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ORIGINAL RESEARCH

Predictors of Medication-Related Emergency Department Admissions Among Patients with Cardiovascular Diseases at Mbarara Regional Referral Hospital, South-Western Uganda

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Background: Medication-related emergency department admissions impose a huge and unnecessary burden on the healthcare system. We sought to determine the prevalence and predictors of medication-related emergency department admissions, among patients with cardiovascular diseases at Mbarara Regional Referral Hospital, Uganda.

Methods: Institutional research ethics approval was secured to conduct a cross-sectional study at the Mbarara Regional Referral Hospital emergency department, between February and September, 2020. All eligible and consenting patients were enrolled in a consecutive manner after a preliminary diagnosis was made by the attending physician. Structured questionnaire interview and comprehensive medication history reviews were used to identify medication therapy problems, in collaboration with a resident physician present on duty. We used sequential categorization for medication therapy problem(s). Descriptive and logistic regression analyses were used to determine prevalence and predictors of medication-related emergency department admissions.

Results: Out of the 128 patients interviewed, 105 (82%) patient admissions were associated with a medication therapy problem: ineffectiveness of drug therapy (53.3%, 56), medication non-adherence (42.9%, 45), and adverse drug reactions (3.8%, 4). Out of a total of 90 incidences of medication non-adherence, 34.4% (31/90) were due to lack of understanding of patient medication regimen, and 27.8% (25/90) due to unaffordable cost of medicines. Female gender (AOR = 4.31 [1.43, 13.03 at 95% CI]; *P*-value = 0.010]) and a history of tobacco use (AOR = 9.58 [1.14, 80.28 at 95% CI]; *P*-value = 0.037) were statistically significant predictors of medication-related emergency department admissions in adjusted analysis.

Conclusion: Four in five emergency department admissions were associated with medication-related causes, majorly due to ineffectiveness of drug therapy. Knowledge gap on patient medication regimens was the most prevalent cause for medication non-adherence. Female gender and previous or current tobacco use was an independent risk factor for medication-related admissions.

Keywords: adverse drug reaction, ineffective drug therapy, non-adherence, emergency department admission, cardiovascular, Uganda

Introduction

There is a huge public health concern regarding the increasing medication-related emergency department admissions due to failure to manage medication therapy problems (MTPs) among patients with cardiovascular disease in developing

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Received: 4 March 2021
Accepted: 11 June 2021
Published: 29 June 2021

countries.[1,2] MTPs include any undesirable event(s) experienced by a patient, which involves or is suspected to involve drug therapy, thereby interfering with achieving the desired goals of therapy and requires professional judgment to resolve.[3] Optimization of out-patient follow-up management of cardiovascular disease and/or associated complications necessitates accurate and comprehensive diagnosis, treatment, and prevention of medication therapy problems.[4] Medication-related ED (MRED) admissions associated with MTPs have been highly associated with patients on multiple cardiovascular medication,[5] especially, antihypertensive and cardiac glycoside medications.[6–8] These admissions impose an unnecessary extra expenditure on the healthcare system[9] due to prescription cascades, laboratory costs,[10] morbidity and mortality.[11]

Among the diverse categories of MTPs, medication non-adherence has been identified as the single most prevalent and costly cause of hospital emergency admission, resulting from drug treatment failure, sub-optimal disease management, and a compounded risk for disease complications.[12] Similarly, ADR-associated ED admissions have previously been reported at 10.3% in Ethiopia,[13] with the number of medications, comorbid states, and drug therapy changes within the preceding 3 months as strong predictors of ADR-related ED admissions.[14] Actual or potential drug therapy ineffectiveness has been identified as a major cause of hospital admission,[15,16] contributing up to 58% (76/135) of all hospital admissions in a local Ethiopian hospital.[17] However, the burden in Uganda is largely unknown. By and large, there is limited published literature on MRED admissions due to ADR (adverse drug reaction), drug therapy ineffectiveness, or indication in developing countries, possibly due to the underdeveloped surveillance system (ADRs) and the limited human resource capacity to assess prescribed drug therapy effectiveness and indication in out-patient care.

For clinical pharmacists to effectively identify, assess, and quantify the burden of medication-related emergency department admissions among cardiovascular disease patients, there is need for a universal tool or definition to foster a global understanding of the subject. However, this is lacking at the moment, and several MRED admission categorization methods have been developed to that effect.[18,19] However, sequential identification and categorization of medication-related causes of admission, involving issues with drug therapy indication, effectiveness, safety (ADR or dose too high), and adherence in that prioritized order, remains the most trusted system of classification in the literature.[20,21] An MTP of non-adherence is only considered to have potentially resulted in ED admission (MRED) if the medication(s) in question are, firstly, indicated, effective, and safe for the patient. Similarly, an ADR-related admission is only considered if the prescribed medication(s) is indicated and effective for the treated disease condition. Several studies in Africa and related settings have initially narrowed the definition of MRED admissions, as resulting from individual MTPs; like ADRs,[13,22] medication non-adherence,[23] and/or a combination of only two or more varying MTPs,[24] thus missing out on vital information on assessing clinically relevant medication use outcomes among CVD patients. Sequential categorization of MTPs as suggested by Cipolle et al tries to address the challenge of variations in definition and outcomes of research on "Medication or drug-related hospital/ED admissions/visits", as evident in previously published literature. In our study, therefore, we operationalized medication-related ED (MRED) admissions, as causes of admissions related to either medication effectiveness, adherence, or adverse drug reactions for medications indicated. Medication-related problems associated with drugs not indicated were excluded.

Due to a dearth of research on MRED admissions in sub-Saharan Africa, this study sought to determine the prevalence and predictors of MRED admissions among patients with cardiovascular disease at MRRH, western Uganda. The study also aimed at identifying the different reasons for non-adherence to medication therapy.

Methods

Study Setting

The study was conducted at the Mbarara Regional Referral Hospital (MRRH) emergency department, Mbarara City, Uganda. MRRH is a 350-bed tertiary hospital and is considered the largest referral center in south-western Uganda. The hospital serves up to four million people from the neighboring districts and countries, like Burundi, DRC, and Tanzania. The hospital ED is a ten-bed facility that is majorly manned by residents under the guidance of senior hospital staff, and comprises both the surgical and medical units. The department runs 24/7 with an estimated annual admission of 4000 patients, both male and female patients ≥18 years of age.

Study Population

All patients admitted at the MRRH ED with a primary diagnosis of cardiovascular disease, between February and September, 2020.

Eligibility Criteria

Inclusion criteria: primary cardiovascular disease diagnosis, age ≥ 18 years, consenting to participate in the study. Exclusion criteria: mentally unstable or unconscious patients, infectious disease exacerbation(s), patients with less than 3 months of out-patient follow-up treatment of cardiovascular disease, incomplete medical records.

Study Design

We conducted a cross-sectional study, between February and September, 2020.

Sample Size Calculation

We used a single proportion formula to determine the sample size,[25] as adopted from previous studies:

$$n = (Z^2\alpha/2XP(1-P))/e^2$$

$$\text{Finite population correction formula } N_o = \frac{n \times N}{n + N - 1}$$

Using an estimate of 165 (N) patients admitted with cardiovascular disease at the MRRH ED in the previous 3 months, 5% margin of error (*e*), an estimated 50% prevalence (p) of MRED admission as no similar study has been done in Uganda or similar settings, and a 5% level of significance, we calculated a sample size (N_o) of 116 participants. By adding 10% for incomplete data or non-response, we obtained a sample size of 128 participants.

Sampling Technique

A consecutive sampling technique was employed involving every consecutive patient who fulfilled the eligibility criteria and consented to participate in the study.

Data Collection Procedure

Study participants were interviewed between 08:00 AM and 5:00 PM (EAT), Monday to Friday. Participants were subjected to a structured questionnaire and checklist interview as soon as the patient or attendant felt convenient and preliminary diagnosis was made by the attending physician. Participant socio-demographic data, history of presenting illness, past history, number of hospital admissions in the past one year, history of allergies and medication history (including over-the counter (OTC) and complementary and alternative medicines) was obtained by pharmacists.

A participant and prescription-oriented medication therapy review was done to identify out-patient MTPs, including medication non-adherence, ineffective drug therapy, and ADRs at the point of admission.

To assess the effectiveness of drug therapy, standard references (Uganda Clinical Guidelines-2016 and UpToDate) and an aggregated system of classification were used to assess appropriateness of prescribed drug (s), appropriateness of dosage form and regimen, issues of drug quality/expiry, and refractoriness of disease to drug therapy, in a prioritized manner.[26]

Using the Naranjo ADR causality algorithm, participants with definite and probable ADR causality scores (≥5) were considered ADR-related ED admissions.[27]

We used the Hill–Bone medication adherence scale to determine any non-adherence that had occurred while the patients were at home.[28] The identified non-adherence was categorized using Cipolle et al's classification of causes of drug therapy problems.[20]

To identify individual MTPs associated with CVD exacerbation, leading to ED admission (MRED admissions), MTPs were sequentially categorized in the precedence of drug therapy indication, ineffectiveness of drug therapy, ADR, and medication non-adherence.[20,21] Non adherence was only considered if drug therapy was indicated, effective, and no concerns of ADRs; similarly, ineffectiveness of drug therapy was only qualified if prescribed drug therapy is indicated.

The above information was verified by a resident physician, who independently interviewed participants and conducted physical assessments whenever requested by the principle investigator.

Patients' enrolment was stopped once the estimated sample size was interviewed.

Data Analysis and Interpretation

Respective participant data were entered and analyzed using statistical software (SPSS version 21, SPSS Inc., Chicago, IL, USA). Prevalence of MRED admissions was determined by dividing the number of MRED admissions by the total sample size. Descriptive analysis was done to determine the frequencies and percentages of the participants, disease, and drug-related factors. The relationship between the dependent (MRED admission) and independent variables were determined using odds ratios

with a 95% confidence interval. Univariate and multivariate binary logistic regression analysis was done to determine predictors of MRED admissions. All variables with *P*-value > 0.25 during univariate analysis were excluded from further analysis. *P*-value <0.05 was considered significant for all analyses.

Ethical Consideration

This study was conducted in accordance with the Declaration of Helsinki.[29] This study was approved by the faculty research ethics committee (FREC) and the Mbarara University of Science & Technology research ethics committee (MUST-REC).

Hospital administration of Mbarara Regional Referral Hospital (MRRH) granted permission for the study to be conducted at the hospital ED.

Informed written consent was obtained from individual patients prior to enrollment into the study.

Participant data were handled in a confidential manner throughout and after the study.

The data collectors adhered to the Ugandan Ministry of Health and MRRH protocols on COVID-19 during the study. This included: donning face masks at all times, sanitizing before and after handling individual patient material(s), maintaining appropriate social distancing during interview, quarantining all questionnaires in a safe and isolated cabin for a duration of 3 days prior to further processing, and regular COVID-19 testing of the data collectors.

Results

General Characteristics of the Participants

Out of the 128 study participants interviewed, 77 (60.2%) were females, 76 (59.4%) were <65 years of age (mean, 59.19; SD ±17.3 years), 84 (65.6%) were unemployed, 65 (50.8%) were uneducated, 89 (69.5%) were married, 85 (66.4%) had a history of present or current alcohol intake, 31 (24.2%) had a history of tobacco use, 69 (53.9%) lived 10 km or more from the nearby hospital, and 75 (58.6%) had been admitted ≤2 times in the past one year (Table 1).

Table 1 Demographic Characteristics of Patients with Cardiovascular Diseases Admitted to the MRRH ED Between February and September, 2020

Variable	Category	Frequency	Percentage (%)
Age (years)	<65	76	59.40
	≥65	52	40.60
Gender	Female	77	60.20
	Male	51	39.80
Occupation	Student/ unemployed	86	67.10
	Employed	18	14.10
	Self-employed	24	18.80
Education level	Uneducated	65	50.80
	Primary	44	34.40
	Secondary	8	6.20
	Tertiary	11	8.60
Marital status	Single	5	3.90
	Married	89	69.50
	Divorced/ widowed	39	30.50
Alcohol	No	43	33.60
	Yes	85	66.40
Tobacco	No	97	75.80
	Yes	31	24.20
Distance from hospital (km)	<10	59	46.10
	≥10	69	53.90

Drug and Disease Characteristics of the Participants

The majority (75, 58.6%) of the participants were admitted 2 or less times in the last one year, 10 (7.8%) had experienced drug allergies, 66 (51.6%) have had new prescribed medications in the last 3 months, 96 (75%) had at least three medications, 62 (49.6%) had a comorbid condition, and 102 (79.7%) had a primary diagnosis of a vascular disease, particularly hypertension (93.1%) (Table 2).

Primary Outcome: Prevalence of Medication-Related Emergency Department (MRED) Admissions

All MTPs due to non-cardiovascular medicines were neither considered as MTPs nor MRED admissions (in case of patient admission). MRED admissions were determined following a sequential identification of MTPs that could have potentially resulted into admission. During the 3-month study period, 82% (105/128) of patients enrolled were considered MRED admissions (Figure 1).

The MTPs associated with MRED admissions, include: ineffectiveness of drug therapy (53.3%, 56), non-

Table 2 Prevalence of Drug and Disease-Related Factors of Patients with Cardiovascular Disease, Admitted at MRRH ED Between February and September, 2020

Variable	Category	Frequency	Percentage (%)
Number of previous admissions in 1 year	≤2 ≥3	75 53	58.60 41.40
Drug allergies	No Yes	118 10	92.20 7.80
New drug prescribed in last 3 months	No Yes	62 66	48.40 51.60
Number of medications	≤2 ≥3	32 96	25.00 75.00
Comorbid condition	No Yes	65 63	50.80 49.20
Previous diagnosis category	Primarily vascular Primarily cardiac	102 26	79.70 20.30
Duration of previous diagnosis category (years)	1–2 ≥3	75 53	58.60 41.40

adherence (42.9%, 45), and ADRs (3.8%, 4). An overall MTP incidence of 1.3 (161/128) was determined, with only 65.2% (105/161) of all identified MTPs potentially associated with patient admissions during the study period. Although some patients had more than one MTP, only the proceeding MTP in the sequential order of MTP categorization was considered as the potential cause of admission (Table 3).

Secondary Outcome: Leading Cause of Medication Non-Adherence

Overall, 90 (70.3%) study participants were not adhering to their prescribed medications while at home. Reasons for non-adherence included: inadequate understanding of medication use instructions (31, 34.4%), unaffordable cost of medicines (25, 27.8%), varying physician diagnosis (9, 10%), forgetting to take medicines (8, 8.9%), unavailability of prescribed medicines (8, 8.9%), and unwillingness to take medicines (2, 2.2%) (Figure 2).

Tertiary Outcome: Predictors of MRED Admissions

Univariate Analysis

Among the factors analyzed for possible association to MRED admissions, female gender (COR = 4.6 [1.7, 12.1 at 95% CI]; *P*-value = 0.002), a single marital status (COR = 0.09 [0.01, 0.93 at 95% CI]; *P*-value = 0.04), ≥3 medications (COR = 2.29 [0.88, 5.97 at 95% CI]; *P*-value 0.09), history of tobacco smoking (COR = 8.8 [1.13, 68.23 at 95% CI]; *P*-value = 0.04), and history of new drug prescriptions within the last 3 months (COR = 1.85 [0.74, 4.64 at 95% CI]; *P*-value = 0.19) qualified for multivariate analysis (Table 4).

Multivariate Analysis

Female gender (AOR = 4.31 [1.43, 13.03 at 95% CI]; *P*-value = 0.010]) and a history of tobacco use (AOR = 9.58 [1.14, 80.28 at 95% CI]; *P*–value = 0.037) were determined to be significant predictors (*P*-value < 0.05) of MRED admissions among patients admitted with cardiovascular conditions. (Table 5). Female participants were about 4.3 times more likely to incur MRED compared to males whereas participants with history of tobacco use were about 9.5 times more likely to experience MRED admissions compared to non-users.

Discussion

Many pharmaco-epidemiological studies on medication-related hospital/ED admissions have been done under varied definitions in the majority of developed countries. However, as the burden of cardiovascular disease continuously increase in low and middle-income countries, there is a growing concern and call for further research to improve drug safety and effectiveness, especially among patients using cardiovascular drugs.[30,31] Outcomes from our study reveal a serious public health threat of medication-related patient admissions in developing countries like Uganda. The findings suggest that four in five (82%) admissions among patients with cardiovascular disease were potentially associated with medication therapy problems. 53.3% (56/105) of all MRED admissions were directly related to ineffectiveness of prescribed drug(s), whereas 42.9% (45/105) and 3.8% (4/105) were potentially associated with non-adherence and ADRs respectively. Although our study finding is justified by a literature review associating medical chart reviews and studies conducted in African settings with a higher medication-related causes of admission,[32] our prevalence still is significantly higher compared to previously

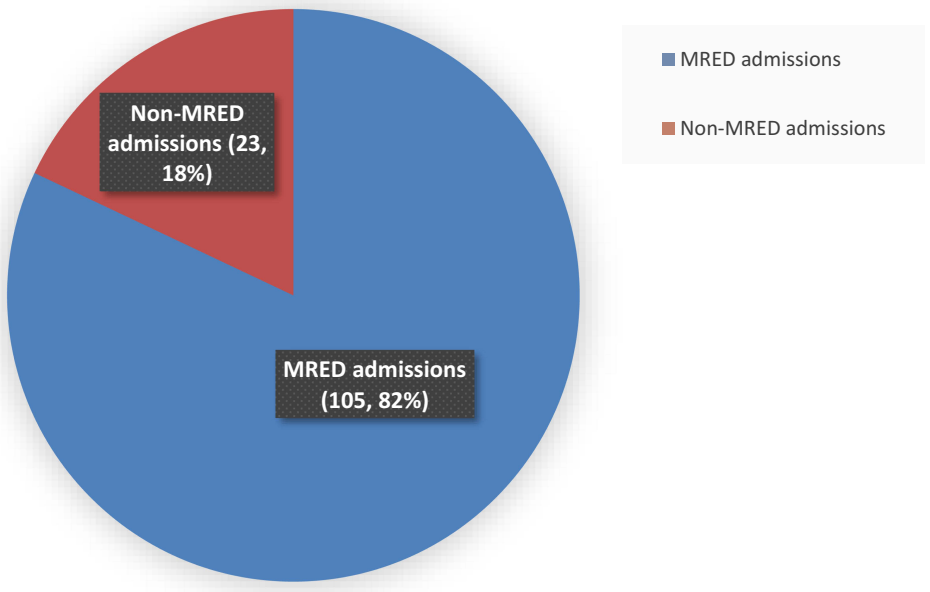

Figure 1 Prevalence of MRED admissions among patients with cardiovascular disease, admitted at MRRH ED between February and September, 2020.

published literature, reporting MRED prevalence of 1.3% to 64%.[33–37] Also, the fact that clinical pharmacy residents were the primary data collectors, and the evidence of higher medication-related admissions among patients on multiple cardiovascular medications,[5] tends to explain the high MRED prevalence in our study. Unlike in our study, several published study characteristics have consistently been associated with lower MRED prevalence, including settings with a higher socio-economic status[23,37–39], meta-analyses and systematic review study outcomes,[22,36,40], specific participant demographic characteristics (pediatrics, urban or semi-urban dwellers),[36,41] and studies adopting only one or two MTPs to define the outcome variable.[13,24,32,41]

Table 3 Medication Therapy Problems Among MRED Admissions of Patients with Cardiovascular Disease, Admitted at MRRH ED Between February and September, 2020

MTP Category	Frequency of MTPs (%)	Proportion Among MRED Admissions
Ineffective drug therapy	56 (34.8%)	56 (53.3%)
Medication non-adherence	90 (55.9%)	45 (42.9%)
ADRs MTP incidence/ admission	15 (9.3%) 161/128 admissions = 1.3	4 (3.8%) 161/105 MRED admissions = 1.5

Ineffectiveness of therapy is one of the most common causes of medication-related ED admissions, due to failure to achieve clinical targets/responses by patients.[15,16] Our study showed that more than half (53.3%) of all MRED admissions were directly associated with ineffectiveness of drug therapy. Our findings do not differ much from previous findings in a similar setting in Ethiopia, reporting a 58% (76/135) prevalence of ineffective drug therapy among hospital admissions.[17] Two in every five MRED admissions were associated with non-adherence to prescribed medications in our study population. Although there exist socio-economic differences among the participant populations and study settings, the individual contribution of non-adherence to overall MRED admissions in our study, is comparable to similar studies, reporting between 14.5% and 47.34% MRED admission prevalence due to non-adherence.[23,37,41,42] A study conducted in Ethiopia, like many other similar studies, report up to 69.7% non-adherence-associated MRED admissions.[43] However, the majority of these studies consider only one MTP as a possible cause of admission, and neither utilized the model by Cipolle et al in assessing medication-related hospitalizations.[20] An approximate 1 out of every 30 MRED (3.8%) admissions potentially resulted from ADRs. This finding does not significantly differ from previously published studies and literature reviews among patients using cardiovascular medicines, with individual ADR contributions as low as 3.3%.[44–46]

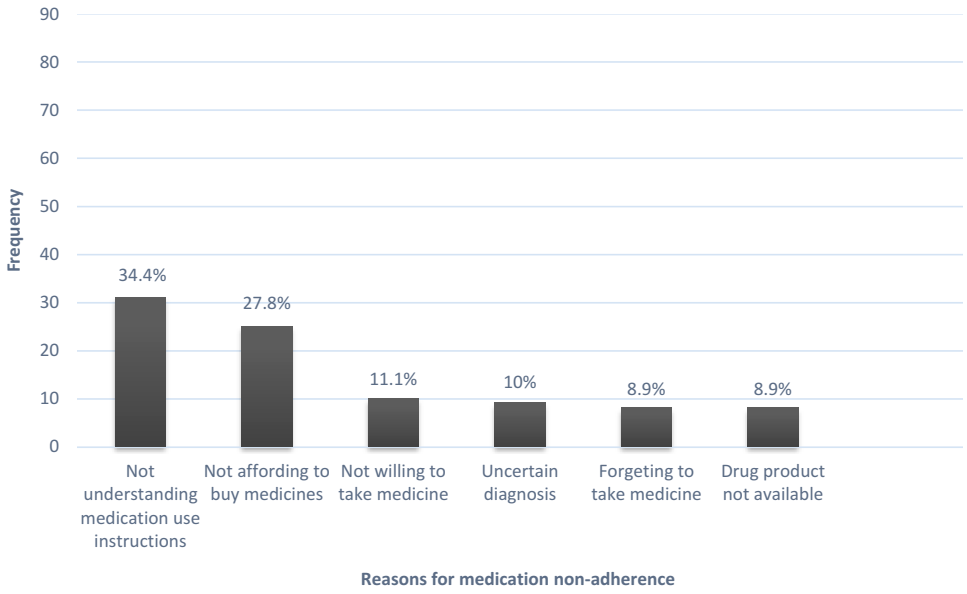

Figure 2 Causes of medication non-adherence among patients with cardiovascular disease, admitted at MRRH ED between February and September, 2020.

Prevalence of MRED admissions across the different participant strata was significantly higher among participants of the female gender (54.7%), those with a positive history of new drug prescribed within past 3 months (44.5%), uneducated (40.6%), married (54.7%), unemployed/students (54.7%), diagnosis of primary disease within the past 2 years (48.4%), and age < 65 years (46.9%). Previous studies conducted in similar settings associated poor socio-economic status and literacy levels with high MRED prevalence.[47,48] However, although old age (>65 years) is a known predictor of MRED admissions,[49] our results state otherwise. This can be explained by the small sample size and the larger younger population in our setting (Table 1). According to categorized outcomes of all participant diagnoses on admission (Table 1), 79% of all MRED admissions had vascular disease diagnosis, of which 7 in every 10 (74%) ED admissions presented with uncontrolled hypertension (with or without complications) and considered MRED admissions. Previous studies implicate hypertensive patients as more likely to visit the ED due to non-adherence (AOR = 11.06, 95% CI: 3.99–30.61), thus MRED admission.[8,41] The low levels of medication adherence among hypertensive patients has been prior reported as resulting from patients' knowledge gaps on their medicines and disease, poor health-seeking behaviors among the general population, mistrust of the healthcare system, inaccessibility to medicines in public hospitals, and poor continuum of care among patients with cardiovascular diseases in Uganda.[50–53]

Previous studies have established an association between medication non-adherence with a complicated cardiovascular disease course (AOR = 2.062, 95% CI: 1.030–4.129), ED admission (OR = 7.5 [95% CI: 5.3, 11.0)[23] and an all cause-mortality (RR 0.71, 95% CI: 0.64–0.78).[54–56] Our study identified an overall 70.3% (90/128) prevalence of non-adherence. This implies that 7 out of every 10 cardiovascular disease ED admissions were non-adherent to their prescribed medications. Our finding is consistent with previous reports of 63.35% (95% CI: 38.78–87.91) prevalence of medication non-adherence, and as the most likely cause of MRED admissions among patients with cardiovascular disease (AOR = 11.06, 95% CI: 3.99–30.61).[41,57,58] Likewise, previous studies in Ethiopia, DRC, and Uganda report that up to 73.2% patients are non-adherent to their medications due to inadequate understanding of medication use instructions (AOR = 7.67, 95% CI = 2.48–23.73, *P*-value < 0.001) (OR = 1.7; 95% CI 1.1–2.7).[59–61] The leading cause of medication non-adherence was the inadequate understanding of medication use instructions among patients (31, 34.4%). This is anticipated as the majority (109, 85.5%) of our participants were uneducated, coupled with the under-resourced health care associated with limited essential medicines in the hospitals.[48,52,62] This demonstrates an urgent need to utilize pharmacist-led comprehensive patient counseling, and strengthen transition-of-care

Table 4 Univariate Analysis of Patient, Disease and Drug-Related Factors Among Patients with Cardiovascular Disease, Admitted at the MRRH ED Between February and September, 2020

Variable	Category	Medication-Related ED (MRED) Admissions		COR (95% CI)	*P*-value
		No	Yes		
Age (years)	<65	16	60	0.60 (0.22, 1.54)	0.28
	≥65	7	45	1	
Gender	Female	7	70	4.60 (1.70, 12.10)	0.002
	Male	16	35	1	
Occupation	Unemployed/student	16	70	0.88 (0.26, 2.91)	0.88
	Employed	3	15	1.00 (0.19, 5.15)	1.00
	Self-employed	4	20	1	
Education	Uneducated	13	52	0.40 (0.05, 3.41)	0.40
	Primary	7	37	0.53 (0.06, 4.81)	0.57
	Secondary	2	6	0.30 (0.02, 4.06)	0.37
	Tertiary	1	10	1	
Marital status	Single	2	3	0.09 (0.01, 0.93)	0.04
	Married	19	70	0.23 (0.05, 1.05)	0.06
	Divorced/widowed	2	32	1	
Distance to hospital (km)	<10	9	50	1.41 (0.56, 3.55)	0.46
	≥10	14	55	1	
Previous admissions in one year	≤2	14	61	0.89 (0.35, 2.24)	0.81
	≥3	9	44	1	
Tobacco	No	1	30	1	
	Yes	22	75	8.8 (1.13, 68.23)	0.04
Alcohol	No	10	33	1	
	Yes	13	72	1.68 (0.67, 4.22)	0.27
Drug allergy	No	22	96	0.49 (0.06, 4.03)	0.50
	Yes	1	9	1	
New drug in 3 months	No	14	48	1	
	Yes	9	57	1.85 (0.74, 4.64)	0.19
Number of medications	≤2	9	23	1	
	≥3	14	82	2.29 (0.88, 5.97)	0.09
Previous diagnosis	Vascular	19	83	0.79 (0.25, 2.58)	0.70
	Cardiac			1	
Duration of previous diagnosis (years)	1–2	13	62	1.11 (0.45, 2.76)	0.82
	≥3	10	43	1	
Comorbid conditions	No	13	52	0.76 (0.30, 1.87)	0.54
	Yes	10	53	1	

systems, as reported to reduce MRED admissions to as low as 3% (*P*-value = 0.002) in previous similar studies.[49,63]

Our predictive analysis results show that the female gender (AOR = 4.31 [1.43, 13.03 at 95% CI]; *P*-value = 0.010) and present or past tobacco users (AOR = 9.58 [1.14, 80.28 at 95% CI]; *P*–value = 0.037), were at least 4 and 9 times more likely to be admitted to ED due to medication therapy problems respectively. These are consistent with previously published studies, identifying

Table 5 Multivariate Analysis of Patient, Disease and Drug-Related Factors Associated with MRED Admissions Among Patients with Cardiovascular Disease, Admitted at the MRRH ED Between February and September, 2020

Variable	Category	MRED Admissions		COR (95% CI)	*P*-value	AOR (95% CI)	*P*-value
		No	Yes				
Gender	Female	7	70	4.60 (1.70, 12.10)	0.002	4.31 (1.43, 13.03)	0.010
	Male	16	35	1		1	
Tobacco	Yes	1	30	8.8 (1.13, 68.23)	0.040	9.58 (1.14, 80.28)	0.037
	No	22	75	1		1	

female gender[8,64] and tobacco use or smoking[65] as predictors of MRED admissions. Although 66.7% (70/105) of all MRED admissions were females in our study, previous studies have suggested otherwise, with an expected lower CVD risk among females, owing to the potential cardioprotective role of estrogen (reduction of oxidative stress levels),[66] higher anti-oxidant potential,[67] and the good health seeking behaviors.[68] However, the female gender has also been associated with the increasingly high non-traditional CVD risks (eg depression, gestational diabetes, acute and chronic emotional stress, menopause, hypertensive disorders of pregnancy etc.),[69] and the increasing psychosocial and economic pressures (financial dependence, high family responsibilities, discriminative cultural norms),[70] which is most likely in our community setting. Smoking is one of the leading modifiable risk factors of CVD, and has been associated with development and progression of CVD through different pathophysiological processes of endothelial dysfunction, atherogenesis and atherosclerosis, hemodynamic effects, inflammation, hypercoagulable state, and dyslipidemia.[71] This could primarily lead to disease refractoriness to drug therapy, or influence the pharmacokinetics of certain CVD drugs used by patients in the out-patient settings, thus leading to medication-related ED admissions.

Because of the short study duration and, thus, smaller study population, a random sampling technique was not used. The potential recall bias and incomplete information were the other important limitations of the study. There is also a possibility that some medication, disease, or patient-related factors failed to qualify for multivariate analysis due to the smaller number of participants, and the limitations/restrictions owing to interruptions by the SARS-CoV-2 pandemic, on patient enrollment. The poor documentation habits in our study setting would have further compromised on the quality of data and outcomes.

Conclusion

Ineffectiveness of drug therapy is the largest sole cause of MRED admissions among patients admitted with cardiovascular diseases. Patients understanding gap of the disease and treatment constitute the largest reason of medication non-adherence. Participants of the female gender, and those with a history of tobacco use were more likely to be admitted due to medication-related causes.

Because most admissions were related to the medication therapy problems experienced at home, there is clear need to focus on optimization of chronic care in Uganda and related settings.

Ethical Approval

This study was approval by the Mbarara University of Science and Technology Research and Ethics Committee (MUST-REC) with a letter with Ref. No. MUREC1/7.

Acknowledgments

The authors are sincerely grateful to the patients and caregivers that offered to participate in this study. And most importantly, the authors are thankful for the support and approval granted by the administration of Mbarara Regional Referral Hospital (MRRH) for allowing us to conduct the study. We are sincerely grateful for all the support offered by Dr. Kushemererwa Oliver, a clinical pharmacy resident at Mbarara University of Science & Technology.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Funding

The authors received no specific funding for this work.

Disclosure

The authors declare no conflicts of interest.

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