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Prevalence and predictors of drug-related hospitalisation among patients visiting emergency departments of Addis Ababa city hospitals in Ethiopia: a multicentre prospective observational study

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ABSTRACT

Objectives This study aimed to determine the prevalence, categories and predictors of drug-related hospitalisation (DRH) among patients visiting emergency departments of Addis Ababa city hospitals, Ethiopia.

Design A multicentre prospective observational study was conducted through patients' interview and chart review.

Settings The study was undertaken in three tertiary care hospitals in Addis Ababa, Ethiopia.

Participants A total of 423 patients fulfilling the inclusion criteria were included.

Outcome measures Prevalence and preventability of DRH, categories of drug-related problems causing DRH, medications and diseases involved in DRH, and factors significantly associated with DRH.

Result More than half of the patients (216, 51.1%) were female. The mean age (SD) was 47.50 (±17.21) years. The mean length of hospital stay (SD) was 10.29 (±8.99) days. Nearly 60% (249) of them were hospitalised due to drug-related problems, of which 87.8% were preventable. The cause for hospitalisation for more than half (130, 53%) of them was a failure to receive drugs, and 37.85 (94) patients were categorised as untreated indications. Age ≥65 years (adjusted OR (AOR)=7.451, 95% CI: 1.889 to 29.397), tertiary educational level (AOR=0.360, 95% CI: 0.141 to 0.923), participants who did not have any occupation (AOR=3.409, 95% CI: 1.120 to 10.374) and presence of comorbid conditions (AOR=2.004, 95% CI: 1.095 to 3.668) were predictors of DRH.

Conclusion Nearly 90% of DRH was deemed to be preventable in the study settings. Older age, lower educational level, unemployment and presence of comorbid conditions in hospital as an inpatient were predictors of DRH.

Strengths and limitations of this study

- ► The strength of this study is the study design which is a prospective observational study.
- ► This is a multicentre study with sufficient sample size, increasing representativeness of the findings.
- ► The main limitation of this study is lack of standardised procedures for immediate recording and reporting of drug-related hospitalisation.
- ► Patients who visited other than the emergency ward were excluded from participation, which can also be considered as a limitation of the study.

INTRODUCTION

Though drugs can be ordered for the intention of achieving desired health outcomes that improve patients' quality of life, symptoms and signs of diseases causing drug-related hospitalisation (DRH) as a result of drug-related problems (DRPs) could be apparent.[1–3] DRP is defined according to Hepler and Strand as 'an undesired event or circumstance due to drug therapy that actually or potentially interferes with desired health outcomes'.[4]

Medication use has been increasing across the globe due to the presence of a large number of treatable diseases, and this has contributed to the production of more advanced medications by the pharmaceutical industry. Therefore, advances in drug therapies could lead to an apparent increase in the incidence of DRPs, which in turn leads to hospitalisation.[5] Hospitalisation can be defined as drug related if it is straightforwardly linked to one of the eight predefined Hepler and Strand's classifications of DRPs: adverse drug reaction (ADR), drug interaction, improper drug selection, untreated indication, subtherapeutic dosage, supratherapeutic dosage, failure to receive drugs and drug use without indication.[6–12] Those DRPs can arise when a medicine is prescribed aptly and used correctly (eg, ADR), due to errors involving prescribing (including

inappropriate or overtreatment, and failure to prescribe the indicated treatment or undertreatment), dispensing, administering, reconciling or monitoring of medicines as well as from poor patient adherence.[2 13 14] According to the WHO, an ADR is any harmful, undesired and inadvertent drug effect that occurs at doses used in human for therapy, diagnosis or prophylaxis.[15]

Over the past decades, DRH has been considered as wide spreading.[16] In the USA, DRPs accounted for 17 million emergency department (ED) visits and 8.7 hospitalisation events annually.[17] It increases morbidity and mortality rates, and healthcare cost; decreases income and household productivity; and reduces quality of life.[2 18 19]

Studies carried out in different areas of the globe estimated the extent of DRH to be between 16% and 41.3%. Of these, 50%–95% were preventable. Supratherapeutic dosage (10.3%–12.7%), non-compliance (10.6%–65.8%), ADRs (10.7%–45.5%) and untreated indications (10.7%–13.3%) were frequently identified as the causes of DRH.[6 9 18 20–22]

DRPs resulting in DRH were defined as preventable if the following would not take place: patient failed to take a drug that is known to reduce or prevent symptoms according to the prescribed directions, took a drug for which a patient had a known allergy, drug treatment was obviously improper, dosage differed from accepted recommendations, took a drug that was not indicated and if there was a failure to monitor by a physician at reasonable time intervals due to financial difficulty. If there was, however, no reasonable action to prevent DRPs, it is then termed as non-preventable.[20 23]

In many studies, drug-related hospitalised patients had mainly cardiovascular diseases and diabetes, suggesting that cardiovascular and hypoglycaemic medications were involved in DRH.[6 10 11 18 20 21 24 25] Previous studies also identified polypharmacy, advanced age and comorbid conditions as factors that exacerbate the occurrence of DRH.[3 6 20 21]

It is thus important to determine DRH prevalence to improve treatment outcomes and prevent unnecessary admissions. To the best of our knowledge, there are no studies conducted about DRH in Ethiopia. The present study therefore aimed to determine the prevalence, categories and predictors of DRH among patients admitted to an ED of three selected hospitals in Addis Ababa, the capital of Ethiopia.

METHODS

Study settings

The study was carried out in the ED of Tikur Anbessa Specialized Hospital (TASH), Zewditu Memorial Hospital (ZMH) and Yekatit 12 Hospital Medical College (Y12HMC), Addis Ababa, Ethiopia. TASH has 700 beds and it is a tertiary care teaching hospital affiliated with Addis Ababa University. In TASH, outpatient, inpatient and emergency services are delivered. The ED provides services for about 13 920 patients per year. Y12HMC is also a tertiary care level referral and teaching hospital that provides both inpatient and outpatient treatment for a large number of people coming from Addis Ababa as well as other places of the country. The hospital has a total of three ED rooms. The adult medical ED is collocated with adult surgical ED. It serves around 10 560 patients per year. The third hospital is ZMH, which is one of the teaching and general referral hospitals in Ethiopia and its ED serves about 10 560 patients per year.

Patient involvement

Patients did not participate in the initial conception and design of the study. However, based on the participating patients' comments during the pretest (5% of the sample size), we made a correction on the patient approach and timing for an interview at ED during data collection. Patients who participated actively in this study determined the medication use, level of adherence and medical history.

Study design and population

A prospective observational study design was used to collect data from August to September 2020. All patients admitted to the ED of the three selected hospitals during the study period and fulfilled the inclusion criteria were included.

Inclusion and exclusion criteria

Patients having a medical history with completed data and aged ≥14 years old were included. Patients with incomplete or no medical records, refused to participate, presented with trauma and injuries associated with accidents (eg, road traffic accidents, beaten by stick, getting stabbed and shot by a bullet) and poisoned/intoxicated (for instance, snake bite, alcohol intoxication or use of pesticide) were excluded. During the data collection period, about 2655 patients were being admitted to the ED, out of which 423 participants fulfilled the inclusion criteria.

Sample size determination and techniques

Since there was no study done on DRH in Ethiopia, the sample size was estimated using the general formula for single population proportion.

$$n = [(Z_{\alpha/2})2 \times p\,(1-p)]\sqrt{d^2}$$
$$= [(1.96)^2 \times 0.5 \times 0.5]/0.05^2 = 384$$

Hence, n=required sample size, Zα/2=critical value for normal distribution at 95% CI, which equals 1.96 (*Z* value at alpha=0.05), p=proportion of DRH=0.5, d=margin of error of 5%=0.05. The calculated sample size using this formula was 384. Adding 10% contingency (for non-response rate) to compensate for participants who could refuse to participate brought the final sample size to 423. The sample size was distributed to the three hospitals based on the patient load of hospital's ED per annum as mentioned in the Study settings section. Accordingly, 169

participants were included from TASH, 127 participants from ZMH and 127 participants from Y12HMC.

Data collection procedures

A structured questionnaire was developed from carefully evaluated published articles in the literature. For instance, categories of DRPs that lead to hospitalisation and factors having association with DRH (eg, sociodemographic and clinical characteristics) were extracted from the literature. All the necessary data including patients' demographic details (age, sex, marital status, education level, employment), and clinical information like the number of medications being taken prior to admission were collected and documented using data collection tools through interviewing the patients/family members. Furthermore, patients' medical records were reviewed by data collectors to obtain clinical information (disease history, allergic status, admission diagnosis, length of hospital stay during admission, number of medications being taken prior to admission, data on laboratory investigations). Supplemental information and clarifications on some patients' medical information were obtained through discussion with the treating physicians and residents. By applying those data-gathering approaches, different categories of DRPs resulting in hospitalisation with their possible causes were determined.

Data were collected by three pharmacists having Master of Science degrees in Clinical Pharmacy. They had basic knowledge and skill in pharmaceutical care services and also received training on how to obtain data from patients' medication charts and approach the patients and healthcare professionals. Updated Ethiopian Standard Treatment Guidelines for Hospitals, third edition, 2014; Ethiopian Antiretroviral Therapy and Tuberculosis Guidelines; Cancer Treatment Protocols prepared by TASH oncologists; pharmacotherapy textbooks; Medscape and UpToDate were used as a guide for disease management. Micromedex online database was used to check drug interactions. Furthermore, updated guidelines released from the American Cardiology Center, American Heart Association, European Cardiology Society and American Diabetic Association were used as a guide to treat different diseases. Clinical pharmacists along with physicians determined subtherapeutic and supratherapeutic dosage outcomes using medical charts, laboratory tests, clinical outcomes, medication dose and frequency. Participants' hospitalisation attributed to failure to receive drugs was decided using physicians' recording documentation, clinical pharmacists' knowledge and patient-reporting evidence. Untreated indications and improper drug selection were evaluated and interpreted using treatment guidelines. For instance, if patients presented with untreated or improperly treated cardiac diseases, treatment was initiated and optimised using the American Heart Association guidelines and UpToDate latest version. To minimise bias, the three pharmacists at each hospital independently evaluated the identified DRPs that resulted in hospitalisation. Decision was then reached by a consensus after a series of meetings and discussions as well consultations with physicians and residents. Once DRPs resulting in DRH were identified, they were recorded and classified using DRP registration format according to Hepler and Strand's classification.

Data collection management

Pretest was performed on 5% of patients in TASH prior to the actual data collection period, and amendment was made accordingly. The data collection process was supervised, and the information gathered via data abstraction formats was reviewed and checked for their completeness every day to ensure quality. Urgent correction was made, if any errors were identified.

Data analysis

The data were entered and analysed using SPSS V.26. Mean and SD for continuous variables and frequency and percentage for categorical variables were computed by using descriptive statistics in SPSS to summarise sociodemographic and relevant clinical characteristics of the study participants. Tables and charts were used to present the results. Furthermore, univariate and multiple binary logistic regressions were performed to analyse factors that predict DRH. Variables with p values of <0.2 in the binary univariate analysis were included in the multiple binary logistic regressions to control the effect of confounders. The level of significance was set at $p \leq 0.05$, and results were reported as ORs with 95% CIs.

RESULTS

Sociodemographic and clinical characteristics

From 2655 participants enrolled in the study, a total of 423 study participants were included for analysis. Of them, 169 participants from TASH, 127 from ZMH and another 127 from Y12HMC were included (figure 1).

Sociodemographic and clinical characteristics of the participants are depicted in table 1. More than half of the participants (216, 51.1%) were female. The mean (SD) age of the participants was 47.5 (±17.21) years and nearly two-thirds (275, 65%) were ≥40 years of age. More than 70% (301, 71.1%) of the total participants' level of education was below secondary school. Nearly three-quarters of them (304, 71.9%) resided in Addis Ababa city. Out of the total study participants, 58% (245) of them were taking ≥3 and 30% (127) were taking ≥5 drugs prior to admission, which is termed as polypharmacy. Above half of the participants (213, 50.4%) had comorbid diseases, including hypertension (108, 22.5%), cardiac diseases (59, 13.5%) and diabetes mellitus (53, 12.5%). The mean (SD) length of hospital stay was 10.28±8.99 days and ranges from 2 to 96 days.

Prevalence and categories of DRH

From a total of 423 enrolled patients, DRH was identified in 245 (57.9%) participants, of which 87.8% were deemed preventable. A total of 322 DRPs rendering

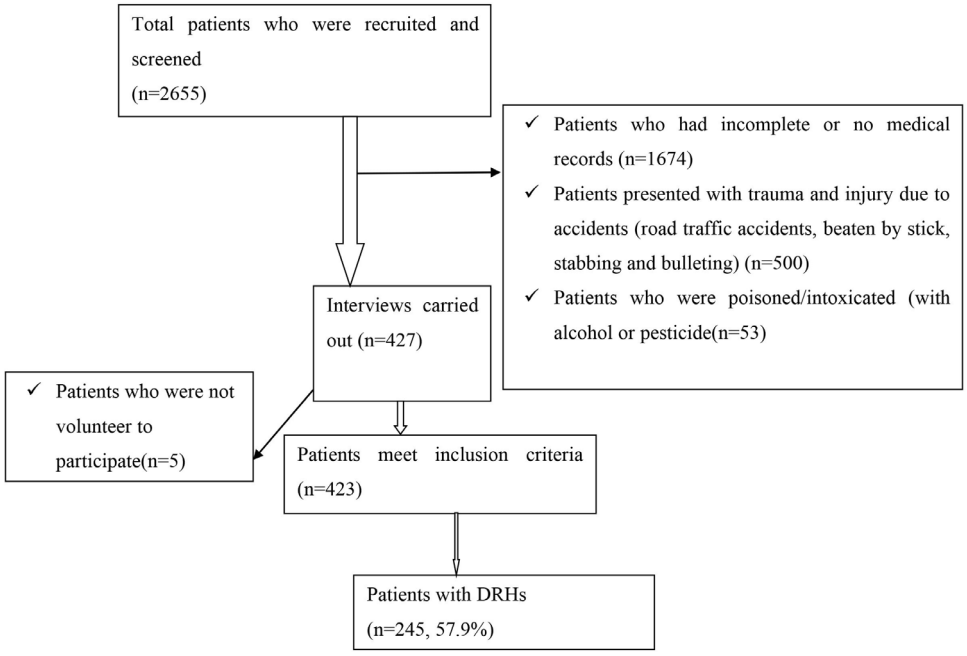

Figure 1 Patients' inclusion information flow chart in the emergency ward at TASH, ZMH and Y12HMC, Addis Ababa, Ethiopia, August–September 2020 (n=423). DRH, drug-related hospitalisation; TASH, Tikur Anbessa Specialized Hospital; Y12HMC, Yekatit 12 Hospital Medical College; ZMH, Zewditu Memorial Hospital.

DRH were observed in 245 participants, representing 1.31 DRPs per patient (figure 2). Out of 245 drug-related hospitalised patients, more than half (130, 53%) of them were due to failure to receive drugs, followed by untreated indication (94, 37.8%) and subtherapeutic dosage (30, 12.2%). The main reasons for failure to receive drugs included the following: patients preferred not to take the medication (43, 33.1%), feared adverse events (18, 13.8%) and drug products were not available (17, 13.1%) (table 2).

Medications and diseases involved in DRH

Out of a total of 245 drug-related hospitalised patients, nearly one-third of them had cardiovascular diseases (80, 32.6%), followed by endocrine disorders (47, 19.2%) and cerebrovascular diseases (26, 10.6%) (see table 3).

Medication classes and specific drugs implicated in DRH are depicted in table 4.

A total of 497 drugs were implicated in 245 drug-related hospitalised patients, providing an encounter of 2.03 drugs per drug-related hospitalised patient. Cardiovascular, antimicrobial, antineoplastic and endocrine drug classes were the most frequently involved drugs in the hospital admissions. Among cardiovascular drugs, furosemide (59, 24.1%), ACE inhibitors (ACEIs) (48, 19.1%), and antiplatelets and anticoagulants (44, 18%) were the most frequently mentioned followed by drugs acting on the endocrine system like oral hypoglycaemic agents (37, 15.1%) and insulin (24, 9.8%). Antibiotics (25, 10%), anticancer drugs (23, 9%) and combination of antiretroviral therapy (15, 6.1%) had also contributed to admission to varied extent.

Factors associated with the occurrence of DRH

According to the multivariate logistic regression analysis, the variables age, employment, presence of comorbid diseases and educational level were significantly associated with the occurrence of DRH (see table 5). Age >64years (adjusted OR (AOR)=7.451, 95% CI: 1.889 to 29.397), tertiary educational level (AOR=0.360, 95% CI: 0.141 to 0.923), participants who did not have any occupation (AOR=3.409, 95% CI: 1.120 to 10.374), students (AOR=6.331, 95% CI:1.375 to 29.153) and presence of comorbid diseases (AOR=2.004, 95% CI: 1.095 to 3.668) were predictors of DRH.

DISCUSSION

The aim of optimising pharmacotherapy is to achieve the desired therapeutic outcomes in the absence of morbidity and mortality associated with a drug. To the best of our knowledge, this study is the first to explore the prevalence, categories and rate of preventability of DRH in the ED of three selected hospitals that are responsible for the provision of medical and surgical care to patients in need of immediate care.

The occurrence of DRH reported in this study (245, 57.9%) is substantially higher than studies conducted elsewhere, including America (16.2%), Brazil (31.6%), Denmark (10.8%), Norway (38%), Sweden (41.3%), India (17.2%) and Malaysia (39%).[3 6 7 18–20 26 27] The high prevalence in the current study could be explained by a number of reasons: (1) the categories of DRPs causing DRH in this study were comprehensive, while other studies investigated particular types of DRPs that resulted

Table 1 Sociodemographic and clinical characteristics of the participants in the emergency ward at TASH, ZMH and Y12HMC, Addis Ababa, Ethiopia, August–September 2020 (n=423)

Variables	DRH (245), n (%)	Non-DRH (178), n (%)	Total (423), n (%)
Gender			
Male	119 (48.6)	88 (49.4)	207 (48.9)
Female	126 (51.4)	90 (50.6)	216 (51.1)
Age* (in years)			
Mean±SD	48.23±17.85	46.5±16.3	47.5±17.2
14–24	24 (9.8)	14 (7.9)	38 (8.98)
25–39	51 (20.8)	59 (33.1)	110(26)
40–64	100 (40.8)	74 (41.6)	174 (41.1)
>64	70 (28.6)	31 (17.4)	101 (23.9)
Marital status*			
Single	64 (26.1)	34 (19.1)	98 (23.2)
Married	129 (48.6)	105(59)	234 (55.3)
Widowed	20 (8.2)	9 (5.1)	29 (6.7)
Divorced	42 (17.1)	31 (16.9)	73 (17.3)
Educational level*			
No formal education	116 (47.3)	72 (40.4)	188 (44.4)
Elementary	66 (26.9)	47 (26.4)	113 (26.7)
Secondary	31 (12.7)	35 (19.7)	66 (15.6)
Tertiary	32 (13.1)	24 (13.5)	56 (13.2)
Residence			
Addis Ababa	177 (72.2)	127 (71.3)	304 (71.9)
Out of Addis Ababa	68 (27.8)	51 (28.7)	119 (28.1)
Religion			
Orthodox	186(76)	136(76)	322 (76.1)
Muslim	42 (17.1)	31 (17.4)	73 (17.3)
Catholic	1 (0.4)	1 (0.6)	2 (0.5)
Protestant	16 (6.5)	10(6)	26 (6.1)
Employment status*			
Salaried worker	111 (45.3)	83 (46.6)	194 (45.9)
Unemployed	87 (35.5)	74 (41.6)	161 (38.1)
Student	18 (7.3)	7 (3.9)	25 (5.9)
Other†	29 (11.8)	14 (7.9)	43 (10.2)
Social habit (smoking cigarette)			
Yes	29 (11.8)	15 (8.4)	44 (10.4)
No	216 (88.2)	163 (91.6)	379 (89.6)
Social habit (drinking alcohol)			
Yes	71 (29)	57 (32)	128 (30.3)
No	174 (71)	121 (68)	295 (69.7)
Any physical activity			
Yes	170 (69.4)	132 (74.1)	302 (71.4)
No	70 (30.6)	46 (25.9)	106 (28.6)
Home remedies (herbals)			
Yes	3 (1.2)	0 (0)	3 (0.7)
No	242 (98.8)	178 (100)	420 (99.3)

Continued

Table 1 Continued

Variables	DRH (245), n (%)	Non-DRH (178), n (%)	Total (423), n (%)
Number of medications taken per patient*			
Mean±SD	3.4±2.4	3.2±2.1	3.3±2.3
0	24 (9.8)	12 (6.7)	36 (8.5)
1	41 (16.7)	26 (14.6)	67 (15.8)
2	35 (14.3)	40 (22.5)	75 (17.7)
3–4	61 (24.9)	57(32)	118 (27.9)
≥5	84 (34.3)	43 (24.2)	127 (30)
Polypharmacy			
Yes	84 (34.3)	43 (24.2)	127 (30)
No	161 (65.7)	135 (75.8)	296 (70)
Comorbid condition*			
Yes	137 (55.9)	76 (42.7)	213 (50.4)
No	108 (44.1)	102 (57.3)	210 (49.6)
Comorbid condition (hypertension)			
Yes	68 (27.8)	40 (22.5)	108 (25.5)
Comorbid condition (diabetes mellitus)			
Yes	31 (12.7)	22 (12.4)	53 (12.5)
Comorbid condition (cardiac diseases)			
Yes	38 (15.5)	21 (11.8)	59 (13.9)

*Represent variables having significant bivariate associations.
†Participants who did not have any occupation rather they lived depending on other people.
DRH, drug-related hospitalisation; TASH, Tikur Anbessa Specialized Hospital; Y12HMC, Yekatit 12 Hospital Medical College; ZMH, Zewditu Memorial Hospital.

in DRH such as therapeutic failure[27] and ADR[2 26 28 29]; (2) the prospective design of this study helps to ensure the gathering of all information required to accurately classify the events; (3) detailed histories of drug therapy obtained by clinical pharmacists might have improved detection of DRH; and (4) use of the Hepler and Strand's comprehensive classification system has likely boosted the probability that all possible drug-related causes of hospitalisation be identified. In addition, the wide variability in the rate of DRH could also be attributed to the variations in the extent of study population, inclusion criteria, study settings, participants' level of education and awareness, level of health professional expertise, methods of evaluating DRH attributed to DRPs, study designs (prospective vs retrospective) and the study duration. These variations are also reported by other studies.[2 10 11 28 29]

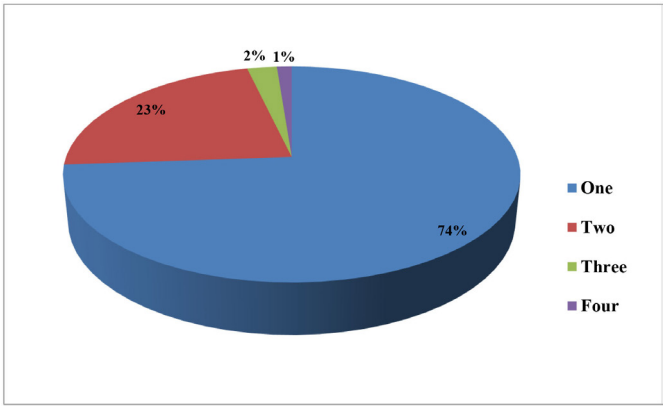

Figure 2 Numbers of drug-related problem occurrence per patient leading to hospitalisation in the emergency ward at TASH, ZMH and Y12HMC, Addis Ababa, Ethiopia, August–September 2020 (n=245). TASH, Tikur Anbessa Specialized Hospital; Y12HMC, Yekatit 12 Hospital Medical College; ZMH, Zewditu Memorial Hospital.

In this study, 87.8% of DRH was deemed to be preventable and this is in line with other international studies in which preventability of DRH has been by far greater than 50%.[10–12 18 21 22 29 30] The reason why DRH preventability was high could be attributed to failure to take appropriate measurements before drug-related diseases were apparent. For instance, the principal categories of DRH in our study were failure to receive drugs (130, 53.5%) and untreated indication (94, 38.5%). Hence, both categories of DRH attributed to DRPs could be avoided by providing awareness for patients about their drug use, applying good prescribing and dispensing practice, and providing appropriate pharmaceutical care plan.

The majority of DRH were most commonly seen among female patients, which is concordant with a previous study.[31] However, in a study done in Saudi Arabia, DRH was largely found in male patients.[2 22] Elderly patients

Table 2 Categories of drug-related hospitalisation (DRH) in the emergency ward at TASH, ZMH and Y12HMC, Addis Ababa, Ethiopia, August–September 2020 (n=245)

Categories of DRH	Causes of DRH	Frequency (%)
Untreated indications		94 (38.5)
	Untreated medical condition existed	34 (36.2)
	Synergistic/potentiating drug needed	42 (44.7)
	Preventive/prophylactic drug needed	18 (19)
Improper drug selection		16 (6.5)
	More effective alternative drug is available	6 (37.5)
	Condition is already refractory to drug	2 (12.5)
	The drug is not effective for condition	6 (37.5)
	Others*	2 (12.5)
Subtherapeutic dosage		30 (12.2)
	Wrong dose (too small) of the drug	24 (80)
	Frequency is inappropriate (long)	5 (16.7)
	Duration of drug use is too short	1 (3.3)
Supratherapeutic dosage		13 (5.3)
	Wrong dose (too high) of the drug	11 (84.6)
	Frequency is inappropriate (short)	2 (15.4)
Adverse drug reaction		38 (15.5)
	Undesired effect from the drug is found	34 (89.5)
	Unsafe drug for patient existed	1 (2.6)
	Dosage is administered too rapidly	1 (2.6)
	Allergic reaction is found/ reported	2 (5.3)
Drug interactions		1 (0.4)
	There is (are) major drug interaction/s	1 (100)
Failure to receive drugs		130 (53.5)
	Does not understand instructions	6 (4.6)
	Patients prefer not to take	43 (33.1)
	Patients forget to take	3 (2.3)
	Drug product not available	17 (13.1)
	Cost of medication too expensive	16 (12.3)
	Does not believe in the drug effectiveness	1 (0.8)
	Patients felt better	17 (13.1)
	Patients felt worse	1 (0.8)
	Fear of adverse events	18 (13.8)
	Failure to follow up due to COVID-19	8 (6.2)
Total number of DRPs leading to DRH		322
Total number of participants with DRH		245
Average number of DRPs per drug-related hospitalised patient		1.31
Preventability of DRH		215 (87.8)

*Patients who were using expired drugs like insulin and albuterol.
DRPs, drug-related problems; TASH, Tikur Anbessa Specialized Hospital; Y12HMC, Yekatit 12 Hospital Medical College; ZMH, Zewditu Memorial Hospital.

developed more DRPs leading to DRH than patients in other age groups, which is also in line with other studies.[6 16 27] The main reasons could be increased deterioration of physiological functions and likelihood of comorbid conditions with age. These conditions may warrant taking of multiple drugs, which ultimately serves as a basis for contracting medication side effects and interactions (drug–drug or drug–food).

In this study, patients whose educational level was elementary and below were more prone to develop DRH

Table 3 Diseases associated with drug-related hospitalisation in the emergency ward at TASH, ZMH and Y12HMC, Addis Ababa, Ethiopia, August–September 2020 (n=245)

Disease categories	n (%)
Cardiovascular diseases	80 (32.6)
CNS diseases	8 (3.2)
Cerebrovascular diseases	26 (10.6)
Infectious diseases	21 (8.5)
Endocrine system diseases	47 (19.2)
Cancer	25 (10.1)
Diseases of the respiratory system	21 (8.5)
GI diseases	10 (4)
Others*	7 (2.8)

*Includes anaemia, chronic kidney disease, systemic lupus erythematosus and haemophilia.
CNS, central nervous system; GI, gastrointestinal; TASH, Tikur Anbessa Specialized Hospital; Y12HMC, Yekatit 12 Hospital Medical College; ZMH, Zewditu Memorial Hospital.

Table 4 Medication classes and specific drugs implicated in drug-related hospitalisation (DRH) in the emergency ward at TASH, ZMH and Y12HMC, Addis Ababa, Ethiopia, August–September 2020 (n=245)

Drug class	Specific drugs	n (%)
Cardiovascular drugs		
	Atorvastatin	31 (12.7)
	Antiplatelets (aspirin, clopidogrel)	24 (9.8)
	Furosemide	59 (24.1)
	Spironolactone	33 (13.5)
	Anticoagulants (warfarin, heparin)	20 (8.2)
	Beta-blockers (metoprolol, atenolol)	21 (8.6)
	Digoxin	15 (6.1)
	ACE inhibitors (enalapril/ lisinopril)	48 (19.6)
	Calcium channel blockers (nifedipine, amlodipine)	34 (13.9)
	Hydrochlorothiazide	11 (4.5)
Drugs for the respiratory system		
	Long-acting beta-blockers	15 (6.1)
	Bronchodilator	10 (4.1)
Central nervous system drugs		
	Antiepileptics	5 (2)
	Antipsychotics	5 (2)
	Amitriptylin	2 (0.8)
Antimicrobial drugs		
	Antibiotics (piperacillin/ tazobactam, meropenem, amoxicillin, amoxicillin/ clavunicacid, ceftriaxone, benzathine penicillin)	25 (10.2)
	Combination of antiretroviral therapy	15 (6.1)
	Anti-tuberculosis	13 (5.3)
Antineoplastic agents	Cyclophosphamide, imatinib, methotrexate, doxorubicin	23 (9.4)
Immunosuppressants		
	Mycophenolate	1(.4)
	Corticosteroids (prednisolone, budesonide)	9 (3.7)
Endocrine drugs		
	Oral hypoglycaemic drugs (metformin, glibenclamide)	37 (15.1)
	Insulin	24 (9.8)
	Propylthiouracil	4 (1.6)
Gastrointestinal drug	Proton pump inhibitors	7 (2.9)
Others	Potassium chloride	1 (0.4)
	Non-steroidal anti-inflammatory drugs	3 (1.2)
	Opioids	1 (0.4)
Others		
	Ferrous sulfate	1 (0.4)
Total number of medications involved in DRH		497
Total number of drug-related hospitalised participants		245 (57.9)
Average number of medications per drug-related hospitalised patient		2.03

TASH, Tikur Anbessa Specialized Hospital; Y12HMC, Yekatit 12 Hospital Medical College; ZMH, Zewditu Memorial Hospital.

than those who had high school education or above, which was consistent with studies done previously.[3 18] This could be related to the fact that high level of education is useful for better socioeconomic status and to understand appropriate medication use.

Out of a total of 245 drug-related hospitalised patients, the foremost categories of DRH were failure to receive drugs (130, 53.5%), followed by untreated indication (94, 38.5%), ADRs (38, 15.5%) and subtherapeutic dosage (30, 12.2%). Similar findings were reported by other studies.[5 12 18 20–22 25 27 30] The major reasons for failure to receive drugs in this study were the following: preference for cultural and religious therapies over conventional medicines, drug products were not available, cost of medications was too expensive, fear of adverse events, failure to follow up due to COVID-19, feeling better and illiteracy (near to half of drug-related hospitalised patients were illiterate). Thus, inability to recall regimens is another important reason associated with increased risk of hospitalisation related to failure to receive drugs, as reported elsewhere.[3 11 21]

The second frequent category of DRH was untreated indication (94, 38.5%) as reported in other studies.[9 22] Reasons were patients remained untreated, and prophylaxis and synergistic medications were not indicated. This might be due to incorrect diagnosis, patients did not come to the health setting on time and treating physicians did not follow the management guidelines/protocols. For example, patients having moderate persistent asthma were being treated with albuterol inhalation alone. Statins have not also been prescribed for patients with atherosclerotic cardiovascular diseases like peripheral arterial disease, stroke, ischaemic heart disease and whose age is ≥40 years with diabetes mellitus and high/low-density lipoprotein level as per the guidelines. In addition, some compelling indication like hypertension remains untreated and subsequently results in DRH owing to stroke and other cardiovascular diseases. Furthermore, since only cancer diagnosis and management are carried out in one of this research's hospital, which is TASH, patients coming from different corners of the country remained untreated and/or treated with

Table 5 Predictors involved in drug-related hospitalisation (DRH) in the emergency ward at TASH, ZMH and Y12HMC, Addis Ababa, Ethiopia, August–September 2020 (n=245)

	Predictors of patient hospitalisation			OR	
	DRH (245)	Non-DRH (178)	Total (423)	AOR (95% CI)	P value
Variables	n (%)	n (%)	n (%)		
Age (years)					
Mean±SD	48.24±17.86		47.50±17.21		
14–24	24 (9.8)	14 (7.9)	38 (8.98)	1	
25–39	51 (20.8)	59 (33.1)	110(26)	1.55 (0.51 to 4.66)	0.435
40–64	100 (40.8)	74 (41.6)	174 (41.1)	2.567 (0.82 to 8.06)	0.106
>64	70 (28.6)	31 (17.4)	101 (23.9)	7.45 (1.89 to 29.40)	0.004
Marital status					
Single	64 (26.1)	34 (19.1)	98 (23.2)	1	
Married	129 (48.6)	105(59)	234 (55.3)	0.60 (0.29 to 1.23)	0.16
Widowed	20 (8.2)	9 (5.1)	29 (6.7)	0.49 (0.20 to 1.18)	0.109
Divorced	42 (17.1)	31 (16.9)	73 (17.3)	0.35 (0.19 to 0.75)	0.983
Educational level					
No formal education	116 (47.3)	72 (40.4)	188 (44.4)	1	
Elementary	66 (26.9)	47 (26.4)	113 (26.7)	0.57 (0.23 to 1.43)	0.229
Secondary	31 (12.7)	35 (19.7)	66 (15.6)	0.57 (0.23 to 1.39)	0.215
Tertiary	32 (13.1)	24 (13.5)	56 (13.2)	0.36 (0.14 to 0.92)	0.033
Employment status					
Salaried worker	111 (45.3)	83 (46.6)	194 (45.9)	1	
Unemployed	87 (35.5)	74 (41.6)	161 (38.1)	0.29 (0.09 to 0.89)	1
Student	18 (7.3)	7 (3.9)	25 (5.9)	6.33 (1.38 to 29.15)	0.018
Others*	29 (11.8)	14 (7.9)	43 (10.2)	3.41 (1.12 to 10.37)	0.031
Polypharmacy					
Yes	84 (34.3)	43 (24.2)	127(30)	1.48 (0.72 to 3.04)	0.284
No	161 (65.7)	135 (75.8)	296(70)	1	
Comorbid condition					
Yes	137 (55.9)	76 (42.7)	213 (50.4)	2.00 (1.09 to 3.67)	0.024
No	108 (44.1)	102 (57.3)	210 (49.6)	1	

*Participants who did not have any occupation.
AOR, adjusted OR; TASH, Tikur Anbessa Specialized Hospital; Y12HMC, Yekatit 12 Hospital Medical College; ZMH, Zewditu Memorial Hospital.

various empirical therapies that also lead to improper drug selection until they start anticancer drugs in TASH.

ADRs (38, 15.5%) were also commonly reported as the common classification of DRH, which is also mentioned in other studies.[11 19–21 29 30 32] This might be associated with numerous number of patients with cardiac disease and diabetes in our study population and poor awareness of patients with regard to cardiac medications' untoward effects such as diuretics-induced electrolytes disturbance and hypoglycaemic symptoms of antidiabetics. Some ADRs could result from failure to follow direction for use of the medications. For example, a patient with diabetes mellitus who was on metformin experienced epigastric burning sensation pain and vomiting after taking metformin without meal. Overall, the plausible explanation for DRH might be the absence of pharmaceutical care services in many health institutions including emergency wards of the study settings, which is very important for optimising drug therapy and patient safety. There was also poor collaboration among patients, clinical pharmacists and physicians about patients' medication use process involving medication use, their side effects, adherence issue and consequences of not taking their medication properly. Therefore, the better opportunity for clinical pharmacists to add value in patient care roles is through ensuring medication management services according to evidence-based guidelines. In the present study, both failure to receive drugs and untreated indication were

reported under the DRP category of needing additional drug therapy that resulted in DRH, which is supported by other studies.[7 9 18]

In this study, medication classes frequently observed to cause DRH were cardiovascular medicines, antimicrobials, antineoplastics, endocrine drugs, respiratory medicines and central nervous system drugs. Among these classes of drugs, cardiovascular drugs were predominantly involved in DRH, which was in line with other studies.[3 5 6 21 25 27]Cardiovascular drugs, antidiabetics and antiasthmatics were most commonly associated with DRH, which was supported by the previous studies.[2 24 26 27] The most common drugs associated with DRH mentioned in this study finding were furosemide, ACEIs, insulins, oral hypoglycaemic agents, warfarin, spironolactone, aspirin and central nervous system agents, and these are also implicated in several other studies.[5 7 10 21 22 24 29] The main reason might be connected with the common diseases found in the study area, which were heart failure, diabetes mellitus, stroke, HIV and asthma.

Moreover, the most common organ system involved in DRH was the cardiovascular system (80, 32.6%), with the most common specific disease, that is, heart failure (55, 22.5%), which is consistent with previous studies.[6 25] Moreover, hypertension was mentioned for DRH which was implicated in the previous study.[5 22 27] This is due to the fact that cardiovascular diseases require multiple medicine regimens and this contributed to DRPs. Among hospitalised patients attributed to endocrine systems were due to hypoglycaemia, hyperglycaemia and diabetic ketoacidosis, which are also cited in other studies.[22 27] It might be due to the patients' poor awareness about the hypoglycaemic symptoms of antihypoglycaemic agents, poor monitoring control and patients prefer not to take the medications.

In this study, age, educational level and presence of comorbid diseases had statistically significant correlation with the occurrence of DRH. The findings are consistent with other studies.[18 20 30 33]

In the multiple binary logistic regression analysis, patients aged ≥65 years were 7.45 times more likely to be hospitalised due to drug-related morbidity than non-drug related as compared with those aged between 14 and 24 years. This might be due to age-related physiological changes and larger number of coexisting disease conditions which require multiple medications, and this in turn is associated with an increased risk of DRH.

From the employment factor, students were 6.3-fold more likely exposed to DRH than non-drug related as compared with the employed. This might be explained by the nature of the disease they had which means students in this finding have majorly contracted heart failure disease secondary to chronic rheumatoid valvular heart disease. Out of a total 16 students, 9 (56.3%) of them had heart failure owing to valvular heart diseases. Consequently, it needs lifelong and multiple medication treatment and then they faced various DRPs leading to hospitalisation. Moreover, participants who did not have any occupation were 3.4 times more likely to be hospitalised owing to drug-related diseases than non-drug related as compared with those who were employed.

The other factor was educational level in which patients with tertiary education were 64% less likely to be hospitalised because of drug-related issues as compared with participants who did not have formal education. This could be related to the fact that high level of education might be useful to understand about appropriate medication use. This was supported by the studies conducted in Brazil.[3 11 18] Patients with comorbid disease were also twofold more likely to be hospitalised because of drug-related than non-drug-related issues as compared with patients without comorbid disease. As implicated in the previous studies,[18 30 33] comorbidity increases vulnerability towards DRPs. These results clearly indicate the necessity of managing DRH in multimorbid patients.

In terms of drug-related hospital stay, the overall length of hospital stay in the present study was 4352 days with an average length of hospital stay of 10.28±8.99 days, which is longer than what has been reported in other studies.[12] This might be due to the fact that the data in the previous study are in a single hospital and for a relatively short period of time (28 days); while in this finding, the study was carried out at three tertiary care hospitals for the period of 60 days. Therefore, avoiding preventable DRH is also a very cost-effective tool for healthcare systems and could reduce the problem of bed crisis in hospitals.

Among factors which have not demonstrated an association in the multivariate analysis, polypharmacy was mentioned. This agree with what have been reported in other studies.[21 25] In contrast, polypharmacy has been reported having positive association with the occurrence of DRH in previous studies.[3 6 11 21 22 30] This lack of significance could be the result of variations in the number of used medications and identified DRPs causing DRH. In this study, around two-thirds of drug-related hospitalised patients used none to four drugs per patient. Accordingly, to say polypharmacy, ≥5 drugs should be concomitantly taken. Furthermore, the identified DRPs causing DRH were failure to receive drugs and untreated indication. So, both categories reveal not taking medications and the patients might not use polypharmacy. Additionally, marital status did not illustrate significant association with DRH.

Conclusion

The prevalence of DRH was higher in this study than studies conducted elsewhere among emergency ward patients in the study settings. Among those, the majority of DRH were deemed to be preventable. These findings provide valuable insight about category of DRPs and class of drugs that causes DRH. Age, educational level, participants who did not have any occupation and presence of comorbid conditions have had significant association with DRH. Hence, researches regarding DRH should be conducted in different Ethiopian hospitals to demonstrate its impact.

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Patient consent for publication Obtained.

Ethics approval Prior to study initiation, letter of ethical approval (Ref No: ERB/SOP/172/08/2020) was obtained from the Ethical Review Committee of the School of Pharmacy, College of Health Sciences, Addis Ababa University. Verbal consent from patients was obtained after the provision of information regarding the purpose of the study and its risk for the interviewed which could be time to be spent during the interview (maximum of 30 min). Names were not used, rather codes were used to maintain confidentiality of the information throughout the study period. Patients were told the reasons of being selected to be included in the study and assured that waning participation would not have any influence on the right to get treatment. Patients were also told about their right to withdraw from the study at any time.

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