Cross-sectional Study

"Childrens are not just "little adults". The rate of medication related problems and its predictors among patients admitted to pediatric ward of southwestern Ethiopian hospital: A prospective observational study

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ABSTRACT

Background: The rate of medication related problems is high in developing countries due to the complexity of pediatrics medication management. Pediatric population should have their own dosage regimens. The pediatric dosage regimens were derived from the adult dose that might lead to sudden reach of sub or supra-therapeutic doses. As the result, the medication therapy management is difficult in this populations. Despite this, a scanty of studies were conducted on medication related problems among pediatric populations. Therefore, this study examined the prevalence and risk factors for the occurrence of the medication related problems among patients admitted to pediatric ward of Mettu karl referral hospital.

Patients and methods: The pediatric population who were received the pharmacotherapy for their disease was observed and followed for the occurrences of medication related problems at pediatric wards of Mettu karl referral hospital from February 12, 2020 to February 24, 2021. Patients whose age was less than or equal to 18 years and who were on drug therapy or who needs drug therapy during study period were included. The possibility of adverse drug reactions developed from the drug was assessed by using the Naranjo scale. Multivariable logistic regression analysis was used to determine the predictors of medication related problems.

Result: Over the study period, a total of 189 pediatric populations were included. Among these, 115 (60.8%) were males, and the mean age of the patients was 1.4339 ± 0.864 years. The medication related problems was found among 121(64.01%) of pediatric patients. Among seven types of drug therapy problems unnecessary drug therapy, need additional drug therapy, ineffective drug therapy and dose too high were the most predominantly occured DRP that accounted 74 (27.72%), 67 (25.09%), 43 (16.10%), 36 (13.48%), respectively. The mean number of hospital stay was 4.29 days with minimum and maximum stay of 2 and 9 days and antibiotics 364 (51.3%) were the most common class of drugs that was associated with drug related problems. Being a neonate (AOR = 1.48, 95CI%: 1.69–7.42, P = <0.001), hospital stay greater than or equal to seven days (AOR = 1.98, 95CI%: 2.471–12.644, P = 0.016), and the presence of co-morbidity(AOR = 2.507, 95CI%: 3.270–4.949, P = 0.080) were the predictors of the medication related problems.

Conclusion: The prevalence of medication-related problems in pediatrics patient was found to be high. Being neonatal, prolonged hospital stay and the presence of a multiple disease were the predictors of medication-related problems in pediatric patients. Therefore special attention should be given for newborns, prolonged hospital stay and patients having co-morbidity. Besides this, the drug information service and the patients round activity should be started by clinical pharmacist to decrease the occurences of any preventable medication related problems.

1. Background

Drug related problem(DRP) is a problem that interferes with a patient's pharmacotherapy that results in poor treatment outcomes [1–3]. MRP that are catagorised as actual, if observable harms are reach the patients and potential if there is a possibility to affect the patients in the future [4,5]. This includes need additional drug therapy, unnecessary drug therapy, ineffective drug, dose too low or too high, adverse drug reactions, and non-compliance [6].

MRP can have a negative impact on the patients quality of life and health care budgets as the result of decreased effectiveness of therapy [7]. MRPs can affects the patients goals of therapy and increases the patients demand for additional drug prescription that results in poly-pharmacy, and increased the hospitalization rate [4,8].

Despite the MRPs can affect patients of all ages, high prevalence of the problem in children has become a major concern [9]. This might be due to weight-based dosing, difficulties of dilutions, unability of the pediatrics to communicate and they are easily exposed to the side effects of the drugs as the results of immature organ functions like kidney and liver [6].

"Children are not just "little adults"in which they should have their own pharmacokinetic and pharmacodynamic profile. Extrapolating the adult dose to the pediatrics may lead to the sudden reach of sub or supratherapeutic doses and make medication monitoring difficult [3].

Many of the drugs that are used in pediatrics were off-label due to lack of clinical trials studies on this special populations [10]. The drug use in children may be accompanied by many adverse reactions not observed in adults [2]. Therefore, appropriate medication should be given for pediatric patients [6].

Generally, unresolved MRP can affects the childrens quality of life, increases the social and economic burden of disease, patients re-admission, prolonged hospital staay, and finally leads to mortality [3, 11].

The rate of medication related problems in developing countries is high that accounts from 31.57% to 80.1% as the result of the complexity of pediatrics medication management [9]. Despite this, limited studies conducted on pediatric populations and no finding on our study area related to pediatric medication use problem. Hence, this study aimed to assess the rate of medication-related problems and associated factors among patients admitted to the pediatric ward of MKRH.

2. Patients and methods

2.1. Study area, design and period

The pediatric population who were received the pharmacotherapy for their disease was observed and followed for the occurrences of medication related problems. The study was conducted at Mettu karl referral hospital (MKRH) from February 12, 2020 to February 24, 2021. MKRH is found in Mettu town, South West Oromia, Ethiopia which is found at 600 km from Finfinne. There are different wards and clinics within MKRH; those include internal medicine ward, surgery ward, pediatric ward, gynecology and obstetrics ward, antenatal clinic, dental clinics, tuberculosis clinic, anti-retro viral therapy clinic and ophthalmic clinic. The work has been reported in line with the strengthening the reporting of cohort studies in surgery (STROCSS) criteria [12].

2.2. Study participants and eligibility criteria

Patients whose age was less than or equal to 18 years and complete registration charts who were on drug therapy or who needs drug therapy during study period and with more than 48 hours of length of hospital stay were included. Pediatric patients whose drug therapy information was incomplete or no drug orders on their charts, and who was admitted to intensive care unit were excluded.

2.3. Study variables and outcome endpoints

The medication related problem was the primary outcome. Hill-Bone Compliance to High Blood Pressure Therapy Scale was used to measure medication adherence [13]. For this study purpose, we had used a 9-item medication-taking sub-scale. Each item is a four-point likert type scale (none of the time, some of the time, most of the time, and all the time). The median split was used and dichotomies into adherent and non-adherent to the treatment.

2.4. Sample size and sampling technique

Single population proportion formula was used to calculate the required sample size by considering the following assumptions: Proportion of drug-related problem P = 0.3157, or 31.57% [14], 95% confidence level, and 5% margin of error (absolute level of precision).

$$n = \frac{(Z\alpha/2)2 \ p \ (1-p)}{d2}$$

z = 1.96
P = 31.57% (0.3157)
d = 0.05

$$n = \frac{(1.96)2(0.6843)(0.3157)}{(0.05)2} = 332$$

Where;

n = sample size
P = Proportion of drug related problems (p) = 31.57%
Z = Z is standardized normal distribution value at the 95% CI: 1.96
d = The margin of sample error tolerated = 5%

The expected number of populations in the study period (N), based on the average number of patients coming to the hospital in 3 months was 355. The corrected sample size (nf), was calculated by using correction formula as follows:

$$nf = \frac{(n*N)}{(n+N)}$$

$$nf = \frac{(332*355)}{(332+355)}$$

nf = 172. After adding a 10% contingency it becomes 189. A conscequative sampling technique was used to include study participants.

2.5. Data collection process and management

A semi-structured data collection tool was prepared to collect the data. Two medical doctor and three clinical pharmacist pharmacists were recruited for data collection; one clinical pharmacist was assigned to supervise the data collection process. Different guidelines like Ethiopian STG and WHO guidelines, drug formulary were employed to identify the medication related problem. DRP registration format was used to identify and record different types of DRPs [15]. To assure the consistency of the data collection tool it was pretested at nearby hospital called Bedele general hospital prior to normal data collection.

2.6. Data processing and analysis

The data were entered into a computer using EPI-data version 3.1. The principal investigator has daily checked and cleaned the data before analysis. The data was then exported to the statistical software for social sciences (SPSS) 24.0 for analysis. Multivariate logistic regression was

used to analyze the variable by using COR and AOR with 95% CI. All variables associated with the medication therapy problem at a P-value ≤0.25 on the bivariate analysis were entered into a multivariate logistic regression analysis to control for confounders. Finally, the predictors of drug therapy problem were declared if a P value of ≤0.05.

2.7. Ethics approval and consent-to-participate

Ethical approval was obtained from the Research Ethics Review Committee(RERC) of the Mettu University with reference number of MEU/CHS/RERC05/2012. Written informed consent was obtained from parents of the participants. The study protocol was performed accordance with the declaration of Helsinki. The study was registered resear chregistry.com with a unique reference number of "researchregistry7047".

2.8. Operational definitions

Drug-related problem: Includes ADR, non-adherence, inappropriate indication and dose, and ineffective drug therapy.
ADR was assessed using Naranjo algorithm of ADR probability scale [16]. Accordingly, ADR Probability scale was categorized by taking sum the of 10 questions and grouped as.

- Definite ADR if the total score is ≥ 9
- Probable ADR if the total score is 5–8
- Possible ADR if the total score is 1–4
- Doubtful ADR if the total score is 0

Poly-pharmacy: The daily consumption of 5 or more medications [17].
Co-morbidity: Patients diagnosed with two or more diseases [18].
Prolonged hospital stay: If the patients stay ≥ 7 days [19].

3. Results

3.1. Socio-demographic factors and clinical characteristics of study population

A total of 189 patients were included in the study, of which 115 (60.85%) were males and 74 (39.15%) were females. Most of them 73

Table 1
Socio-demographic factors and clinical characteristics of patients admitted to pediatric ward of MKRH from February 12, 2020 to February 24, 2021.

Variables		Frequency	Percent
Age	Neonate(birth to 28 days)	27	14.29
	Infant(29 days to 1 year)	73	38.62
	Children(>1 year to 14 years)	69	36.51
	Adolescents(>14 years–18 years)	20	10.58
Sex	Male	115	60.85
	Female	74	39.15
Residence	Urban	83	43.92
	Rural	106	56.08
Past medical history	No	74	39.15
	Yes	115	60.85
Past medication history	No	85	44.97
	Yes	104	55.03
Immunization	No	58	30.69
	Yes	131	69.31
Length of hospital stay	<7	99	52.38
	≥7	90	47.62
Co-morbidity	No	80	42.33
	Yes	109	57.77
Number of medications per patient	<5	85	44.97
	>5	104	55.03

Table 2
Commonly diagnosed disease and prescribed medication of patients admitted to pediatric ward in MKRH from February 12, 2020 to February 24, 2021.

Variables		Frequency	Percent
Diagnosis	Severe community acquired pneumonia	118	31.5
	Acute gastroenteritis	53	14
	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
	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,plumpynut, lasix,vancomycin, augmentin, cimetidine, folic acid.

(38.62%) were infant, whereas adolescent covered the least 20 (10.58%) from all age groups admitted during the study. The mean age of patients was 1.434 years, ranging from 1 day to 18 years. A total of 106(56.08%) were from rural area. Regarding to their clinical characteristics a total of 115 (60.85%) of them had a past medical history and 104 (55.03%) patients had past medication history. Most of patients 131 (69.31%) were immunized and 90(47.62%) have taken greater than five medication per diagnosis. The mean number of hospital stay was 4.29 days with minimum and maximum stay of 2 and 9 days respectively(Table 1).

3.2. Incidence and types of DRPs in pediatric patients admitted to pediatric ward

Out of 189 patients 121(64.01%) had at least one drug therapy problem. During the study period a total of 267 medication related problems were identified. Therefore, the ratio of the no of medication related problems to patient was 1.41. Among seven types of drug therapy problems unnecessary drug therapy, need additional drug therapy, ineffective drug therapy and dose too high were the most predominantly encountered DRPs accounted 74 (27.72%), 67 (25.09%), 43 (16.10%), 36 (13.48%), respectively. Dose too low, Adverse drug reaction and non-compliance were the least DRP identified which accounts 25(9.36),12

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
Bronchodilators	21	4.8
Minerals and vitamins	13	3
Diuretics	4	1
Anti-epileptic drug	8	1.8
Antimalarial agents	5	1.2
Others	4	1
Total	435	100

Others. Anti-emetic, anti-anemic, H_2 antagonists.

Table 4

Bivariable and Multivariable logistic regression analysis result of factors associated with DRPs among pediatric patients admitted to pediatric ward 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)l			
Age	Adolescents	13(65%)	7(35%)	1	1	0.612
	Children	40(57.9%)	29(42.1%)	1.35(0.33–2.474)	1.94(0.333–2.638)	0.93
	Infant	50(68.5)	23(31.5%)	0.63(0.189–10.984)	0.92(0.831–12.42)	0.091
	Neonate	18(66.6%)	9(33.3%)	1.09(1.35–5.85)	1.48(1.69–7.42)	<001
Sex	Female	47(63.5%)	27(36.5%)	1	1	0.346
	Male	80(76.2%)	25(23.8%)	0.54(0.398–2.388)	0.93(0.698–2.78)	
Residency	Urban	52(71.2%)	27(28.8%)	1	1	0.417
	Rural	70(66%)	36(34%)	0.99(0.495–1.635)	10.762(0.395–1.47)	
Past medical history	No	49(57.6%)	36(42.4%)	1	1	0.513
	Yes	68(65.4%)	36(36.6%)	0.72(0.698–2.32)	1.254(0.626–2.523)	
Immunization	No	41(70.7%)	17(29.3%)	1	1	0.724
	Yes	90(68.7%)	41(31.3%)	1.098(0.518–1.876)	1.142(0.547–2.385)	
Length of hospital stay	<7days	52(56.5%)	40(43.5%)	1	1	0.016
	≥7days	52(53.6%)	45(46.4%)	1.13(1.463–10.522)	1.98(2.471–12.644)	
Poly pharmacy	No	49((55.7%)	39(44.3%)	1	1	0.834
	Yes	57(56.4%)	44(43.6%)	0.97(0.487–1.603)	0.834(0.443–1.57)	
Co-morbidity	Yes	43(61.4%)	27(38.6%)	1.15(1.856–2.914)	2.507(3.270–4.949)	0.008
	No	69(57.9%)	50(42.1%)	1	1	

AOR: Adjusted odd ratio; CI: Confidence interval; COR: Crude odd ratio.

(4.49%,10(3.75%), respectively.

3.3. The most common diagnosis and prescribed medications in patients admitted to pediatric ward

Of the total cases diagnosed during the study period severe pneumonia, bronchial asthma and acute gastro enteritis were the leading case accounted 118 (31.5%), 62 (16.5%) 53(14%), respectively. Ceftriaxone and Paracetamol were the most frequently prescribed drug which is accounted 272 (30%), 112 (12.4%), respectively. The mean numbers of drugs prescribed were 4.79 per patient ranging from 2 to 9 for minimum and maximum respectively(Table 2).

3.4. The common class of medication drugs involved in DRPs

In our study area, a 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 antipyretics 69(15.8) (Table 3).

3.5. Determinants of medication related problems among pediatric patients

Multivariable logistic regression result revealed that the predictors of medication related problems among pediatric patients were age (neonate), prolonged hospital stay, and presence of co-morbidity. The presence of medication related problems among neonates were 1.5 times more likely than infants (AOR = 1.48, 95CI%: 1.69–7.42, P = <0.001). Patients whose hospital stays greater than or equal to seven days were about 2 times more likely to have DRPs than patients whose hospital stay less than seven days (AOR = 1.98, 95CI%: 2.471–12.644, P = 0.016). Lastly, patients who had two or more disease were about 2.5 times more likely to have DRPs than patients who had less than two disease (AOR = 2.507, 95CI%: 3.270–4.949, P = 0.080) (Table 4).

4. Discussion

The change in the pharmacokinetics and pharmacodynamics of the drugs in children can results in medication related problems in hospitalized patients [14]. The magnitude of medication related problems in the study was quite high that accounts 121(64.01%) which is higher than the study of Brazil 6.8% [20]. However, it was lower than the study of Jimma University Medical Center 74.3% [21] and Dessie Referral

Hospital 87.7% [22]. The occurrence of the medication related problem was comparable with that of Vietnam 65.7% [9]. The difference in the prevalence of medication related problems might be due to variance in age classification of pediatrics, study setting and a variation in classification of medication related problems.

Among different types of medication related problems unnecessary drug therapy 42 (34.7%) and need additional drug therapy 26 (21.5%) were the most commonly occur problems. This is consistent with southwestern Ethiopian hospitals [17,19]. However, in Jimma University Medical Center, Hiwot Fana Specialized University Hospital, Saudi Arabia, and Zewditu Memorial Referral Hospital dosing error was commonly reported [6,14,23,24] and in Brazil ineffectiveness was the widely occur medication related problem [3]. The difference in the prevalence of medication related problems among different studies might be due to difference in prevalence of medical conditions and the presence of organ dysfunction like kidney and liver that changes the pharmacokinetics of the drugs.

Antibiotics was the most class of drug associated with drug related problems that accounts 212 (48.7%). This is consistent with India, University of Gondar Teaching Hospital, Zewditu Memorial Referral Hospital, and Dessie referral hospital, hong kong [14,25–28]. The mis-use of antibiotics in the pediatrics wards were commonly due to the patients were presented with infectious aetiology and given antibiotics by empirical therapy without considering the causative agents for their infections.

The significant association was obtained between medication related problem and the patients age. The medication related problems was prevalent in neonate than other age groups. On the contrary, being a neonate was not a predictors of medication related problem in the study of Hiwot fana specialized university hospital [6]. Similar finding was obtained in Vietnam, Sauidi Arabia, and Brazil in which drug related problems was prevalent in younger age than child school age and childrens [9,20,24]. This may be because MRPs resulting from inappropriate indication or inadequate dosage form were more likely to occur in neonates than other age groups.

Pediatric patients with increased length of hospital stay was more likely to be exposed with medication related problems. This was consistent with the study conducted in Wollega University Referral Hospita, southwestern Ethiopian hospitals and university of Gondar [17–19,26]. This is due to the more the pediatric patients stay in hospital the more likely to be developed hospital acquired infections which made the therapy complex than naïve patients.

In our study the presence of two or more disease was the predictors of

medication related problems. This is inline with the study of Zewuditu memorial referral hospital [14,21,23,29]. On the contrary, patients with comorbidities were less likely to have DRPs than patients with no comorbiditiesin Vietnam [9]. Similarly, the presence of two or more disease was not a determinants of medication related problem in Hiwot fana specialized university hospital [6]. In our study area the more the patients presents with additional disease the more unnecessary drug and needs additional drug therapy problems were likely to occur.

In our study, the rate of drug therapy problems was found to be high. This implies that the complexity of diseases management in this special populations. Therefore, further researcher should conduct the study on the impact of medication related problems on treatment outcome of the pediatric populations.

4.1. Limitation of the study

As limitation the cause and effect relation ships was not identified and the impact of drug related problem on the patients treatment outcome was not assessed. The other weakness was a fear of COVID-19 among data collectors and supervisors since the study was conducted during this pandemic disease.

5. Conclusion

The prevalence of medication-related problems in pediatrics patient was found to be high. Inappropriate indication and ineffective drug therapy were the widely occurred medication related problems. Among the different class of medication involved in medication related probles antibiotics were commonly reported. Being a neonate, prolonged hospital stay and the presence of multiple disease were a predictors of medication-related problems in pediatric patients. Therefore special attention should be given for newborns, prolonged hospital stay and patients having co-morbidity. Besides this, the drug information service and the patients round activity should be started by clinical pharmacist to minimize the occurences of any preventable medication related problems.

Acknowledgment

Abbreviations

ADR	Adverse drug reaction
AOR	Adjusted odds ratio
COVID-19	Coronavirus disease-19
CI	Confidence interval
COR	Crude odds ratio
MRP	Medication-related problem
MKRH	Mettu karl referral hospital
SPSS	Statistical package for social sciences
STG	Standard treatment guideline;
WHO	World health organization

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102827.

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The following information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories then this should be stated.

Please state any conflicts of interest

The authors declared that they have no competing interest.

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Ethical approval

Ethical clearance was obtained from the Institutional Review Board (IRB) of mettu University, college of health science.

Consent

Not applicable. No individual person's personal details, images or videos are being used in this study.

Author contribution

FB, GB and LT contribute in the preparation of proposal, methodology, and statistical analysis. BAG and DJ were participated in preparing the first draft of the manuscript and contributed to the methodology and editing of the manuscript. All authors checked and confirmed the final version of the manuscript.

Registration of research studies

1. Name of the registry: RESEARCH REGISTRY, https://www.researchregistry.com
2. Unique Identifying number or registration ID: researchregistry7047
3. Hyperlink to the registration (must be publicly accessible):https://www.researchregistry.com/register-now#home/registrationdetails/5d70f2520791fb0011b79e9f/

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References

[1] O. Urbina, O. Ferrández, S. Luque, S. Grau, S. Mojal, R. Pellicer, M. Riu, E. Salas, J. Comin-Colet, Patient risk factors for developing a drug-related problem in a cardiology ward, Therapeut. Clin. Risk Manag. 11 (2015) 9.

[2] L. Daniel, L. Rarichan, M. Jose, M.S. Binoy, B. Rajalingam, An investigation on drug related problems in pediatrics of a tertiary care, private, teaching hospital at coimbatore, J Clin Case Rep Trials 1 (2018), 01-7.

[3] A.R. Nascimento, R.W. Leopoldino, M.E. Santos, T.X. Costa, R.R. Martins, Drug-related problems in cardiac neonates under intensive care, Revista Paulista de Pediatria 38 (2020).

[4] V. Saldanha, I.B. Araújo, S.I. Lima, R.R. Martins, A.G. Oliveira, Risk factors for drug-related problems in a general hospital: a large prospective cohort, PloS One 15 (5) (2020 May 5), e0230215.

[5] A. Sutherland, D.L. Phipps, S. Tomlin, D.M. Ashcroft, Mapping the prevalence and nature of drug related problems among hospitalised children in the United Kingdom: a systematic review, BMC Pediatr. 19 (1) (2019 Dec) 1–4.

[6] N.D. Agazhi, B.M. Tigabu, Drug therapy problems in pediatric ward of Hiwot fana specialized university hospital, Harari national regional state, Eastern Ethiopia, Int. J. Pharma Sci. Res. 5 (2018) 129, https://doi.org/10.15344/2394-1502/2018/129.

[7] M. Hussein, J. Lenjisa, M. Woldu, G. Tegegne, G. Umeta, H. Dins, Assessment of drug related problems among hypertensive patients on follow up in Adama Hospital Medical College, East Ethiopia, Clin. Pharmacol. Biopharm. 3 (122) (2014) 2.

[8] Y. Ayele, K. Melaku, M. Dechasa, M.B. Ayalew, B.A. Horsa, Assessment of drug related problems among type 2 diabetes mellitus patients with hypertension in Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia, BMC Res. Notes 11 (1) (2018 Dec) 1–5.

[9] T.H. Nguyen, V.T. Le, D.N. Quach, H.G. Diep, N.K. Nguyen, A.N. Lam, S.T. Pham, K. Taxis, T. Nguyen, P.M. Nguyen, Drug-related problems in prescribing for pediatric outpatients in Vietnam, InHealthcare 9 (3) (2021 Mar) 327 (Multidisciplinary Digital Publishing Institute).

[10] E. Kimland, U. Bergman, S. Lindemalm, Y. Böttiger, Drug related problems and off-label drug treatment in children as seen at a drug information centre, Eur. J. Pediatr. 166 (6) (2007 Jun) 527–532.

[11] V. Saldanha, R.R. Martins, S.I. Lima, I.B. de Araujo, A.G. Oliveira, Incidence, types and acceptability of pharmaceutical interventions about drug related problems in a general hospital: an open prospective cohort, BMJ open 10 (4) (2020 Apr 1), e035848.

[12] R. Agha, A. Abdall-Razak, E. Crossley, N. Dowlut, C. Iosifidis, G. Mathew, for the STROCSS Group, The STROCSS 2019 guideline: strengthening the reporting of cohort studies in surgery, Int. J. Surg. 72 (2019) 156–165.

[13] Y. Song, H.R. Han, H.J. Song, S. Nam, T. Nguyen, M.T. Kim, Psychometric evaluation of hill-bone medication adherence subscale, Asian Nurs. Res. 5 (3) (2011 Sep 1) 183–188.

[14] M.K. Birarra, T.B. Heye, W. Shibeshi, Assessment of drug-related problems in pediatric ward of Zewditu memorial referral hospital, Addis Ababa, Ethiopia, Int. J. Clin. Pharm. 39 (5) (2017 Oct) 1039–1046.

[15] R.J. Cipolle, L.M. Strand, P.C. Morley, Pharmaceutical Care Practice: the Patient-Centered Approach to Medication Management, McGraw Hill Professional, 2012.

[16] C.A. Naranjo, U. Busto, E.M. Sellers, P. Sandor, I. Ruiz, E.A. Roberts, E. Janecek, C. Domecq, D.J. Greenblatt, A method for estimating the probability of adverse drug reactions, Clin. Pharmacol. Ther. 30 (2) (1981 Aug) 239–245.

[17] F. Bekele, T. Tsegaye, E. Negash, G. Fekadu, Magnitude and determinants of drug-related problems among patients admitted to medical wards of southwestern Ethiopian hospitals: a multicenter prospective observational study, PloS One 16 (3) (2021 Mar 16), e0248575.

[18] B.M. Tigabu, D. Daba, B. Habte, Drug-related problems among medical ward patients in Jimma university specialized hospital, Southwest Ethiopia, J. Res. Pharm. Pract. 3 (1) (2014 Jan) 1.

[19] F. Bekele, G. Fekadu, K. Bekele, D. Dugassa, J. Sori, Drug-related problems among patients with infectious disease admitted to medical wards of Wollega University Referral Hospital: prospective observational study, SAGE open medicine 9 (2021 Jan), 2050312121989625.

[20] R.D. Leopoldino, M.T. Santos, T.X. Costa, R.R. Martins, A.G. Oliveira, Drug related problems in the neonatal intensive care unit: incidence, characterization and clinical relevance, BMC Pediatr. 19 (1) (2019 Dec) 1–7.

[21] D. Feyissa Mechessa, D. Dessalegn, T. Melaku, Drug-related problem and its predictors among pediatric patients with infectious diseases admitted to Jimma University Medical Center, Southwest Ethiopia: prospective observational study, SAGE open medicine 8 (2020 Nov), 2050312120970734.

[22] G.K. Bizuneh, B.A. Adamu, G.T. Bizuayehu, S.D. Adane, A prospective observational study of drug therapy problems in pediatric ward of a referral hospital, northeastern Ethiopia, Int. J. Pediatr. 2020 (2020 Mar 20).

[23] D. Feyissa, B. Kebede, A. Zewudie, Y. Mamo, Medication error and its contributing factors among pediatric patients diagnosed with infectious diseases admitted to Jimma university medical center, southwest Ethiopia: prospective observational study, Integrated Pharm. Res. Pract. 9 (2020) 147.

[24] A. AlAzmi, O. Ahmed, H. Alhamdan, H. AlGarni, R.M. Elzain, R.S. AlThubaiti, M. Aseeri, A. Al Shaikh, Epidemiology of preventable drug-related problems (DRPs) among hospitalized children at KAMC-Jeddah: a single-institution observation study, Drug Healthc. Patient Saf. 11 (2019) 95.

[25] S. Mohammed, S. Poudel, F. Laloo, A. Madhur, R. Robert, B. Mathew, Assessment of drug-related problems in a tertiary care teaching hospital, India, Asian J. Pharmaceut. Clin. Res. 10 (2017) 310.

[26] A. Srikanth, Assessment of drug related problems and its associated factors among medical ward patients in university of gondar teaching hospital, northwest Ethiopia: a prospective cross-sectional study, J. Basic Clin. Pharm. 8 (2017).

[27] Y.M. Belayneh, G. Amberbir, A. Agalu, A prospective observational study of drug therapy problems in medical ward of a referral hospital in northeast Ethiopia, BMC Health Serv. Res. 18 (1) (2018 Dec) 1–7.

[28] A.N. Rashed, L. Wilton, C.C. Lo, B.Y. Kwong, S. Leung, I.C. Wong, Epidemiology and potential risk factors of drug-related problems in H ong K ong paediatric wards, Br. J. Clin. Pharmacol. 77 (5) (2014 May) 873–879.

[29] Y.L. Niriayo, K. Kumela, T.D. Kassa, M.T. Angamo, Drug therapy problems and contributing factors in the management of heart failure patients in Jimma University Specialized Hospital, Southwest Ethiopia, PloS One 13 (10) (2018 Oct 23), e0206120.