

Research Article

Evaluation of Patients Pharmaceutical Care Needs Unmet and Associated Factors in Pediatric Ward of Mettu Karl Referral Hospital, South Western Oromia, Ethiopia: A Prospective Observational Study, 2021

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Keywords

- Pharmaceutical care
- Pediatrics
- Associated factors
- Mettu Karl Referral Hospital
- Ethiopia

Abstract

Background: Pharmaceutical care is a practice in which the practitioner takes responsibility for a patient's drug-related needs, and is held accountable for this commitment. Responsible drug therapy is provided for the purpose of achieving positive patient outcomes. In pediatrics there is not much information, but it has been estimated that from 20 to 50% of children suffer some drug related problem during the hospital stay, although the majority of drug related problem are preventable.

Objective: To ascertain evaluation of patients pharmaceutical care needs unmet and associated factors in pediatric ward of Mettu Karl Referral Hospital.

Methods: A prospective observational study design was carried out from February 12//2020 to February 24/2021. Data was collected cleared, coded and analyzed by statistical packages for social sciences 23.0 version statistical software. Based on the univariate analysis, the variables that were significant ($P \leq 0.25$) were included in the multivariate analysis to control for confounders and to identify factors independently associated with the occurrence of drug related problems. P - Value <0.05 was considered as statistically significant.

Results: Of the study 189 study participants, 115 (60.8%), were males, and the participants mean age was 1.4339 ± 0.864 years. A total of 189 pediatric patients were included in the study, of these 121 (64.01%), patients had at least one drug therapy problem. The most frequently identified drug related problems were unnecessary drug therapy 42(34.7%), and need additional drug therapy 26(21.5%). Most 95 (50%), of patients were diagnosed for one case and the mean number of diagnosis per patient were 2.28. Ceftriaxone were the most frequently prescribed class of drugs accounted 272 (30%) from the total of 903 drugs prescribed. Out of 375 diagnosis encountered during the study severe pneumonia and bronchial asthma were the leading case accounted 118 (31.5%), and 62 (16.5%), of the total cases diagnosed respectively. Polypharmacy ≥ 5 medications (AOR=3.834, 95% CI= 0.443-7.57, $p=0.034$), length of hospital stay ≥ 5 days (AOR=1.48, 95%CI= (0.471-1.644), $p=0.018$), and co-morbidity (AOR =2.507, 95% CI: 1.270-4.949, $p=0.008$) were the independent predictors of drug therapy problem occurrence.

Conclusion and recommendations: Unnecessary drug therapy problem was mostly occurred in this study due to in appropriate indication of the medications and antibiotics is the class of drugs mostly encountered in drug therapy problem due to it was prescribed empirically. Comorbidity had been identified as major risk factors for occurrence of drug related problems. The health sector policy makers should continue to include clinical pharmacists in the hospital to involve and strengthen ward based clinical pharmacy services.

ABBREVIATIONS

ADE: Adverse Drug Events; ADR: Adverse Drug Reaction; Drps: Drug Related Problems; EFMHACA: Ethiopian Food, Medicine And Health Care Administration And Control Authority; ICU: Intensive Care Unit; JUSH: Jimma University Specialized Hospital; MKRH: Mettu Karl Referral Hospital; MMAPS: Morisky

Medication Adherence Predictor Scale; PEMPL: Pediatric Essential Medicine List; SSLR: Serum Sickness-Like Reaction; WURH: Wollega University Referral Hospital; ZMH: Zewditu Memorial Hospital.

INTRODUCTION

Drug Therapy Problem is an event or circumstance involving

drug therapy that actually or potentially interferes with desired health outcomes. An actual DTP is an event that the patient is currently experiencing even if they are well controlled, whereas a potential DTP is an event that the patient is not currently experiencing, but is at risk of developing due to either drug therapy prescribed or concurrent disease states [1,2]. Different drug therapy problem classification systems are published in literature up to date there is no consensus & uniform methods of classification of drug therapy problem. However, according to Cipolle, Morley & Strand all drug therapy problems are usually classified as; adverse drug reaction, dosage too low, ineffective drug therapy, needs additional drug therapy, unnecessary drug therapy, dosage too high, & non convenience. They are a major safety issue for hospitalized patients [3,4]. Many studies demonstrate the consequences of DRPs, which include additional physician office visits, long-term care admissions, hospitalizations, additional prescriptions, and emergency department visits [5]. Factors that contributes for occurrence of drug therapy problems in pediatric patients include : poly-pharmacy, certain infectious & parasitic diseases, type of admission, length of hospital stay,& number of disease condition [6], & also includes, missing information, poor patients knowledge of the drug use, administration of drug with a narrow therapeutic range, poly-morbidity, hepatic [7]. Patients suffering from chronic pain that are prescribed Opioids painkillers may build up a tolerance to the effect of the painkillers, requiring higher doses to achieve the same reducing effect. This risky practice of dose escalation can led to drug overdoses, some drug reduce the body's absorption of essential nutrients from food, which could lead to nutritional deficiencies [8]. Cefaclor, an oral second-generation cephalosporin, is commonly used to treat respiratory and skin infections in children. Recently a unique ADR, cefaclor induced serum sickness-like reaction (SSLR), in which the child develops urticaria, arthralgia and facial oedema on receiving a second or third course of cefaclor, has been identified [9]. In Pediatrics there is not much information, but it has been estimated that from 20 to 50% of children suffer some DRP during the hospital stay [10], children, and especially small children, receive considerable amounts of drugs and several studies indicate that drug related problems in children are of great clinical relevance and that many of them are preventable [11]. The differences in drugs pharmacokinetics & pharmaco-dynamics observed in children influence the choice of the drug, dose, dosage form & dosing interval [12]. The pediatric medication use process is complex & error prone because of the multiple steps required in calculating, verifying, preparing, administering doses [13]. These factors make the pediatrics to be at high risk for drug related problem. Therefore, all pediatric prescriptions & medication orders must be checked for its appropriateness of the dose, route, & frequency with a pediatrics dosing reference [14]. Pediatric inpatients may have three times more medication errors than adult in patients, and these errors are frequently harmful [15,16]. Neonates also show prolonged gastric emptying. Thus during the neonatal period, acid-labile medicines like benzyl penicillin and ampicillin are well-absorbed, while the absorption of medicines like phenytoin, Phenobarbital and Rifampicin is low. Moreover re flux of gastric contents retrograde into the esophagus is very common during the first year of life [17]. Children should not be treated as "miniature men and women. The spectrum extends

from the very small preterm newborn infant to the adolescent [18], although it is believed that DRPs are more frequent and severe in neonates than in older children and adults [19,20]. This is because of the physiological immaturity, which interferes with drug pharmacokinetics (absorption, distribution, metabolism and excretion), the rapid body growth combined with the administration of drug doses based on body weight, and the frequent use of off-label drugs [21,22]. In general lines, DRPs may involve errors in the drug therapy process (medication errors), or may result from a harmful effect of the drug (adverse drug reaction) [23]. Children, particularly small children, may be unable to express their sensations and complaints, a high proportion medicines used are off-label and unlicensed, many poorly evaluated phytotherapeutic, ayurvedic, anthroposophic, traditional and homeopathic medications are popular because they are perceived as "soft" and less toxic medicines by many parents, caretakers, and even health professionals, there is irrational use of medicines, e.g. antibiotics, clinical trials are lacking and experience and skills in reporting ADRs and ADEs are insufficient, a pediatric essential medicine list (PEML), has yet to be developed, appropriate medicine formulations and administration devices for, children are lacking [24,25]. However, children have therapeutic needs which probably cannot be met if medicines representing major therapeutic advances in adults are not tested and labeled for pediatric use. Once a medicine becomes available on the market for adults, it is possible to use it in children in an off label way. Thus use of unlicensed and off label medicines for children has been common practice for decades; this does not offer children the same quality, safety and efficacy of medicines as adults. This situation is not consistent with the United Nations convention on the rights of child [26]. This study could provide information for health care professionals to focus on DTP of medicine and also will help them by providing useful information for development of effective DTP reporting system and for awareness creation forums and training for them, and all essential activities for optimizing patient safety and to control the impact of DTP s on the patients and the society in the study area.

METHODOLOGY

Study design, period and study area

A Hospital based prospective cross sectional study was conducted in MKRH, Mettu town, South West Oromia, Ethiopia which is found at 600 km from Addis Ababa. Mettu, located in the Illu babor Zone of the Oromia Region along the Sor River, this town has a latitude and longitude of 8°18'N 35°35'E and an altitude of 1605 m. The hospital can give service for around 1.4 million clients. There are different wards and clinics within MKRH; those include internal medicine ward, surgery ward, pediatric ward, gynecology and obstetrics ward, Ante natal clinic, dental clinics, tuberculosis clinic, anti-retro viral therapy clinic and ophthalmic clinic. The study was conducted from February 12//2020 to February 24/2021.

Study subjects

All patients who admitted to the pediatric ward of MKRH during the data collection period & that fulfilled the inclusion criteria were target population. Patient who were on drug therapy or who needs drug therapy during study period,

Patients whose age was less than or equal to 18 years & complete registration charts, A patient whose hospital stays was greater than 2 days (48hrs), were included in the study. Patients whose back ground information was incomplete or no drug orders on their charts, pediatric patients who were admitted to intensive care unit, patients discharged before cross checking the collected data were excluded.

Sample size determination and sample technique

The sample size was determined by using the single population proportion formula: The sample size was determined based on 'P' value which was taken from ZMH, P=0.3157, or 31.57%, $n = \frac{(Z\alpha/2)^2 P(1-P)}{d^2}$. Where: n= sample size, P=prevalence

of drug therapy problem (p=0.3157), d=margin of sampling error tolerated (d=0.05), z=the standard normal value at confidence interval of 95% (z=1.96), So, $n = (1.96)^2(1- 0.3157) \times (0.3157) / (0.05)^2 = 332$, Since the total patients medical record cards from September 2020 to December 2020 is less than 10,000, which is 355, reduction formula(correction formula) was applied as follow; $n_f = n / (1+(n/N))$, $n_f = 332 / (1+(332/355)) = 172$, Where; n_f = final sample size, n=total study population, N=source of population, When 10% contingency is added to minimize non response rate, $172+(172 \times 0.1) = 189$, the total sample size was 189. Convenience sampling method was used to select sample arbitrarily & easy to use, less cost, & to get accurate results when the population is homogeneous

Study variables

Dependent variable was occurrence of drug therapy problems and independent variables were age, sex and family income, past medical history, poly pharmacy, duration of hospital stay, medication history, co-morbidity, number of drugs, drug type, and disease type.

Data extraction and procedure

Data was taken from patient medical charts & medical records. Structured data format (semi-structured check list) was employed to collect the required data for this study. The checklist had two parts. Part I (case identification), and part II (subjective data, objective data, laboratory results, assessment, prescribed medications and identified DTPs). Data was collected through medical record reviews of patients and asking care giver by using structured format. Data entry form was used to obtain information on demographics of patient (e.g. patient name, age, gender, height, weight, date of admission and date of discharge), presenting complaints, laboratory test reports, provisional/confirmed diagnosis, drug therapy given (with brand names and generic names of each drug, dose, duration and route of therapy). The content of the format include patient details, investigations, procedures, current and past medication and disease conditions. Drug related problems were identified by evaluating the appropriateness of prescriptions in terms of indication, dosage, untreated indication, safety, and efficacy. In order to evaluate the clinical significance of DRPs in neonates, each DRP was classified according to its safety-relevance, that is, the potential risk of a DRP for causing serious damage to the patient's health. Finally the existence of DTPs was identified using Ethiopian guide line,

the Pharmaceutical Care Network Europe (PCNE) classification of drugs related problems (DRPs) version 5.01 (PCNE, 2006). The principal investigator reviewed all filled format so that any suggestion and corrections was given soon. The two pharmacists who were involved in collecting the data in the inpatient setting had received similar professional training.

Data quality assurance

In order to assure quality of data important measures was undertaken including: the patient card number was used, to check for if there is invalid and incomplete pertinent response and these cards were also coded so over or under count was not matter. The data collected was checked for completeness and consistency on daily basis.

Statistical Analysis and interpretation

The gathered quantitative data was cleared, arranged, coded, and then analyzed through employing statistical packages for social sciences 23.0 version statistical software. Categorical variables were expressed by percentage and frequency, whereas continuous variables were present by mean and standard deviation. Model fitness was checked using the Hosmer-Lemeshow goodness of fit test (p = 0.29), and interpreted as a model fitted. Bi-variant and multivariable logistic regression was used to analyze the associations between dependent variable and independent variables. Among the uni-variate analysis, those variables with P< 0.25 were selected for multi variable binary logistic regression analysis. A p-value of less than 0.05 is considered statistically significant.

Ethical clearance

The study was commenced after approved by department of pharmacy, college of health sciences, and a formal letter was given to MKRH in order to get permission to conduct the study, and all the process was started after getting permission from MKRH. A letter was submitted to MKRH management then transferred to concerned bodies like doctors and nurses who were working in the pediatric ward of the hospital. Privacy and behind the scenes were ensured during data collection process. Patient or caregivers were informed about the study and their written consent was obtained using appropriate forms. Patient consent was obtained prior to data collection and no personal identity was disclosed. The instruments and procedure was not cause any harm to the study subject. Thus, name and address of the patient was not recorded in data collection checklist.

Operational definitions

Pediatrics: are those age groups less than or equal to 18 years including premature [27]

Drug therapy problem: is defined as, an event or circumstance involving drug treatment that actually or potentially interfere with desired health outcomes of patient and require professional judgment to resolve through careful assessment of patients, drugs, and disease information to determine the appropriateness of each medication regimen[28]

Hospital stay: The time gap will be spent by the patient in the hospital from his/her admission till his/her discharge (discharge

date will be determined by looking his/ her discharge date from his/her medical chart) [29].

Medication Error: Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient or consumer [30].

Pharmaceutical care: The process through which a pharmacist cooperates with a patient and other professionals in designing, implementing and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient [31].

Poly Pharmacy: The daily consumption of 5 or more medications [32].

Needs additional drug: this could occur when a patient needs more medication to treat their condition or Preventive therapy is needed to reduce the risk of developing a new condition or a medical condition requires combination therapy to achieve synergism or additive effect [33].

Unnecessary drug therapy: No valid medication indication for the drug at this time or this could occur when the patient has been placed on too many medications for their condition and the drug is simply not needed [34]

Ineffective drug therapy: The drug is not the most effective one for the medical problem or when a patient is given medication that does not treat the patient's condition or the condition is refractory to the drug product being used or the dosage form is inappropriate [35].

Dosage too high

The dose is too high for the patient or the dosing frequency is too short or the duration of therapy is too long or a drug interaction causes a toxic reaction to the drug product or the dose was administered too rapidly & this could occur when a patient is given medication that is too strong & is causing detrimental effects or is simply not necessary [36].

Noncompliance: This could occur when a patient chooses not to or forgets to take a medication or the patient does not understand the instructions or the patient prefers not to take the medication or Drug product is too expensive or the patient cannot swallow or self-administer the medication properly [37].

ADR: The drug product causes an undesirable reaction that is not dose-related or this could when a patient has an allergic response to a medication or safer drug is needed because of patient risk factor or a drug interaction causes an undesirable reaction [38].

Dosage too low: The dose is too low to produce the desired outcome or the dosage interval is too infrequent or this could occur when a patient is given medication that is not strong enough to get beneficial or therapeutic effects & a drug interaction reduces the amount of active drug available or the duration of therapy is too short [39].

RESULTS

Socio-demographic factors and clinical characteristics of respondents

A total 189 of patients were included in this study, of which

115 (60.8%), were males and 74 (39.2%), were females. Most of 73(38.6%), them were infant, whereas adolescent covered the least 20 (10.6%), from all age groups admitted during this study. The mean age of patients was 1.4339 years, ranging from 1 day to 18 years and the mean weight of patients was 10.6799 kg with minimum and maximum range of 1.5 kg to 29 kg respectively. From the total 189 of patients 106(56.1%), & 83 (43.9%) lives in rural and urban respectively. From the total 189 of patients 115 (60.8%), of them had a past medical history and 104 (55%), patients had past medication history. Most of 131 (69.3%), patients were immunized and 90(47.6%) was take greater than five medication per diagnosis. From the total 189 of patients the laboratory values were done for 95(50.3%), patients. The mean age, weight, and number of medication 1.4339, 10.6799, and 4.79 respectively. The mean number of hospital stay was 4.29 days with minimum and maximum stay of 2 and 9 days respectively. Out of 189 patients 121(64.01%), had at least one drug therapy problem. The eight item MMAPS was shows 148(78.3%), is low which is mostly adherent to medication. The ten naranjo adverse drug reaction probability scale was show most adverse reaction predictor scale was doubt fully 119(63.0%) (Table 1).

Types of DRPs in pediatric patients admitted to pediatric ward

DTPs were classified in to seven types along with respective magnitude such as unnecessary drug therapy, need additional drug therapy, dose too high and ineffective drug therapy were the most predominantly encountered DRPs accounted 42 (34.7%), 26 (21.5%), 15 (12.4%), 15(12.4%) of the total DTPs respectively. Adverse drug reaction drug therapy and non-compliance drug therapy were the least DRP identified 6.6%, 3.3% respectively (Figure 1).

Diagnosis and medication use status of pediatric patients

Out of 375 diagnosis encountered during this study period severe pneumonia and bronchial asthma were the leading case accounted 118 (31.5%), 62 (16.5%), of the total cases diagnosed respectively. Acute gastro enteritis and Malaria were also common, with a magnitude of 53(14%), and 43(11.5%), respectively. Most 95 (50%), of patients were diagnosed for one case and the mean number of diagnosis per patient were 2.28. Ceftriaxone were the most frequently prescribed class of drugs accounted 272 (30%), from the total of 903 drugs prescribed. Paracetamol were also the second common drug class prescribed contained 112 (12.4%), and less frequently prescribed drugs accounted 43(4.8%), of the total drugs prescribed. The mean numbers of drugs prescribed were 4.79 per patient ranging from 2 to 9 for minimum and maximum respectively (Table 2).

Class of drugs mostly cause DRPs in pediatric patient ward

Total of 435 drugs were involved in different types of DRPs. Among these the classes of drugs mostly involved in DRP were antibiotics 212 (48.7%), followed by fluid and electrolytes 18(18.7%), and diuretics 4(1.0 %), were involved in DRP followed by Antimalarial agents 5(1.2%) (Table 3).

Table 1: Socio-demographic factors and clinical characteristics of drug related problem in patients admitted to pediatric ward of MKRH from February 12/2020 to February 24/2021.

Variables	Category	frequency	percent
Age	Neonate(birth to 28 days)	27	14.3
	Infant(29 days to 1 year)	73	38.6
	Children(>1 year to 14 years)	69	36.5
	Adolescents(>14 years to 18 years)	20	10.6
Sex	Male	115	60.8
	Female	74	39.2
Residence	Urban	83	43.9
	Rural	106	56.1
Past medical history	No	74	39.2
	Yes	115	60.8
Past medication history	No	85	45.0
	Yes	104	55.0
Laboratory values	No	94	49.7
	Yes	95	50.3
Immunization	No	58	30.7
	Yes	131	69.3
Length of hospital stay	<5 days	99	52.4
	>5 days	90	47.6
Co-morbidity	No	80	42.3
	Yes	109	57.7
Number of medications per patient	<5 medications	85	45.0
	>5 medications	104	55.0
Drug therapy problem prevalence	No	68	35.6
	Yes	121	64.01
Morisky medication adherence predictor scale	Low	148	78.3
	Moderate	27	14.3
	High	14	7.4
Naranjo adverse drug reaction predictor scale	Doubtfully	119	63.0
	Possible	13	6.9
	Probable	50	26.5
	Definite	7	3.7

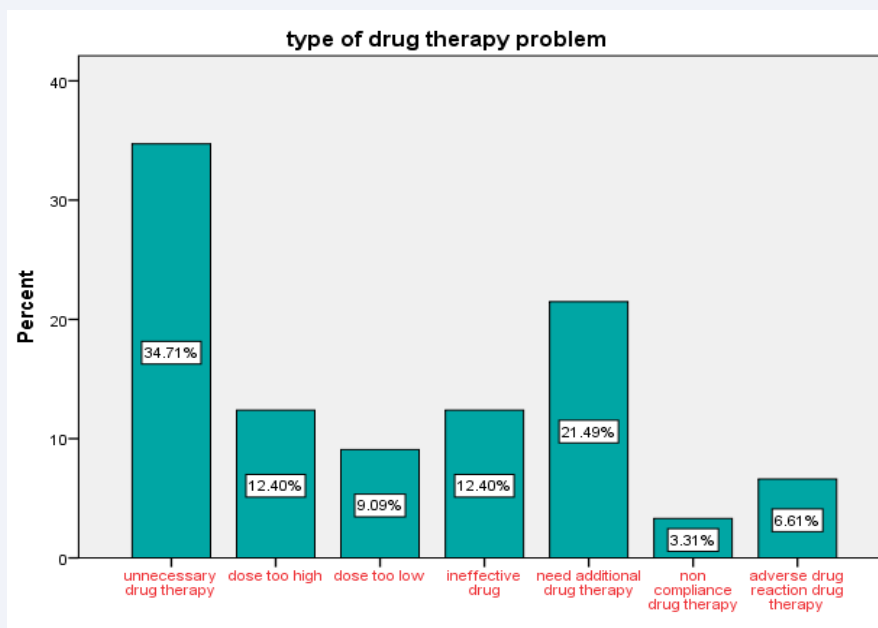


Figure 1 Types of DRPs encountered in pediatric patients admitted to MKRH February 12/2020 to February 24/2021.

Predictors of drug related problems of patients in medical ward

Bivariable logistic regression was conducted to comprehend variables which associated with presence of drug therapy problem among medical ward patients in MKRH. Polypharmacy ≥ 5 medication were 4 time more likely cause DTPs (AOR=3.834, 95% CI= 0.443-7.57, $p=0.034$), than who taken < 5 medication, length of hospital stay ≥ 5 days were 1.5 times more likely cause DTPs (AOR=1.48, 95%CI= (0.471-1.644), $p=0.018$) than who stayed < 5 days. Patients who had at least one comorbidities were 3.67 times more likely cause DTPs (AOR=2.507, 95%CI= 1.270-4.949, $p=0.008$) than who hadn't comorbidities (Table 4).

DISCUSSION

The goal of drug therapy is to achieve defined therapeutic outcomes and improve the patient's QOL while minimizing patient risk. But inappropriate use of drugs during disease management may lead to drug therapy problems. Identification of common types of DRPs and common drugs involved in DRP is an important component of drug therapy and contributes to reduction of drug related morbidity and mortality. Majority of studies conducted at different countries showed higher prevalence of drug related problems and indicated different drugs and drug classes involved

in DRPs [40]. Different factors are associated with the occurrence of DRPs in pediatric patients. This study was tried to identify the magnitudes and determinants of this DRP among pediatric patients admitted to pediatric wards. The prevalence of DRP in our study was 121 (64.01%), which higher than the study done in Malaysia (52.9%), and Hong Kong (21%) [41,42]. Because in this study pharmacists perhaps don't round with doctors in pediatric ward and they don't critically helping patients get the best results from their medications. In addition, the prevalence was lower than the study done in college university referral hospital (71.57%), Jimma University Specialized Hospital (74.3%), Dessie Referral Hospital (87.7%), Wollega university referral hospital (71.51%) [43-46]. However, comparable findings were reported from Northern Sweden (66%) [47]. The difference in magnitudes of DRP observed across different countries might be due to a variation in DRPs classifications and study settings. Despite this difference observed, the interventions should be done to resolve DRPs to improve patients' treatment outcomes, and future researchers should use similar DRPs classification systems to generate evidence-based recommendations.

The second encountered drug therapy problems in this study was need additional drug therapy 21.5%, and the ceftriaxone is the most encountered drug in drug therapy problems in this

Table 2: Diagnoses and Medication use status of pediatric patients admitted to pediatric ward in MKRH from February 12/2020 to February 24/2021.

Variables	Category	Frequency	Percent
Diagnosis	Severe community acquired pneumonia	118	31.5
	Acute gastroenteritis	53	14.0
	Bronchial asthma	62	16.5
	Meningitis	21	5.6
	Neonatal sepsis	37	9.8
	Severe acute malnutrition	13	3.5
	Febrile seizures	10	2.6
	Acute febrile illness	12	3.4
	Malaria	43	11.5
	Others*	6	1.6
	Total	375	100
Medication	Ceftriaxone	272	30.0
	Paracetamol	112	12.4
	Artesunate	43	4.8
	Hydrocortisone	80	8.9
	Fluid and electrolytes	75	8.4
	Ampicillin	67	7.4
	Gentamycin	77	8.5
	Dexamethasone	55	6.1
	Vitamins' and minerals	53	5.9
	Others**	69	7.6
	Total	903	100

Others*.diabetes mellitus, urinary tract infections, chronic liver disease, anemia, juvenile arthritis

Others**.Metoclopramide, Insulin, Plump nut, Lasix, Vancomycin, Augmentin, Cimetidine, Folic acid

Table 3: Class of drugs mostly cause DRPs in pediatric patients admitted to pediatric ward in MKRH from February 12/2020 to February 24/2021.

Class of drugs	frequency	percent
Antibiotics	212	48.7
Antipyretics	69	15.8
Fluid and electrolytes	81	18.7
Corticosteroids	18	4.0
Bronchodilators	21	4.8
Minerals and vitamins	13	3.0
Diuretics	4	1.0
Anti-epileptic drug	8	1.8
Antimalarial agents	5	1.2
Others	4	1.0
Total	435	100

Others. Anti-emetic, anti-anemic, H₂ antagonists

Table 4: Bi variate and Multi variate logistic regression analysis result of factors associated with DRPs among pediatric patients admitted to pediatric wards of MKRH from February 12/2020 to February, 24/2021.

Variables	Category	DRPs		COR(95%CI)	AOR(95%CI)	P-value
		Yes (n=121)	No(n=68)			
Age	neonate	18(66.6%)	9(33.3%)	ref	ref	1
	infant	50(68.5)	23(31.5%)	2.933(0.789-10.984)	3.213(0.831-12.42)	0.091
	children	40(57.9%)	29(42.1%)	0.903(0.33-2.474)	0.937(0.333-2.638)	0.93
	adolescents	13(65%)	7(35%)	1.25(0.45-3.476)	1.314(0.457-3.778)	0.612
Sex	Female	47(63.5%)	27(36.5%)	ref	ref	0.346
	Male	80(76.2%)	25(23.8%)	1.291(0.698-2.388)	1.393(0.698-2.78)	
Residency	Urban	52(71.2%)	27(28.8%)	ref	ref	0.417
	Rural	70(66%)	36(34%)	0.899(0.495-1.635)	10.762(0.395-1.47)	
Past medical history	No	49(57.6%)	36(42.4%)	ref	ref	0.513
	Yes	68(65.4%)	36(36.6%)	1.272(0.698-2.32)	1.254(0.626-2.523)	
Immunization	No	41(70.7%)	17(29.3%)	ref	ref	0.724
	Yes	90(68.7%)	41(31.3%)	0.986(0.518-1.876)	1.142(0.547-2.385)	
Length of hospital stay	<5	52(56.5%)	40(43.5%)	ref	ref	0.018*
	>5	52(53.6%)	45(46.4%)	0.84(0.463-1.522)	1.48(0.471-1.644)	
Poly pharmacy	No	49((55.7%)	39(44.3%)	ref	ref	0.034*
	Yes	57(56.4%)	44(43.6%)	0.884(0.487-1.603)	3.834(0.443-7.57)	
Co morbidity	No	69(57.9%)	50(42.1%)	ref	ref	0.008**
	Yes	43(61.4%)	27(38.6%)	1.579(0.856-2.914)	2.507(1.270-4.949)	

AOR: Adjusted odd ratio; CL: Confidence interval; COR: Crude odd ratio, ref: reference
 *P-value <0.05, **P-value <0.01

study, which was comparably similar with the study done in Wollega university referral hospital which shows need additional drug therapy was the widely occurred drug related problem that accounts for 22.77%, and the most common drug associated with the drug therapy problem was ceftriaxone 44.77% [46]. Because in pediatric patients ceftriaxone prescribed empirically to manage the infectious diseases and several diseases were not treated well, so it needs additional treatment to be managed. The most frequently encountered drug related problems in this study were unnecessary drug therapy, needs for additional therapy, and dose too high, ineffective drug therapy. From those needs

for additional drug therapy was the leading DTP isolated in this study accounted 22.5% this is less than with study conducted in four French speaking countries and 5 pediatric clinics in Greece which explained needs additional drug as the most common with 25% and 28% respectively [48]. Due to sample size variation and study area means this study solely conducted in one hospital contrary to four French speaking countries and 5 pediatric clinics in Greece and also due to physicians prescribed the medication without right indication and more medication once to manage various pediatrics diseases. Noncompliance was most common DRP explored in Victoria and Bangkok 50% and 36%

respectively, but in this study it accounted 3.3% which was less than in Victoria, because due to majority of this study subjects was infants intravenous route of administration which had rare noncompliance type of drug related problems, and in the present study, unnecessary drug therapy (42(34.7%)), need additional drug therapy (36(21.5%)) and dose too high (15(12.4%)) were the most commonly occurred DRPs. This was similar to the finding of Hiwot Fana Specialized University Hospital in which inappropriate indication was the commonly occurred DRPS [49]. Due to pediatric patients experience unique differences from the adult population in pharmacokinetic parameters and consequently, require individualized dosing. Medications useful in pediatric medicine often lack a therapeutic indication and dosing guideline for this population. In addition, a study from the University of Gondar showed inappropriate dosage was the most commonly occurred type of DTP 39.1% [50].

According to the finding of Dessie Referral Hospital, needs additional drug was the most common DTP and the ineffective drug was the least [51]. Ineffectiveness was the widely occurred DRPs according to the study conducted in Newton Paiva University Center, Brazil [52]. Because most drugs administered through intravenous rather than oral route of administration which was responsible for noncompliance in this study. In this study, the most common drugs associated with at least one of the DRPs were ceftriaxone (272(30%)), paracetamol (112 (12.4%)), and hydrocortisone (80 (8.9%)). Similarly, the study conducted in Dessie Referral Hospital revealed that antibiotics, cardiovascular drugs, and non-steroidal anti-inflammatory drugs were the most common class of drugs associated with DRPs. Specific to the drugs ceftriaxone; spironolactone, Enalapril, and furosemide were highly associated with DRPs. Because pediatrics patients were vulnerable to different infectious diseases in which antibiotics especially ceftriaxone were highly prescribed empirically. On the contrary, to the study conducted in the University of Gondar showed that the most common agents associated with DRPs were Omeprazole, heparin, and acetylsalicylic acid [53]. Perhaps due to geographical locations and the diseases mostly occurred in the pediatric patients. Finally, our study show patients who had co-morbidity had 2.5 times more likely to had at least one DRPs than patients who hadn't co-morbidity (AOR=2.507,95% CI:1.270-4.949,P=0.008), which is higher than the study conducted in WURH shows patients who had co-morbidity had 2 times more likely to had at least one drug therapy problems [46]. Because patients who had comorbidities facing drug disease interaction which exaggerated the illness due to fear of adverse drug disease interaction they were not adherent to the medication then DRPs were finally occurred. In this survey bivariable logistic regression was conducted to comprehend variables which associated with presence of drug therapy problem among medical ward patients in MKRH. Polypharmacy ≥ 5 medication were 4 time more likely cause DTPs (AOR=3.834, 95% CI= 0.443-7.57, p=0.034) than who taken < 5 medication, length of hospital stay ≥ 5 days were 1. 5 times more likely cause DTPs (AOR=1.48, 95%CI= (0.471-1.644), p=0.018) than who stayed < 5 days. Because polypharmacy perhaps decrease pediatric patients medication adherence due to missing understanding and unable to afford if expensive medications and also due to forgetfulness frequency, dose or time interval, cause drug-drug/diseases/food interaction, and

minimize safety of medication by causing side effects/adverse events. Length of hospital stay ≥ 5 days perhaps also increasing patients staying in hospitals /made them hospitalized patients in which patients facing others infectious diseases which seeking additional medications to manage the diseases occurred in hospitals, then drug related problems perhaps also occurred due others medication added to their first used regimen.

CONCLUSION

It is concluded from this study, drug related problems are common in pediatric wards. Unnecessary drug therapy was the top ranking DRP followed by Needs for additional drug therapy, dosage too high, and ineffective drug therapy respectively. The most common drug classes prescribed in this study and involved in DRPs were anti-bio tics, followed by Antipyretics. Co-morbidity was the major independent risk factors for the occurrence of drug therapy problems in pediatric wards, and also infants were the risk factors for DRPs occurrence. MKRH should be prepared formal policy for dug procurement to maintain stable medication availability. The role of clinical pharmacists should also be accounted to ascertain, figure out, and avert DRPs. A strategy to prevent the occurrence and consequences of DRPs including education of nurses/physician's is a paramount importance.

RECOMMENDATIONS

Based on the findings of this study, the following recommendations are suggested

The health sector policy makers should continue to include clinical pharmacists in the hospital to involve and strengthen ward based clinical pharmacy services. Clinical pharmacist can play great role in identifying DTPs with other health care providers. MKRH should be prepared formal policy for dug procurement to maintain stable medication availability. Researchers: large and comprehensive studies should be initiated in pediatrics to ensure rational use of drugs by identifying existing DRPs. EFMHACA and WHO: to establish pediatrics drug therapy problem guideline on the national level for effective pharmaceutical services.

Strength

The prospective observational study was following up and it compares the exposure and outcome of disease and also identifies the prevalence of drug therapy problems during this study period accordingly.

LIMITATION OF THE STUDY

Unavailability of some laboratory investigations challenged and made it difficult to ascertain the severity of the problem. The study did not show the overall prevalence of DRPs for a patient rather it shows DRPs up to patients discharge. Because of time limitation the authors couldn't pretest this questionnaire. Lack of drug related problems policy at national level is also other limitation of this study.

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DATA AVAILABILITY

The data used in this study can be obtained on written request to the corresponding author.

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