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Clinical pharmacists' interventions about drug therapy problems and its acceptability by prescribers among pediatric hospitalized patients with infectious diseases in resource-limited settings

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Abstract

Background Infectious disease continues to be a major cause of death among pediatrics. Drug therapy problem (DTP) is a significant public health challenge that is highly prevalent in pediatrics, and it has an impact on the effectiveness and safety of drug therapy to a greater extent than in adults. Thus, this study aimed to determine the magnitude of DTPs, types and acceptability of pharmaceutical interventions by prescribers and its associated factors among hospitalized pediatric patients with infectious diseases at pediatric wards of Public comprehensive specialized hospitals (PCSHs).

Methods This multicenter crosssectional study was conducted among pediatric patients with infectious disease admitted to PCSH pediatric wards from December 01, 2023, to February 30, 2024. Cipolle's and Strand's DTP classification methods were used for the identification of DTPs. Pharmaceutical interventions and their acceptance rate by prescribers were classified according to the Pharmaceutical Care Network Europe (PCNE) 2019. Data was entered and analyzed into SPSS version 27. To identify predictors of DTP occurrence, multivariable logistic regression analysis was used. A pvalue of less than 0.05 was considered statistically significant.

Results A total of 389 pediatric patients were involved in the current study, selected from an initial sample size of 405, resulting in a response rate of 96.05%. The overall prevalence of DTPs was 56.56% which occurred in 220 pediatric hospitalized patients with infectious disease. The most commonly encountered type of pharmaceutical intervention provided was adjusting the dose of medication (25.2%), followed by patient education/counseling/adherence (23.2%), and discontinuation of medications (20.54%). The acceptance level of interventions by prescribers was high (84.0%). Medication non-compliance (43.6%), unnecessary drug therapy (16.0%), and dose too high (12.0%) were common types of DTPs. Patients with the prolonged hospital stay (6–10 days) [AOR = 2.02, 95%CI: 1.33–7.80] and more

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than ten days in hospital [AOR = 2.89, 95%CI: 1.90-11.23]; patients with high number of medications (≥ 5) [AOR = 4.60, 95%CI: 1.89–8.82]; those who paid for their medications [AOR = 2.19, 95%CI: 1.18, 3.31], and patients with comorbidity [AOR = 3.90, 95% CI: 1.56–8.15] were the predictors of the occurrence of DTPs.

Conclusion This study finding revealed that the magnitude of DTPs was high in pediatric inpatients with infectious diseases at PCSHs. The presence of comorbidity, source of medication fee, polypharmacy, and prolonged hospital stays were factors associated with the occurrence of DTPs. The acceptance rate of interventions by the prescribers was high. Clinical pharmacists' involvement in direct patient care responsibility astutely reduces drug therapy problems and hence increases patient safety.

Keywords Drug therapy problem, Pediatrics, Infectious disease, Patient safety, Intervention

Introduction

Infectious diseases constitute a public health threat worldwide to humans [1]. Infectious diseases continue to be a major cause of death among pediatrics [2]. They are among the greatest health problems affecting pediatrics these days [3, 4]. According to global estimates, of the 6.3 million children who died before 5 years of age, about 3.26 million (51.80%) children died of infectious diseases, with pneumonia, diarrhea, malaria, meningitis, and neonatal sepsis being the leading infectious diseases [5].

Pediatric patients are at a higher risk of developing drug therapy problems (DTPs) compared to adult patients due to their body surface area, weight, and development of organ function, which vary from adults and within their age groups, and this variation impacts the effectiveness and safety of pharmacotherapy [6]. Organ systems like the liver and kidneys are immature in pediatrics, which can significantly affect the pharmacokinetics and dynamics of drugs [7]. DTPs are undesirable events following drug therapy and prevent the patient from achieving a therapeutic plan. They include unnecessary drug therapy, need for additional drug therapy, ineffective drug therapy, dosage too low, adverse drug reactions, dosage too high, and non-compliance [8]. Globally, DTP has increased significantly over the past few decades [9], and it may occur at any time, such as during medication use, and from prescription to follow-up treatment [8].

The different steps required for calculating, reviewing, preparing, and administering dosages, as well as the more complex handling of medications intended for children, contribute to the increased risk of DTP in children [10]. When pediatric medications are optimized without solid research evidence or appropriate formulations of drugs, there is a greater likelihood of harm [11–14]. It is essential to understand and take into consideration the role that growth and development play in drug disposition and actions to provide children with safe and effective drug therapy [15]. It's crucial to understand that because processes related to absorption, distribution, metabolism, and excretion alter during the course of growth and development, extrapolation may result in an estimation that is wrong dose either dose too low or dose too high [16].

DTPs can lead to adverse drug event which is a prevalent patient safety issue, increased length of hospital stay, higher total treatment cost, high demand for more drugs, and patient morbidity and mortality [17–20]. Identifying the determinants of DTPs in pediatrics is crucial for developing targeted interventions to optimize medication use and improve patient outcomes [17, 19, 21]. Various factors contribute to the occurrence of DTP including but not limited to; polypharmacy, number of infectious diseases, prolonged hospital stay, number of diseases, comorbidities, and number of drugs per patient [17, 19, 22–24]. The annual estimated cost of drug-therapy problem-related morbidity and mortality resulting from non-optimized drug therapy was $528.4 billion in 2016 US Dollars (USD) [25].

Interventions by clinical pharmacists have been considered as a valuable contribution by the community in patient care by minimizing medication errors, optimizing medication therapy, and reducing the total cost of therapy [26]. Involvement of clinical pharmacists in patient care is used to reduce medication errors and adverse drug events, while treating physicians approve the majority of clinical pharmacist interventions in many clinical conditions [27]. The level at which prescribers accept clinical pharmacist interventions is a big issue for assessing the role of the clinical pharmacist in the detection and identification of DTPS.

In Ethiopia, the burden of infectious diseases remains high, particularly among pediatrics, and this group of inpatients with infectious diseases is likely to be exposed to complex drug regimens, increasing the risk of DTPs [17–19, 28]. However, there is limited evidence on the magnitude, level of clinical pharmacist interventions' acceptability by prescribers, and determinants of DTPs in the pediatric hospitalized patient population with infectious diseases in Northwest Ethiopia. Therefore, this study aimed to determine the magnitude of DTPs, types, and acceptability of pharmaceutical interventions by prescribers and their associated factors among hospitalized pediatric patients with infectious diseases in

comprehensive specialized hospitals (CSHs) in Northwest Ethiopia.

Methods

Study design, period, and settings

This multicenter-institutional based crosssectional study was conducted from December 01, 2023, to February 30, 2024, at the pediatric ward of public comprehensive specialized hospitals (PCSH) in Northwest Ethiopia. PCSHs include the University of Gondar, Debre Tabor, Felege Hiwot, Tibebe Ghion, and Debre Markos. The University of Gondar CSH is located 750 km northwest of Addis Ababa, and the hospital serves more than 7 million people in the Amhara region. Debre Tabor CSH which is located at a distance of 667 km from the capital city, Addis Ababa, and 104 km from Bahirdar City, provides service for more than 3 million people in the area. Felege Hiwot and Tibebe Ghion CSHs are located in Bahir Dar City, the capital of the region, which is 565 km from Addis Ababa, and the hospital serves about 5 million people. Debre Markos CSH is located 300 km from Addis Ababa and provides service for an estimated population of 5 million.

Source population and study population

The population source was all pediatric infectious disease patients admitted to PCSH pediatric wards in northwest Ethiopia. The study population comprised all pediatric patients with infectious diseases who were admitted to pediatric wards of PCSHs during the study period and who fulfilled the inclusion criteria.

Inclusion and exclusion criteria

Pediatric patients (age < 18 years) admitted to the pediatric wards of PCSHs and stayed for more than 24 h, diagnosed with at least one infectious disease, and received at least one medication, and pediatric patients whose parent/guardian signed the written informed consent were included in the study. Pediatric hospitalized patients who were readmitted, patients who stayed less than 24 h, were admitted to the intensive care unit (ICU) and those not signed written informed consent were excluded from the study.

Variables of the study

The outcome variable was drug therapy problems (yes/no) and types and acceptability of pharmaceutical interventions by prescribers about drug therapy problems. The explanatory variables included the gender, age, weight, duration of hospital stay, number of drugs used, presence of comorbidity, number of infectious disease, number of disease condition, class of drug prescribed, place of residence, involvement of family in the childcare, previous history of medical illness, source of medication fee, severity of the disease, level of consciousness and type of admission to the hospital.

Sample size and sampling technique

Single population proportion formula was used to estimate the sample size required for the study

Where,

n = required sample size.

z = confidence level of 95% (95%).

p = estimated prevalence from the previous study.

d = estimated margin of sampling error with the assumption of 95% confidence interval (CI), marginal error (d) of 5%, Zα/2 = 1.96, and p = 60.2% from the study was conducted among pediatric patients admitted to Wolaita Sodo University Comprehensive Specialized Hospital [17]. Then, by considering a 10% non-response rate, the required total sample size is 405. Having this minimum study sample size, proportional allocation of samples to the total population of each PCSH pediatric ward was applied using the formula as follows (Fig. 1):

$n = \frac{ni*Ni}{N}$ Where; n =total sample size to be selected, N =total population, Ni = total population of each PCSH pediatric ward for the period of four months, and ni =sample size from each PCSH pediatric ward.

Debre Tabor; n1= (405*430)/ 2610 = 67
University of Gondar; n2= (405*683)/2610 = 106
Felege Hiwot; n3= (405*588)/2610 = 91
Tibebe Ghion; n4= (405*467)/2610 = 72
Debre Markos; n5= (405*442)/2610 = 69

Total sample size = n1 + n2 + n3 + n4 + n5 = 405, but in the current study 389 pediatric inpatients were involved by using a simple random sampling technique with a response rate of 96.05% (389/405), sixteen study participants were withdrawn because of unwillingness to take part in the study.

Drug therapy problem (DTP) detection among pediatric inpatients

The DTP evaluation tool was prepared based on Cipolle's and Strand's DTPs category classification system, a widely accepted patient- centered tool, which is the standardized guideline for clinical pharmacists in clinical practice during provision of pharmaceutical care [8]. DTPs were identified by using the Pocketbook of Pediatric Hospital Care [29], Ethiopian Standard Treatment Guidelines 2021 [30], and textbook of Pediatrics (Nelson 21st edition). The identified DTPs were classified and defined [31] as follows: [1] Unnecessary drug therapy: Is a DTP that occurs when there is no valid medical indication for the drug at the time, multiple drug products are used when only single-drug therapy is appropriate, or the condition is best treated with nondrug therapy [2], Needs

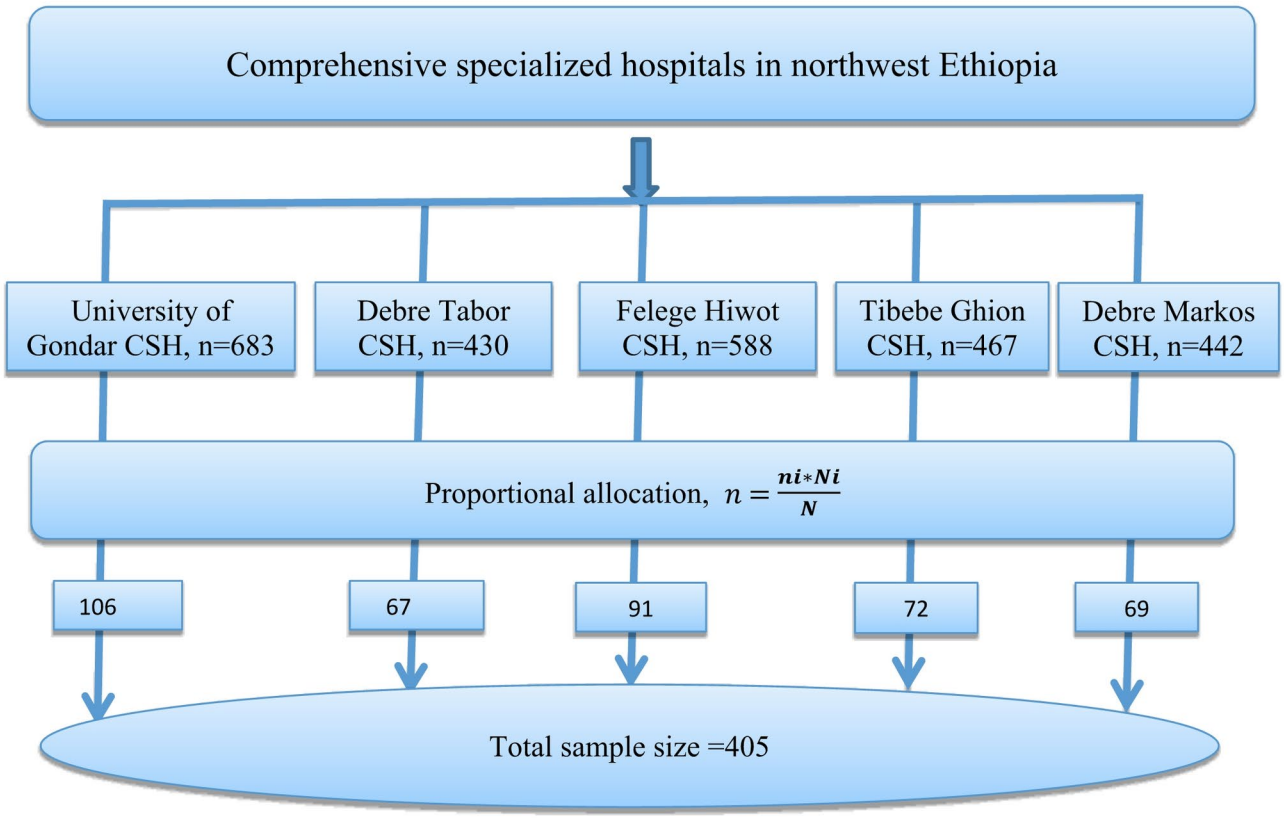

Fig. 1 Diagrammatic representation of the sampling procedure at PCSHs in Northwest Ethiopia

additional drug therapy: Is a DTP that occurs when there is a medical condition needing new drug therapy, preventive therapy is needed to reduce the risk of developing a new condition, or a medical condition requires combination therapy for better efficacy [3], Ineffective drug therapy: Is a DTP where the drug is not the most effective for the medical problem, the drug product is not effective for the medical condition, the condition is refractory to the drug product being used, or the dosage form is inappropriate [4], Dose too low: Is a DTP that occurs when the dose is too low to produce the desired outcome, the dosage interval is too infrequent, a drug interaction reduces the amount of active drug available, or the duration of therapy is too short [5], Dose too high: Is a DTP where the dose is too high or the dosing frequency is too short or the duration of therapy is too long for the patient, a drug interaction causes a toxic reaction to the drug product, or the dose was administered too rapidly [6], Adverse drug reaction: Is a DTP where the drug product causes an undesirable reaction that is not dose related, a safer drug is needed because of patient risk factors, a drug interaction causes an undesirable reaction that is not dose-related, or the regimen was administered or changed too rapidly, and [7] Non-compliance: Is a DTP that occurs when the patient does not understand the instructions, the patient prefers not to take or forgets to take the medication, the cost of the drug product is not affordable for the patient, the patient cannot swallow, or the drug product is not available for the patient.

Polypharmacy: According to WHO polypharmacy is defined as the usage of more than or equal to five medications per patient.

Pediatrics: In the present study pediatrics were defined as those less than 18 years including.

a. Neonates: Those from birth to 28 days.
b. Infants: Defined as the age group from 1 month to 1 year.
c. Toddler: Defined as the age group between > 1 and ≤ 3 years.
d. Preschool: Defined as the age group between > 3 and ≤ 5 years.
e. School-age: Those with the age group between > 5 and ≤ 10 years.
f. Adolescent: Defined as the age group between > 10 and < 18 years.

Medications and pharmaceutical intervention management

WHO Anatomic Therapeutic Chemical Classification (ATC) system (level 1) was used to classify medications involved in drug therapy problems among patients with

infectious diseases at the pediatric ward of PCSHs [32]. Pharmaceutical Intervention is the process of a clinical pharmacist identifying and rectifying DTPs communicating with other healthcare professionals or patient and or care givers. Pharmaceutical interventions and their acceptance rate by treating physicians, pediatricians in each hospital, were classified according to the Pharmaceutical Care Network Europe (PCNE) 2019 [33].

Data collection procedure and quality control

The data collection tool was prepared by reviewing previous studies for variables that were used to assess DTPs [18, 19, 33, 34]. Data about each patient, including sociodemographic data, clinical characteristics, medical diagnosis, physical assessment, laboratory results, medications, comorbid conditions, previous medical history, and preadmission or home medications, were obtained prospectively either from the patient or family or caregivers, or patient medical records. The data collection tool included details of the patient, physical investigations and laboratory results, medication details (current and past), including management and treatment targets, and comorbidities. Five clinical pharmacists were involved in the data collection, and two MSc clinical pharmacy professionals supervised the process of data collection. The principal investigator and the supervisors were closely following the process of data collection. The principal investigator trained the data collectors and supervisors on the study's objectives, ethical issues, adherence to the data abstraction format, and how and what data were collected from the patients both through interviews and using patient medical records. To ensure consistency and acceptability of the data collection tool, it was pretested on 5% of the total sample size (20 patients) before two weeks of the main data collection at Addisalem Hospital, we found that the tool was clear and consistent, and addressed the objectives of the study and ethical concerns were addressed by have written informed consent.

Data entry and statistical analysis

The collected data were entered using Epi-data version 4.6.0 and analyzed using SPSS version 27. Descriptive statistics were used to describe the results of the study. To describe categorical variables Frequencies/percentages were used, while mean plus standard deviations (mean ± SD) for continuous data. Variance inflation factor and tolerance level were used to test multicollinearity, and Hosmer-Lemeshow test for model fitness. The association between DTP and the explanatory variables was estimated using a binary logistic regression model. For multivariable logistic regression analysis, candidate variables were identified using bivariate logistic regression. Explanatory variables with a p-value < 0.25 in the bivariate regression analysis were analyzed in multivariable logistic regression. Finally, those explanatory variables with a p-value < 0.05 in multivariable regression analysis were declared as statistically significant factors of DTPs.

Results

Socio-Demographic characteristics of the study participants

In the present study, 389 patients were recruited, and more than half of them, 203 (52.2%), were males. More than one third, 145 (37.3%) of patients were preschool with the mean (± SD) age of 2.97 (± 1.53) years, with the range of 3 days to 18 years. More than half (56.8%) of patients were residing in rural areas. The mean weight of patients (± SD) was 11.06 (± 9) kg with the range of 1.12 to 38.9 kg; the majority of them, 246 (63.2%), weight between 5 and 14.99 kg, followed by 55 (14.2%) who weight between 15 and 19.9 kg. The majority of patients were admitted to pediatric wards (80.2%), and the remaining (19.8%) were admitted to the severe acute malnutrition (SAM) ward (Table 1).

Clinical characteristics of study participants

Among 389 pediatric patients included in the study, more than half of the patients had comorbidity, 245 (62.9%). About 53% of patients had stayed between six to ten days in the hospital, with a mean duration of 7.85 (± 4.5) days. Most of the patients, 288 (74%), were newly admitted to pediatric wards of PCSHs, and more than half of the study participants, 222 (57.1%) had one infectious disease (Table 2). The most common infectious diseases diagnosed during the study period were pneumonia (52.2%), followed by meningitis (44.7%) (Fig. 2). A total of 230 different comorbidities were diagnosed among 245 patients. The most common comorbidities were severe acute malnutrition (32.6%), followed by anemia (27.0%) and acute kidney injury (AKI) (18.7%) (Fig. 3).

Types and prevalence of drug therapy problems

The overall prevalence of DTPs was 56.56% which occurred in 220 pediatric patients with infectious disease. A total of 250 DTPs were identified among 220 patients. The most common DTPs identified were noncompliance (43.6%), followed by unnecessary drug therapy (16.0%) and dose to high (12.0%). From 220 patients who had experienced DTPs, majority of the patients 135 (65.9%) had one drug related problem, and 50 (34.2%) patients had two DTPs and 5 (2.0%) patients had three DTPs (Fig. 4).

Drugs involved in drug therapy problems

The most common class of drugs involved in DTPs was antiinfective for systemic use, 168 (43.2%), followed by nervous system, 45 (12.9%). Among 784 medications involved in the occurrence of DTPs, the most common

Table 1 Socio-demographic characteristics of study participants admitted to the pediatric ward of PCSHs from December 01, 2023, to February 30, 2024

Variables	Category	Frequency	Percent
Sex	Male	203	52.2
	Female	186	47.8
Age	Neonate	16	4.1
	Infant	43	11.0
	Toddler	98	25.2
	Preschool	145	37.3
	School age	47	12.1
	Adolescent	40	10.3
Weight (in kg)	< 5	44	11.3
	5-14.99	246	63.2
	15-19.99	55	14.2
	≥ 20	44	11.3
Residency	Urban	168	43.2
	Rural	221	56.8
Involvement of the family in the childcare	Yes	298	76.6
	No	91	23.4
Took immunization as scheduled	Yes	342	95.6
	No	47	4.4
Have home medication	Yes	18	4.6
	No	371	95.4
History of chronic disease	Yes	79	20.3
	No	310	79.7
Ward of admission to the hospital	SAM ward	77	19.8
	Inpatient ward	312	80.2
Source of the medication fee	Payment	202	51.9
	Free	187	48.1

Table 2 Clinical characteristics of study participants admitted to the pediatric ward of PCSHs from December 01, 2023, to February 30, 2024

Variables	Category	Frequency	Percent
Presence of Comorbidity	Yes	245	62.9
	No	144	37.1
Duration of hospital stay (in days)	≤ 5	118	30.3
	6–10	206	53.0
	≥ 11	65	16.7
Level of consciousness	Conscious	340	87.4
	Not conscious	49	12.6
Severity of the disease	Healthy looking	123	31.6
	Acute sick looking	201	51.7
	Chronic sick looking	65	16.7
Previous history of medical illness	Yes	120	30.8
	No	269	69.2
Polypharmacy (≥ 5 medicines)	Yes	121	31.1
	No	268	68.9
Number of disease condition	1	222	57.1
	2	47	12.1
	3	50	12.9
	≥ 4	70	18.0
Type of admission	New	288	74.0
	Transferred	101	26.0

drugs involved in DTPs were ceftriaxone 122 (15.6%), followed by paracetamol 109 (13.9%) (Table 3).

Types of pharmaceutical interventions and level of acceptability

After the detection of DTPs, we have undertaken the intervention by communicating with the treating physicians to improve treatment efficacy, reduce adverse drug events, and optimize patient treatment outcomes. The most commonly encountered type of pharmaceutical intervention provided was adjusting the dose of medication (25.2%), followed by patient education/counseling/adherence (23.2%), and discontinuation of medications (20.5%). Of the proposed 370 interventions, about 74.3% were fully accepted. In general, the acceptance rate was 84.0% (Table 4).

Factors associated with drug therapy problems

Multivariate logistic regression analysis was carried out to identify independent predictors of the occurrence of DTPs among pediatric hospitalized patients with infectious diseases. Patients with a prolonged duration of hospital stay [6–10] were about 2.02 times more likely to have DTPs [AOR = 2.02, 95%CI: 1.33–7.80] whereas those who stayed more than ten days in hospital were

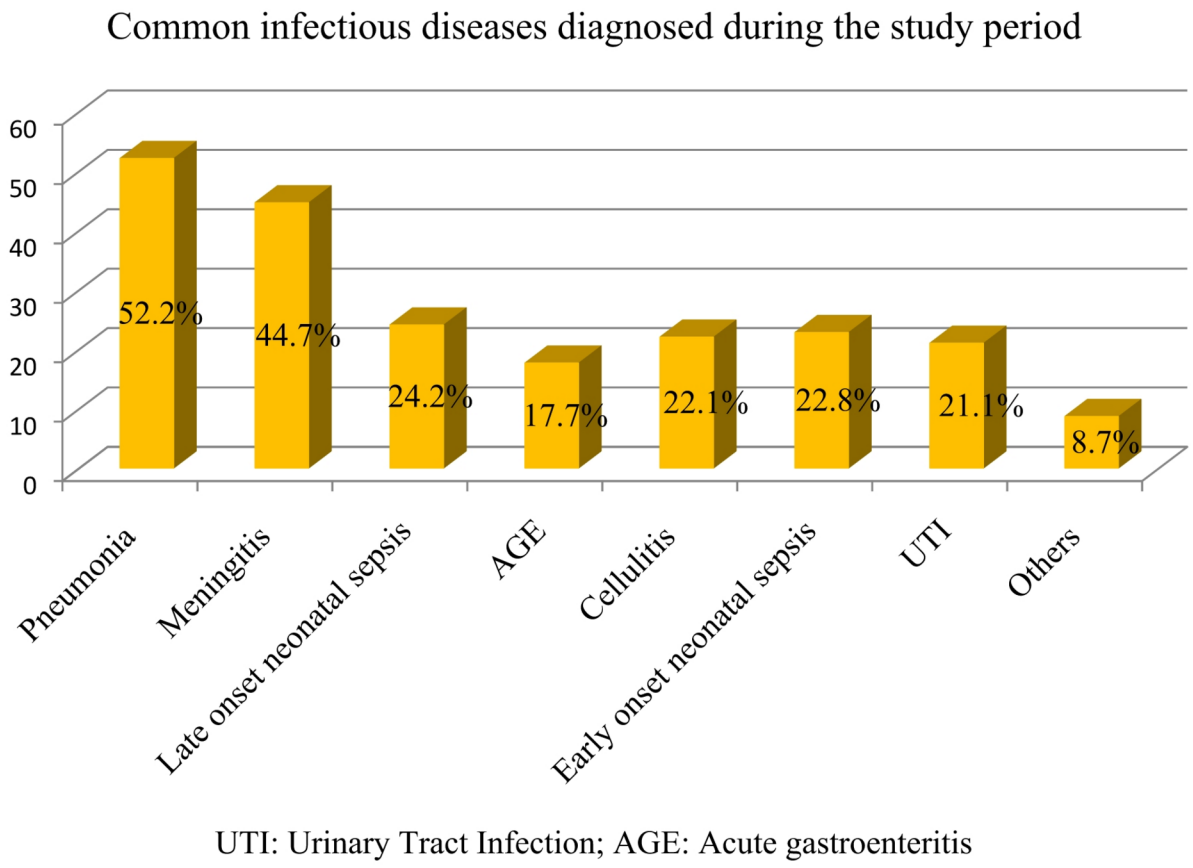

Fig. 2 The top infectious diseases diagnosed among patients admitted to pediatric ward of PCSHs from December 01, 2023 to February 30, 2024

2.89 times more likely to have DTPs [AOR = 2.89, 95% CI: 1.90-11.23] as compared their counterpart (≤ 5 days). It was found that patients with polypharmacy (≥ 5 medicines) were about 3.20 times more likely to have DTPs [AOR = 3.20, 95%CI: 1.70, 5.68] compared to those with less number of medications (< 5 medicines). Patients who paid for their medications were 2.19 [AOR = 2.19, 95%CI: 1.18, 3.31] times more likely to develop DTPs than those who got their medicines for free. Similarly, patients with comorbidity were 3.9 times more likely to experience DTPs [AOR = 3.90, 95% CI: 1.56–8.15] than patients without comorbidity (Table 5).

Discussion

The present study aimed to identify the level of acceptability of pharmaceutical interventions by prescribers about drug therapy problems among hospitalized pediatric patients with infectious diseases in northwest Ethiopia. Understanding the magnitude of DTPs and types, and the acceptability of pharmaceutical interventions by prescribers in these settings can inform the development of strategies to enhance medication safety and improve patient care [35]. The findings of this study will contribute to the existing knowledge on medication management in the pediatric population with infectious diseases in Northwest Ethiopia. Detecting and rectifying DTPs among pediatric hospitalized patients with infectious diseases has the utmost importance in the prevention of potential adverse drug events and complications associated with DTPs. Identifying DTPs in pediatric wards involves recognizing issues that can affect the efficacy and safety of medications for pediatrics [21]. DTPs contribute to not achieving the therapeutic plan, and they are the major causes of the increased cost of health care, prolonged hospitalization, morbidity, and mortality [5, 6, 21, 36].

This study revealed a high prevalence of DTPs, with more than half of the patients (56.56%, 95%CI = 45.21, 68.19) experiencing at least one DTP during their hospital stay. The result of this study was consistent with the previous studies; in the University of Gondar Teaching Hospital [24], and at a clinical pharmacist service-naive Hospital in Northern Sweden [37], and lower than studies conducted at Wollega University Referral Hospital in which 71.51% patients had drug-related problems [18], Dessie Hospital where 75.51% of patients experienced

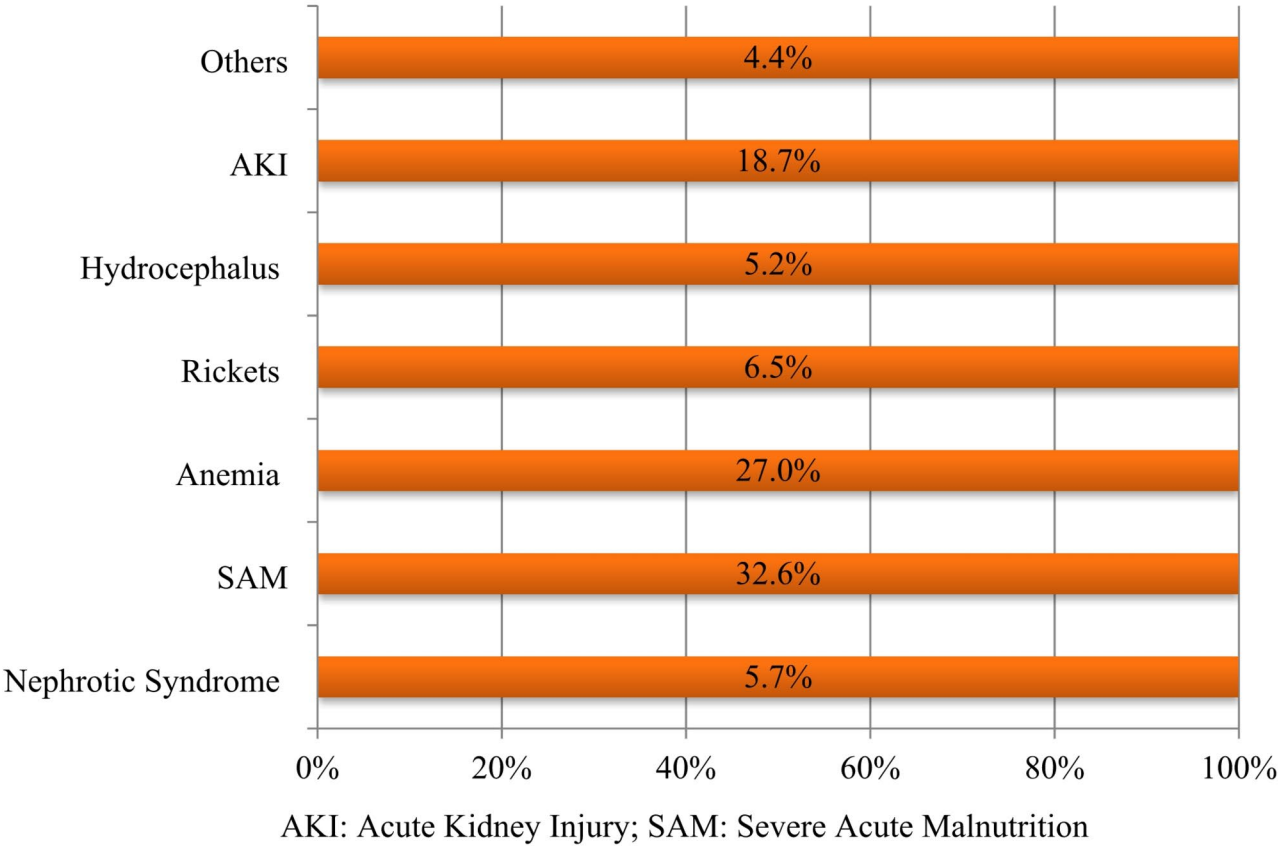

Fig. 3 The comorbidities diagnosed among patient with infectious disease at pediatrics ward of PCSHs from December 01, 2023 to February 30, 2024

at least one drug therapy problem [38], and Kenyatta national hospital (93.8%) [39].

The results of the present study finding were higher than the study in Zewditu Memorial Referral Hospital with an overall rate of drugrelated problems of 31.57% (23) and a study in Hong Kong pediatric wards with an overall incidence of drugrelated problems of 21.0% [22]. The prevalence of DTP variance across the studies might be due to a variation in the DTP classification system, treating physicians' training and adherence to clinical practice guidelines, study settings and sample size, and integration of clinical pharmacists in the ward. Despite all these differences pharmaceutical interventions should be performed to identify and rectify DTPs associated with pediatric patients with infectious diseases to improve patients' treatment outcomes, and prescribers should comply with evidence-based clinical practice guidelines.

The most common types of DTPs identified were non-compliance (43.6%), followed by unnecessary drug therapy (16.0%) and dose too high (12.0%). If patients cannot access or afford their medication, chronic conditions may go unmanaged, leading to complications, prolonged hospitalizations, or even mortality [40]. Patients with low health literacy may not fully understand instructions, leading to incorrect dosage or missed doses, treatments that involve multiple medications or intricate schedules can be confusing or overwhelming, and language barriers may lead to medication nonadherence and this misunderstandings can result in suboptimal treatment, drug interactions, or treatment failure, ultimately worsening the disease condition [41]. Improving medication adherence could significantly enhance patient outcomes, reduce healthcare costs, and improve overall health.

The present study findings regarding the common types of DTPs are consistent with previous studies conducted in Ethiopia [19, 42] and Côte d'Ivoire [43], which have consistently reported non-compliance, dosing inappropriateness, and unnecessary drug therapy as the most prevalent DTPs in pediatric patients. The difference might be in the study setting, and health care professionals' involvement in the counseling and patient education about the rational use of medications. The detected high rate of medication non-adherence in this study underscores the importance of patient education and the involvement of clinical pharmacists in all pediatric wards of hospitals.

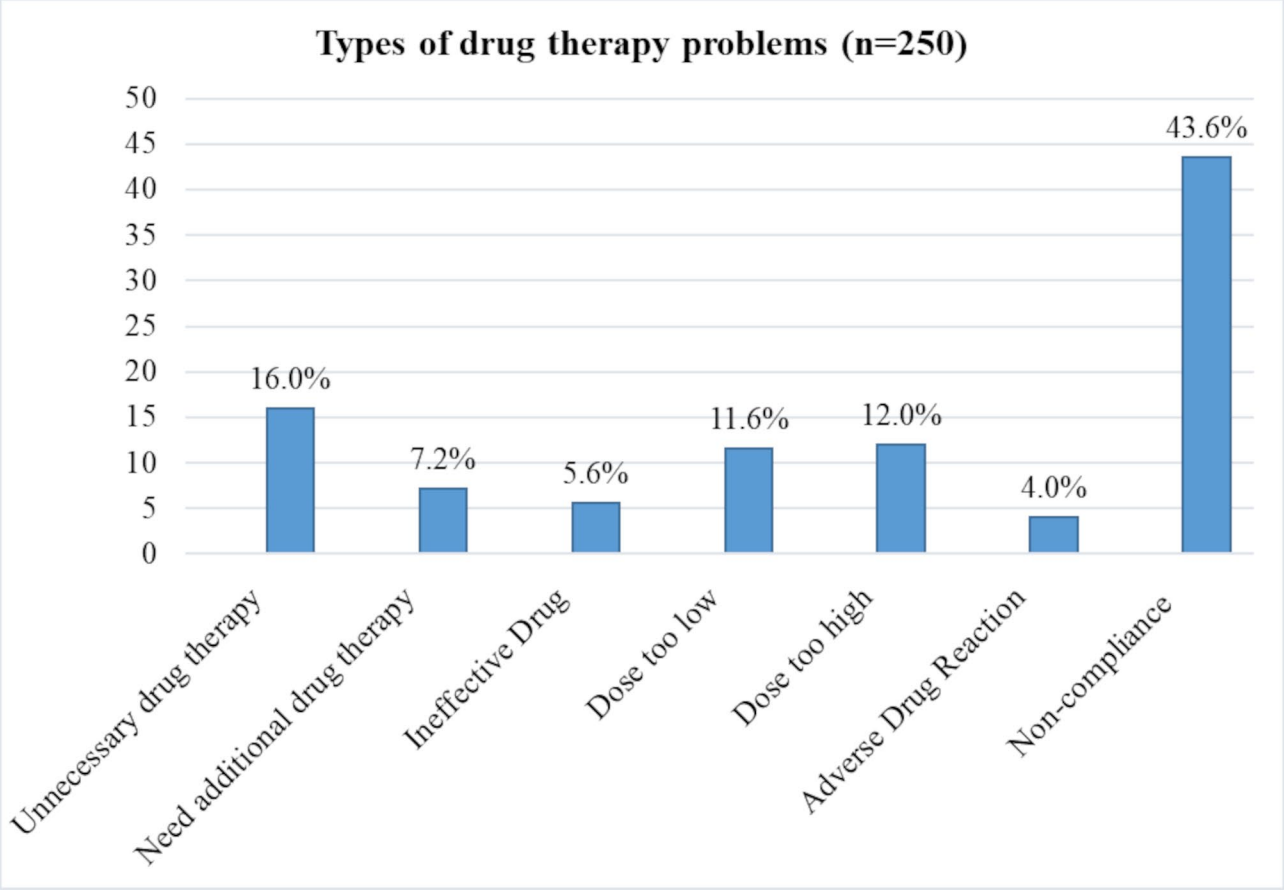

Fig. 4 Drug therapy problems detected among patients with infectious disease at the pediatrics ward of PCSHs from December 01, 2023, to February 30, 2024

Table 3 Class of drugs involved in drug therapy problem among patients with infectious disease at pediatric ward of PCSHs from December 01, 2023 to February 30, 2024

Drug class	Frequency ($n=389$)	Percent
A: alimentary tract and metabolism	48	12.3
B: blood and blood-forming organs	25	6.4
C: cardiovascular system	45	11.6
D: dermatologicals	23	5.9
J: Anti-infective for systemic use	168	43.2
N: nervous system	50	12.9
R: respiratory system	17	4.4
Others [a]	13	3.3

[a]cough medications, fluids, vitamins, and minerals

Table 4 Acceptance level of interventions by prescribers provided for patients diagnosed with infectious disease admitted to pediatric wards of PCSH from December 01, 2023, to February 30, 2024

Type of pharmaceutical interventions	Frequency	Percent
Adjust dose	93	25.2
Adjust frequency	57	15.4
Add a drug	58	15.7
Discontinuation of a drug	76	20.5
Medication adherence and patient education/ counseling	86	23.2
Level of acceptability by prescribers	**Frequency**	**Percent**
Intervention fully accepted	275	74.3
Refused or rejected	59	16.0
Intervention accepted with modification	36	9.7

The study also revealed the classes of drugs most commonly involved in DTPs, with anti-infective agents for systemic use (43.2%) and nervous system drugs (12.9%) being the most prevalent. This is not surprising, as these drug classes are commonly used in the treatment of infectious diseases and often require careful monitoring and dose adjustment, especially in pediatric patients. Anti-infective agents for systemic use are prescribed for the treatment of acute, chronic, or critical infections and the prevention of infections in critically ill patients, especially in pediatrics with low immunity, and increased susceptibility to lethal microorganisms, as well as during surgical and/or medical procedures [17, 44]. Antipyretics and analgesics, particularly paracetamol, for the treatment of fever, which is the most common finding as the signs of infections during presentation to the hospital

Table 5 Multivariable logistic regression analysis of predictors of DTPs in the pediatric ward of PCSHs, 2024

Variable	Categories	COR (95%CI)	AOR (95%CI)	*p*-value
Residence	Rural	1.02 (0.41,7.99)	0.25 (0.20,9.82)	0.081
	Urban	1.00	1.00	
Weight (in kg)	< 5	0.67 (0.43–3.08)	0.80 (0.36–3.44)	0.671
	5-14.99	0.73 (0.19–1.95)	0.66 (0.19–3.78)	0.342
	15-19.99	0.16 (0.18–2.40)	0.41 (0.15–5.88)	0.442
	≥ 20	1.00	1.00	
Ward of Admission to the hospital	Inpatient ward	2.41 (0.88,2.64)	1.29 (0.74,2.63)	0.240
	SAM ward	1.00	1.00	
Comorbidity	No	1.00	1.00	
	Yes	2.25 (2.37–5.81)	3.90 (1.56–8.15)	0.012*
Duration of hospital stay (in days)	≤ 5	1.00	1.00	
	6–10	2.31 (1.09–5.67)	2.02 (1.33–7.80)	0.014*
	≥ 11	3.25 (1.87–6.07)	2.89 (1.90-11.23)	0.003*
Number of infectious disease	1	1.00	1.00	
	2	1.89 (0.68–5.19)	1.17 (0.73–4.26)	0.462
	≥ 3	2.54 (1.15–3.85)	2.13 (0.58–4.96)	0.234
Number of medications for all conditions	≥ 5 medicines	2.46 (1.45,5.18)	3.20 (1.70,5.68)	0.004*
	1–4 medicines	1.00	1.00	
Source of medication fee	Payment	1.57 (0.83,2.78)	2.19 (1.18,3.31)	0.017*
	Free	1.00	1.00	
Number of disease condition	1	1.00	1.00	
	2	0.83 (0.84–2.11)	0.85 (0.27–2.08)	0.243
	3	0.10 (0.18–3.51)	0.39 (0.19–3.36)	0.459
	≥ 4	0.70 (0.82–5.26)	0.92 (0.12–4.94)	0.683

Keys: *= Denotes Significance Statistically ($p < 0.05$); 1.00 = Reference; CI = Confidence Interval; COR = Crude Odds Ratio; AOR = Adjusted Odds Ratio; SAM =Severe Acute Malnutrition

were the commonly involved drugs, next to the aforementioned drugs.

After the detection of DTPs, we have undertaken pharmacotherapeutic intervention by communicating with the treating physicians to improve treatment efficacy, reduce adverse drug events, and optimize patient treatment outcomes. Role of pharmacotherapeutic interventions and the acceptance of these interventions by treating physicians is increasingly recognized as a crucial outcome because it can influence medication adherence, effectiveness, patient satisfaction, and ultimately enhance patient safety [45]. The interventions provided by the study team, such as dose adjustments, medication discontinuation, and patient education, were well-accepted by the treating physicians, with an overall acceptance rate of 84.0%, which was consistent with previous studies [19, 22, 46]. This demonstrates the value of having a dedicated clinical pharmacist team integrated into the pediatric infectious disease management process, as they can play a crucial role in identifying and resolving DTPs, ultimately improving patient outcomes. Clinical pharmacists have an essential role in identifying and rectifying DTPs [17, 21, 36].

The study's findings on the factors associated with DTPs provide important insights for healthcare providers. Identifying the determinants of DTPs is essential for developing targeted interventions to address these issues and improve patient outcomes in addressing prescription and administration errors in children, and this might contribute to the improvement of medication safety and better patient treatment outcomes for pediatric inpatients with infectious diseases [47]. The high number of medications (≥ 5 medications), presence of comorbidity, and prolonged hospital stay were independent predictors of DTPs among pediatric hospitalized patients with infectious diseases. The findings of this study are consistent with previous research [19, 22, 23, 48].

Patients with comorbidities and those receiving multiple medications are more likely to experience medication regimens that are too complex, increasing the risk of DTPs in pediatrics. Additionally, prolonged hospital stays may expose patients to more opportunities for DTPs to occur, underscoring the need for medication monitoring and management during the hospital stay. Accordingly, the source of the medication fee was also one of the associated factors for DTPs in this study, and patients who paid for their medications had a higher chance of having the DTPs, this was in line with the studies conducted so far in Ethiopia [49, 50]. This discrepancy in the association of this variable among the studies across the world might be due to medication availability, cost, and medication awareness among patients. For the safety of

medication use in pediatric inpatients, clinical pharmacists have a valuable responsibility [51].

The role of clinical pharmacists in hospitalized pediatric patients for the safety and proper utilization of medications is indispensable since pediatric patients are at a higher risk of developing DTPs which impacts the effectiveness and safety of pharmacotherapy to a greater extent than adults, and resulting in morbidity and mortality of children across the world [5, 6]. This difference might be due to their immature pharmacodynamic and pharmacokinetic changes implying organ systems like the liver and kidneys are immature in the pediatrics which can significantly affect the pharmacokinetics and dynamics of drugs [7]. This further demonstrates the fact that pediatric patients are at a higher risk of developing drug therapy problems (DTPs) compared to adult patients due to their body surface area, weight, and development of organ function which vary from adults and within their age groups, and this variation impacts the effectiveness and safety of pharmacotherapy [6].

Strengths and limitations of the study

The present study is a multicenter design that enhances the generalizability of the findings. The directionality of causal relationships cannot be verified between variables in cross-sectional study design. The study involved public hospitals, and the results of this study may not be directly applicable to private healthcare institutions. It also did not assess the clinical outcomes associated with the detected DTPs.

Conclusion

This finding showed that the prevalence of drug-related problems was high among pediatric hospitalized patients with infectious diseases at PCSHs in northwest Ethiopia, which needs great attention. The most commonly encountered DTPs were noncompliance, followed by unnecessary drug therapy, and dose too high. A high number of medications (polypharmacy), the presence of comorbidity, and prolonged hospital stays were associated factors with the occurrence of DTPs. The most commonly encountered type of pharmaceutical interventions provided was adjusting the dose of medication, followed by patient education/counseling/adherence, and discontinuation of medications. The acceptance rate of pharmaceutical interventions by the prescribers was high.

Recommendations

Health policymakers should provide community education programs to raise awareness about the importance of adherence to medication regimens in pediatric patients. Public health campaigns and initiatives are urgently needed that engage caregivers and families, ensuring they understand the critical role of medication adherence in preventing DTPs and improving patient outcomes. Hospitals should provide training on drug related problem, medication review and medication administration technique for health care professionals. The hospitals have to establish a forum that encourages physicians, nurses, and pharmacist relationships for better healthcare services, and the integration of clinical pharmacists into the healthcare management teams should be implemented. Future studies should assess the clinical outcomes associated with the detected DTPs.

Abbreviations

AKI	Acute Kidney Injury
AOR	Adjusted Odds Ratio
ATC	Anatomic Therapeutic Chemical Classification
CI	Confidence Interval
COR	Crude Odds Ratio
DTP	Drug Therapy Problem
DTU	Debre Tabor University
ICU	Intensive Care Unit
PCNE	Pharmaceutical Care Network Europe
SAM	Severe Acute Malnutrition

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Author contributions

T.A.M: Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Validation, Writing original draft, Writing review & editingT.S.Y, G.T.A, and T.M.A: Data curation, Formal analysis, Methodology, Writing review & editingS.B.D, F.N.D, K.H.S and S.S.A: Data curation, Formal analysis, Supervision, Validation, Resource, Writing review & editing.

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Data availability

Data is provided within the manuscript or supplementary information files and any additional data will be available upon reasonable request of the corresponding author.

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from the ethical review committee of Debre Tabor University College of Health Sciences with reference number DTU/CBE/297/2016 E.C. All methods were conducted based on the Helsinki Declaration. Written informed consent to participate was obtained from all of the participants in the study after explaining the purpose of the study. If the child is too young to provide informed consent, it was obtained from parents/caregivers. All the responses were kept confidential. Thus, identifiers like the name and address of the patient were not recorded in the data abstraction formats.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

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