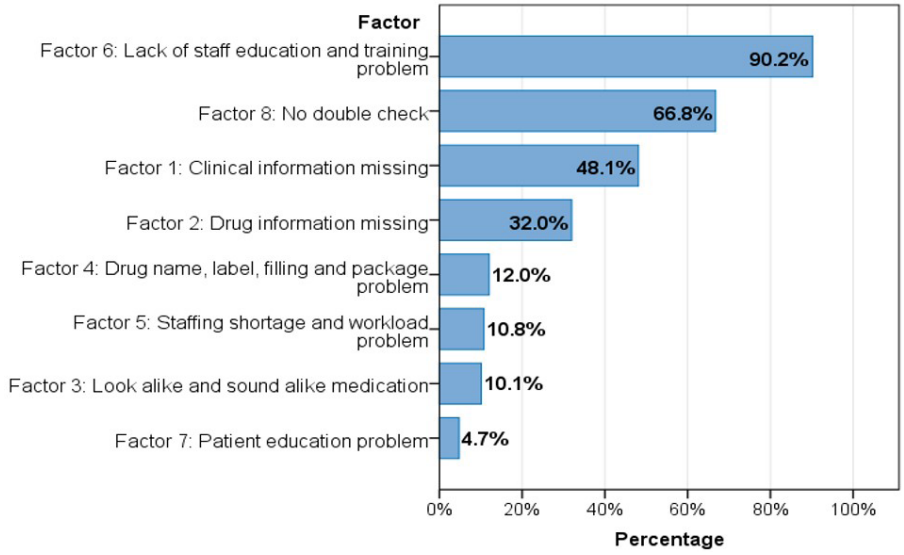

Figure 2: Contributing Factors in Medication Errors

Factors Associated with PRME

PRMEs occurred at the same frequency in the three hospitals (P = 0.241). PRMEs rate was significantly higher in ICU (31.5% vs. up to 13.5%, P = 0.001) and in the case of unconscious patients (38.6% vs. 11.1%, P < 0.001) and absence of caregiver (29.2% vs. 8.8%, P < 0.001), compared to their counterparts respectively; and the rate increased with the number of prescribed medications (P = 0.008). Expectedly, the later the stage of ME occurrence, the more likely it reached the patient (P < 0.001), and PRMEs occurred less likely in MEs occurring on the day of prescription of the involved Medication (13.1% vs. 53.8%, P < 0.001). Further, MEs caused by nurses were more likely to be PRMEs (72.2% vs. up to 34.3%, P < 0.001), whereas those discovered by a pharmacist were less likely to be PRMEs (10.3% vs. 39.5% or more, P < 0.001). High-alert medications were associated with a higher PRME rate (32.7% vs. 11.1%, P < 0.001). Three among the eight contributing factors increased the PRMEs' risk significantly, including drug name, label, filling, and package problem (39.5% vs. 11.4%, P < 0.001), staffing shortage and workload (29.4% vs. 13.0%, P = 0.011), and lack of doublechecking (20.3% vs. 3.8%, P < 0.001) (Table 5).

Table 5: Factors Associated with Medication Errors Reaching the Patient

Factor	Category	Error reached the patient				P-value
		No		Yes		
		N	%	N	%	
Center/Department factors						
Center	CHT	83	89.2	10	10.8	
	KAMC	78	86.7	12	13.3	
	KFSH	110	81.5	25	18.5	.241
Hospital type	Children	83	89.2	10	10.8	
	Tertiary	187	83.6	37	16.4	.193
Department	General Ward	122	86.5	19	13.5	
	ICU	37	68.5	17	31.5	
	ED	33	97.1	1	2.9	
	Outpatient	79	88.8	10	11.2	.001*
Patient-related factors						
Age	030 days	5	55.6	4	44.4	
	31 days - 2 years	100	83.3	20	16.7	
	2-6 years	64	88.9	8	11.1	
	6-12 years	98	86.7	15	13.3	.057
Gender	Male	159	87.4	23	12.6	
	Female	108	81.8	24	18.2	.277

Weight	<5 kg	0	0.0	1	100.0	
	5 10 kg	111	84.1	21	15.9	
	1120 kg	86	85.1	15	14.9	
	>20 kg	69	87.3	10	12.7	.107
Cancer	No	237	84.9	42	15.1	
	Yes	34	87.2	5	12.8	1.000[F]
Haematological disease	No	236	84.9	42	15.1	
	Yes	30	85.7	5	14.3	1.000[F]
Mental disability	No	248	85.5	42	14.5	
	Yes	18	78.3	5	21.7	.362[F]
Other chronic condition	No	112	87.5	16	12.5	
	Yes	153	83.2	31	16.8	.291
Consciousness state	Conscious	240	88.9	30	11.1	
	Unconscious	27	61.4	17	38.6	<.001*
Number of medications	13	78	90.7	8	9.3	
	46	133	86.9	20	13.1	
	7+	54	74.0	19	26.0	.008*
Presence of caregiver	No	68	70.8	28	29.2	
	Yes	196	91.2	19	8.8	<.001*
Factor related to the medication error						
Stage	Prescribing	235	91.1	23	8.9	
	Transcription	3	100.0	0	0.0	
	Dispensing	24	72.2	9	27.3	
	Administration	7	35.0	13	65.0	
	Monitoring	2	50.0	2	50.0	<.001*
Cumulative error	No	259	85.8	43	14.2	
	Yes (2 or more)	12	75.0	4	25.0	.270
Days from prescription	Same day	265	68.9	40	13.1	
	One day or more later	6	46.2	7	53.8	<.001*
Person who discovered the error	Pharmacist	244	89.7	28	10.3	
	Physician	0	0.0	2	100.0	
	Nurse	26	60.5	17	39.5	
	Patient	1	100.0	0	0.0	<.001*
Professional in cause	Nurse	3	27.3	8	72.7	
	Pharmacist	23	65.7	12	34.3	
	Physician	240	90.6	25	9.4	<.001*
Position	Junior	67	90.5	7	9.5	
	Senior	46	82.1	10	17.9	
	Data not available	151	84.4	28	15.6	.332
Factors Associated with the Medication						
Route of administration	Oral	136	86.1	22	13.9	
	Parenteral (IV, IM, s/c)	121	84.0	23	16.0	
	Topical / Local	14	87.5	2	12.5	.852
High alert	No	234	89.0	29	11.0	
	Yes	37	67.3	18	32.7	<.001*
Medication duration	Temporary	188	85.5	32	14.5	
	Chronic	78	83.9	15	16.1	.720

Contributing factors						
Factor 1	No	146	88.0	20	12.0	
	Yes	125	82.2	27	17.8	.151
Factor 2	No	187	86.6	29	13.4	
	Yes	84	82.4	18	17.6	.322
Factor 3	No	246	86.3	39	13.7	
	Yes	24	75.0	8	25.0	.088
Factor 4	No	248	88.6	32	11.4	
	Yes	23	60.5	15	39.5	<.001*
Factor 5	No	247	87.0	37	13.0	
	Yes	24	70.6	10	29.4	.011*
Factor 6	No	28	90.3	3	9.7	
	Yes	242	84.6	44	15.4	.396
Factor 7	No	260	85.8	43	14.2	
	Yes	11	73.3	4	26.7	.252F
Factor 8	No	101	96.2	4	3.8	
	Yes	169	79.7	43	20.3	<.001*

Factor 1: Clinical information missing;
Factor 2: Drug information missing;
Factor 3: Lookalike and sound-alike medication;
Factor 4: Drug name, label, filling, and package problem;
Factor 5: Staffing shortage and workload problem;
Factor 6: Lack of staff education and training problem
Factor 7: Patient education problem;
Factor 8: No double-check.

The test used: [F] Fisher's exact test; otherwise, the chi-square test was used.
* Statistically significant result

Inappropriate drug labelling or packaging (OR=3.13, p=0.042) and a lack of double-checking (OR=5.49, p=0.016) were independently linked with the incidence of PRME, according to multivariate regression analysis (Table 6).

Table 6: Predictors of Medication Errors Reaching the Patient

Predictor	**Level**	**OR**	**95%CI**		**P-Value**
Department	General Ward	Ref			.193
	ICU	0.35	0.07	1.65	.183
	ED	0.37	0.04	3.31	.374
	Outpatient	2.01	0.65	6.26	.227
Consciousness state	Conscious	Ref			
	Unconscious	2.95	0.67	13.07	.155
Number of medications	13	Ref			.970
	46	0.90	0.31	2.65	.852
	7+	0.99	0.27	3.71	.994
Presence of caregiver	No	Ref			
	Yes	0.39	0.13	1.16	.090
Days from prescription	Same day	Ref			
	One day or more later	12.43	2.15	71.70	.005*
Professional in cause	Nurse	7.71	1.37	43.49	.021
	Pharmacist	1.08	0.34	3.46	.892
	Physician	Ref			.061
High alert	No	Ref			
	Yes	2.46	0.95	6.38	.064
Factor 4	No	Ref			
	Yes	3.13	1.04	9.41	.042*

Factor 5	No	Ref			
	Yes	1.55	0.50	4.87	.450
Factor 8	No	Ref			
	Yes	5.49	1.37	21.94	.016*

Multivariate Binary Logistic Regression.
Dependent factor: patient-reaching medication error (yes).
OR: Odds ratio;
95% CI: 95% confidence interval
Ref: Category used as a reference in the calculation of OR
Factor 4: Drug name, label, filling, and package problem
Factor 5: Staffing shortage and workload problem
Factor 8: No double check
* Statistically significant result

DISCUSSION

MEs in the pediatric population constitute a significant health issue. They comprise a high risk of iatrogenic injury, which exposes increased morbidity, mortality, health expenditure, and legal issues. In the current multicenter investigation, we examined the trends and characteristics of all MEs reports from the two tertiary hospitals and the Children's Hospital in Saudi Arabia's Western area over the course of a year. Findings showed that ME Prevalence ranged between 0.35 and 3.5 /1,000 patients, depending on the hospital, and between 0.14 and 14.7 / 1,000 patients, depending on the department. Most MEs consisted of prescribing errors made by doctors and reported by the pharmacist.

Nevertheless, 14.8% of the MEs reached the patient was predicted by several risk factors, notably earlier prescription date, absence of doublechecking, and inappropriate drug labelling or package, with a 3 to 12-fold risk of occurrence. On the other hand, the rate of PHMEs was very low (0.6%), not enabling inferential analysis.

The Prevalence of MEs – Rates and Calculation Methods

Various calculation methods have been used to estimate the Prevalence of MEs in literature, making the comparative analysis difficult across different studies and settings. The Prevalence of MEs was determined in the current study by considering all hospital admissions or visits during the same period, depending on whether the ME occurred in an inpatient or outpatient environment. This calculation method adjusts for the patient flow in the given hospital or department while disregarding the number of medication orders.

A systematic review by Alghamdi *et al.* found that, in every 100 medication orders, approximately 15 MEs were reported in pediatric intensive care units and up to 78 in neonatal ICU (Santesteban *et al.*, 2015). Prescription mistakes were observed in between 5.7% and 35.2% of prescriptions or medicine orders for newborn care, according to three distinct studies, according to a second comprehensive analysis by Santesteban *et al.*. Another study that assessed the efficacy of a pharmacy-led intervention to reduce MEs in the pediatric ward of a Maternity and Children's Hospital, focusing on prescribing errors, found that an intervention was necessary for 10% of the medical orders (Jennifer L Costello 1, 2007). The rates reported in the previously mentioned studies, including the two systematic reviews, can be considered consistent with each other, highlighting an alarming frequency of MEs. These figures seem to be less reflected when using the number of hospital admissions as a denominator, such as in the present study.

Another calculation method that is reported in the literature uses the patient's parameter as the denominator. In the comprehensive systematic review by Alghamdi *et al.*, four studies-two in the PICU and two in the NICU-used this calculating approach and found that the prevalence rates of ME were, respectively, 6.4 to 9.1 and 4 to 35.1 per 1,000 patient days (Santesteban *et al.*, 2015). Compared to the 5.1 to 40.1 per 1,000 hospital admissions rates found in in-patient departments in the present study, the prevalence rates reported in Alghamdi et el. systematic reviews are likely to be considerably high; this is by assuming that patient days are higher than the raw number of hospital admissions. Although such a comparison is inaccurate due to dissimilar calculation methods, this appearing discrepancy may indicate a probable underreporting of MEs in our study population. In an intriguing method, Costello *et al.* demonstrated that underreporting of MEs is a significant limitation of the voluntary reporting strategy in an exciting approach. A pharmacist-led intervention would considerably enhance reporting of MEs while decreasing the severity of the errors reported (Dedefo *et al.*, 2016).

Other calculation methods were used in reporting MEs. For example, a study by Morriss *et al.* reported MEs prevalence in NICU regarding medication doses and found 69.5 MEs per 1,000 doses (Izadpanah *et al.*, 2018); such a method may be more applicable for dispensing errors. Based on nurses' self-reports, another study from Iran estimated the number of MEs involving nurses during the past month in pediatric emergency wards. The authors found that nurses caused an average of ~42 cases of MEs in the studied month (Emily Beth Devine 1 & Kerm Henriksen 1, 2005). Along with this variation in calculating techniques, Alghamdi *et al.* also emphasised a serious lack of uniformity in the definition of MEs used by various research, with several of them employing definitions that were created locally (Santesteban *et al.*, 2015). Such heterogeneity in MEs' definition and reporting systems and the calculation method of MEs prevalence

hinders the comparisons between the different studies and settings. This indicates the need for a standardised practice using evidence-based, homogenous strategies.

Types and Patterns of MEs

The current investigation showed doctors were the most frequently implicated in MEs, with prescription mistakes accounting for over 80% of cases. Second, nurses were engaged in 13.5% of the instances, particularly while giving medicine, which accounted for 10.4% of all MEs. Hence, the study revealed that the most common type of MEs was improper medication dose, strength, frequency, or duration, probably indicating the challenging aspect of the prescribing practice in the pediatric population. Given the frequency of prescribing errors in the pediatric population, several authors were concerned about studying this particular type of ME separately in pediatric settings.

Further, the authors reported that dosing errors were the most commonly reported subtype (Santesteban *et al.*, 2015). A study from South Africa consistently showed that the leading cause of ME in children was dose error, especially in intensive care, as this category of patients requires an individual description of drugs according to age, body, and weight. Medicines that increased the risk of error were antibiotics, sedatives, analgesics, bronchodilators, and cardiovascular medications (Khayam, 2015). A Saudi study in the general pediatric ward and PICU of King Abdulaziz Medical City, Riyadh, found that 56% of the medication orders contained prescribing errors, and 79% were classified as harmful. Additionally, dose and frequency errors accounted for approximately 50% of the cases, and an overdose was detected in 18.7% of the prescribing errors.

Conversely, a study conducted in neonatal care settings in the Tertiary Care Hospital of South India showed significantly higher rates of administration errors reported in some of the included studies, accounting for up to 77% of MEs (B Prakadeesh Bharathi, 2020). In contrast, other studies reported relatively higher rates of drug preparation errors (Morriss *et al.*, 2009). In sum, MEs can happen at any point throughout the administration of a medicine, from prescription to administration and follow-up, and drug interactions can even cause them. Thus, all healthcare professionals are responsible for detecting and prospectively managing the factors causing MEs when dealing with a patient (Abuelsoud, 2019).

Identification and Prevention of MEs Risk

The identification of the associated risk factors constitutes a critical step in the prevention of MEs. As revealed in the current study, among the predominantly identified factors is the lack of staff education and training regarding MEs, found in 90.2% of the cases. This was followed by an absence of doublechecking by the involved healthcare professional, accounting for two-thirds of the cases. Both issues can be corrected using education and awareness interventions targeting the concerned health professionals. Several factors for MEs are highlighted in the literature, such as multiple medications and extended stays in the hospital, which increase the risk of both MEs and drug interactions (Antonucci & Porcella, 2014). Further, neonatal care settings, notably NICU, are reportedly more exposed to MEs than other pediatric settings (B Prakadeesh Bharathi, 2020). Another study in Us revealed that Physicians were had an increased likelihood of major medical errors due to poor well-being, burn-out and low work unit safety grades (Tawfik *et al.*, 2018).

On the other hand, the current study has the particularity to have analysed factors associated with PRME. Finding such variables may be crucial for lowering the incidence and severity of MEs and related morbidity and mortality. Among these factors, we highlight the patient's consciousness status and the caregiver's presence or absence. The clinical significance of these two patient-related factors reflects the potential contribution of the patients or their caregivers in managing the risks of MEs. The adjusted regression model highlighted three other factors: the absence of doublechecking, which was demonstrated to increase the risk of PRME by 5.5 times in an independent fashion, and inadequate drug labelling and packaging, which increased the same risk by 3.1 times. This demonstrates the importance of enhancing the standards of routine practice among health professionals regarding medication use.

Prevention of medication errors should be set in health authorities and institutions. Of the several efforts undertaken to reduce ME rates, a significant focus is on using information technology to mitigate the human factor most commonly underlying MEs (Dedefo *et al.*, 2016; Fernández-Llamazares *et al.*, 2012; Khaemba, 2014). Another encouraged strategy is to increase the number of clinical pharmacists and enhance their training, as these constitute physicians' backup in ensuring the medical prescription's safety and adequacy (Devine EB, 2005). Reports showed that the role of clinical pharmacists in reducing MEs is prominent, owing to their crucial role in identifying issues related to the safe use of drugs and the potential health problems that arise from the misuse (Dedefo *et al.*, 2016). From a larger perspective, reducing MEs requires setting high-level caution at all stages of the mediation process, such as packaging, labelling, description, copying, dispensing, and administration in the internal and external patient settings. Particular attention should be drawn to managing home medication, which increases the risk of human error by involving a third party, including parents and caregivers. Hence, physicians should assess the family environment before prescribing for children to ensure correct administration (Hussain *et al.*, 2014).

STRENGTHS AND LIMITATIONS

The present study is limited by the reliance on a voluntary ME reporting system, resulting in under-reporting and underestimating ME prevalence rates. The study also overlooked potential measures for assessing and improving

ME reporting practises, which may differ between centres and departments. Further, the retrospective design made collecting relevant data a challenging task, notably the assessment of the contributing factors. Nevertheless, the present study has the advantage of being conducted in three referral centres and including all MEs reported in the study year. It supports the good external validity of the findings and provides a reliable baseline figure for further interventional studies in any of the three included centres.

CONCLUSION

Paediatric inpatient care has a significant frequency of MEs, especially in tertiary care facilities, which account for 24% of hospital admissions. Implementing a systematic doublecheck of prescriptions, including recent and older ones, and improving drug labelling and packaging methods may prevent many MEs. The adequate education of health professionals and caregivers regarding MEs should be considered a high-priority tool to improve medication safety among pediatric patients. Further corrective measures and awareness-raising campaigns should be implemented in all referral hospitals to modify the risk factors and improve medication practice at all stages.

Abbreviations

Children's Hospital in Taif (CHT), Confidence Interval (CI), Emergency Department (ED), Factor (F), Intramuscular (IM), Intravenous (IV), Intensive Care Unit (ICU), Institutional Review Board (IRB), Kingdom of Saudi Arabia (KSA), King Abdul-Aziz Medical City (KAMC), King Faisal Specialist Hospital and Research Center (KFSH&RC), Medication Error (ME), The National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP), Neonatal Intensive Care Unit (NICU), Odds Ratio (OR), Patient Harm medication error (PH-ME), Pediatric Intensive Care Unit (PICU), Patient Reaching medication error (PR-ME), Subcutaneous (S/C), Statistical Package for the Social Sciences (SPSS)

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