J. Fac. Pharm. Ankara / Ankara Ecz. Fak. Derg., 49(2): 447-458, 2025
Doi: 10.33483/jfpau.1585631

ORIGINAL ARTICLE / ÖZGÜN MAKALE

PHARMACIST-DRIVEN MEDICATION REVIEW SERVICE IN PATIENTS WITH HEART FAILURE: A PROSPECTIVE STUDY

KALP YETERSİZLİĞİ HASTALARINDA ECZACI ODAKLI İLAÇ İNCELEME HİZMETİ: PROSPEKTİF BİR ÇALIŞMA

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ABSTRACT

Objective: *This study was conducted to detect and prevent drug-related problems (DRP) and potentially inappropriate medication (PIM) in patients with heart failure (HF) through a medication review service provided by clinical pharmacists and to increase drug prescription rates according to guideline-directed medical therapy (GDMT).*
Material and Method: *In this prospective study, which included observation and intervention periods, medication review services were provided to patients with HF between September 2023 and March 2024 by two clinical pharmacists. DRPs were classified according to Hepler-Strand and PIMs were evaluated according to Beers criteria®.*
Result and Discussion: *A total of 162 DRPs (1.8 per patient) were detected in 90 patients. The most common cause of DRPs was untreated indication (66.05%). In the observation period, no recommendations were offered, whereas in the intervention period, recommendations were offered to cardiologists, and 63.3% of them were implemented. DRPs were prevented and decreased by recommendations from two clinical pharmacists (from 1.76 to 0.64; $p < 0.001$). The prescription rates of sodium-glucose co-transporter 2 inhibitors and mineralocorticoid receptor antagonists increased ($p<0.05$). However, there was no difference in the number of PIMs per patient after the intervention ($p>0.05$). Our results provide compelling evidence that clinical pharmacists' assessment of medication use in patients with HF has made a crucial contribution to treatment management aligning treatment management with current guidelines and reducing DRPs.*
Keywords: *Clinical pharmacist, drug-related problems, heart failure, potentially inappropriate medications*

ÖZ

Amaç: *Bu çalışma, klinik eczacılar tarafından sağlanan ilaç inceleme hizmeti aracılığıyla kalp yetersizliği (KY) hastalarında ilaçla ilişkili sorunları (İLİS) ve olası uygunsuz ilaçları tespit etmek*

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Submitted / Gönderilme : 15.11.2024
Accepted / Kabul : 03.03.2025
Published / Yayınlanma : 19.05.2025

*ve önlemek ve kılavuza dayalı tıbbi tedaviye göre ilaç reçete oranlarını artırmak amacıyla yürütülmüştür***.**
Gereç ve Yöntem: *Gözlem ve müdahale dönemlerini içeren bu prospektif çalışmada, Eylül 2023 ile Mart 2024 tarihleri arasında KY hastalarına iki klinik eczacı tarafından ilaç inceleme hizmeti sunulmuştur. İLİS'ler Hepler-Strand'a göre sınıflandırılmış ve olası uygunsuz ilaçlar Beers kriterlerine® göre değerlendirilmiştir.*
Sonuç ve Tartışma: *90 hastada toplam 162 İLİS (hasta başına 1.8) tespit edildi. İLİS'lerin en sık nedeni tedavi edilmemiş endikasyondu (%66.05). Gözlem döneminde herhangi bir öneri sunulmamışken, müdahale döneminde kardiyologlara öneriler sunulmuş ve bunların %63.3'ü uygulanmıştır. Ancak müdahaleden sonra tespit edilen hasta başına düşen olası uygunsuz ilaç sayısında bir fark yoktu. İki klinik eczacının önerileriyle İLİS'ler önlendi ve azaltıldı (1.76'dan 0.64'e; $p < 0.001$). Sonuçlarımız, klinik eczacılar tarafından KY hastalarında ilaç kullanımının değerlendirilmesinin, tedavi yönetimini güncel kılavuzlarla uyumlu hale getirerek ve İLİS'leri azaltarak tedavi yönetimine önemli bir katkı sağladığına dair ikna edici kanıtlar sunmaktadır.*
Anahtar Kelimeler: *İlaçla ilişkili sorunlar, kalp yetersizliği, klinik eczacı, olası uygunsuz ilaçlar*

INTRODUCTION

Heart failure (HF) is a progressive syndrome caused by functional and/or structural changes in the heart that impair its ability to fill or eject blood from the ventricle. HF is considered a global public health issue, affecting approximately 64 million people worldwide, and its prevalence is rapidly increasing owing to population aging [1-3]. It is known that the prevalence of HF is between 1-2% in developed countries. In Türkiye, this rate is 2.9% according to the HAPPY study [4].

It is known that the incidence of HF increases with age. Because more than 80% of patients with HF are individuals aged 65 and older. The prognosis is more severe in geriatric patients than in younger patients due to geriatric syndromes.

Angiotensin receptor neprilysin inhibitors (ARNI), angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), beta-blockers, sodium-glucose cotransporter-2 inhibitors (SGLT-2i), mineralocorticoid receptor antagonists (MRA) are pharmacotherapy options shown in current guidelines to improve hospitalization and mortality in patients with HF [5].

In addition to standard therapy, patients receive many different medications to treat their comorbidities. Due to the polypharmacy common in patients with HF, these patients are at higher risk of potential drug-drug interactions and adverse events. DRPs associated with inappropriate medication management play an important role in the increased prevalence of hospitalization in patients with HF. Data from different healthcare systems show that inappropriate HF treatment according to current guidelines is a global problem [6,7]. Due to pharmacokinetic and pharmacodynamic changes observed particularly in older adults, it is important to assess the appropriateness of medication use in geriatric patients with HF according to geriatric criteria such as Beers®, START/STOPP® and TIME-to-START/TIME-to-STOPP®.

International guidelines recommend a multidisciplinary approach for the management of patients with multiple comorbidities. Therefore, more recent recommendations include the inclusion of clinical pharmacists in the HF multidisciplinary team [8-10]. Clinical pharmacists have a key role in the review of medications in patients with HF. Clinical pharmacists review prescription drugs to verify whether a drug is necessary or appropriate for the treatment of a patient and contribute significantly to the improvement of patient care [11-13]. Studies in the literature where pharmacists evaluate the treatment of patients with HF according to current guidelines are still needed [8,14-16]. This study was aimed to detect and resolve DRPs observed in patients with HF through the medication review service provided by clinical pharmacists, to increase the prescription rates of medications that HF patients should use according to guideline-directed medical therapy (GDMT), and to determine PIMs observed in geriatric patients with HF according to Beers criteria®. The study describes the impact of the role of clinical pharmacists in the care system of patients with HF in a cardiology service in Istanbul.

MATERIAL AND METHOD

Study Design

This prospective study, in which two clinical pharmacists and two cardiologists participated, was conducted between 11 September 2023 and 11 March 2024 in the cardiology service of a 600-bed training and research hospital in Istanbul. The study was completed in two periods: a 3-month observation and a 3-month intervention period. To more accurately interpret the impact of the medicines review service provided by clinical pharmacists, we separately assessed the intervention period before and after the recommendation.

Participants of Study

The sample size was calculated using G*Power (Version 3..9.7) [Computer software] with an alpha of 0.05 and a power of 90%, based on the data in the literature that DRPs can be reduced from an average of 5 (SD 3) to 3 (SD 1) (approximately 40%) per patient in HF patient groups recommended by the clinical pharmacist and was determined as at least 28 patients in each group. Considering a drop-out rate of 15%, a total of 64 patients were included, with at least 32 patients in each group [15,16].

Patients with HF over the age of 18 who presented to the cardiology service and who gave informed consent were included in the study. Pregnant and breastfeeding women, patients younger than 18, and patients with HF in cardiology outpatient clinics were excluded from this study. The first 45 patients with HF, whose written and oral approval was obtained in both periods, were included in the study.

Medication Review Services Provided by Clinical Pharmacists

During the study period, there was a clinical pharmacist who was in the cardiology ward three days a week (Monday, Tuesday, and Wednesday) to provide medical review services to patients with HF and attended physician visits. The second clinical pharmacist contributed to the recommendations submitted for the solution of DRPs detected by the clinical pharmacist in the cardiology ward.

The socio-demographic characteristics of the patients, laboratory parameters, and the medications they used were recorded to account for confidentiality. During the medication review service, patients were assessed for polypharmacy. In our study, polypharmacy was defined as the daily use of five or more medications. The CKD-EPI formula was used to evaluate patients' renal function, and Uptodate® was used for the patient-specific evaluation of the drug dose prescribed during hospitalization. Lexicomp® was used as a primary tool for the detection of potential drug-drug interactions (pDDIs). X, D level potential drug-drug interactions with moderate, major; good, and excellent reliability ratings and clinically significant potential drug-drug interactions were accepted as DRP, and recommendations were presented to physicians for these pDDIs. According to UptoDate®, clinically important pDDIs were also checked on Medscape® before making recommendations to physicians. Only patients were monitored for level C interactions. A and B-level interactions were not considered as DRP.

The '2022 American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Association of America's (HFSA) Heart Failure Management Guidelines' and the '2023 Focused Update of the 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure' were used to evaluate medications prescribed to patients with HF [17]. UpToDate® (Wolters Kluwer Health A.Sh., 2022) was used to improve informed clinical decision-making. The American Geriatrics Society 2023 Beers Criteria® was used to assess the appropriateness of treatment for patients with HF aged 65 years and older. The Beers Criteria® consist of 5 main sections: potentially inappropriate medications for use in geriatric adults, potentially inappropriate medications for use in certain diseases or syndromes, drugs that should be used with caution in geriatric adults, potentially clinically important drug-drug interactions that should be avoided in geriatric adults, medications that require dose adjustment according to renal function in geriatric adults [18].

During the medicine review service provided by the clinical pharmacists, the DRPs detected in patients with HF evaluated in both periods were categorized according to the Hepler and Strand classification system. During the observation period, no intervention was performed by the clinical pharmacist in the treatment process of the patients included in the study, unless there was a vital risk.

When DRPs that could threaten a patient's life were detected, the relevant physician was informed, and the patient was excluded from the study. To prevent and resolve DRPs detected during the intervention period, recommendations on adding and stopping medications, drug dose adjustments, switching to appropriate treatment alternatives, management of potential drug-drug interactions and possible side effects, and drug administration were presented orally and in writing by clinical pharmacists to the two professors of cardiology responsible for the ward (Figure 1).

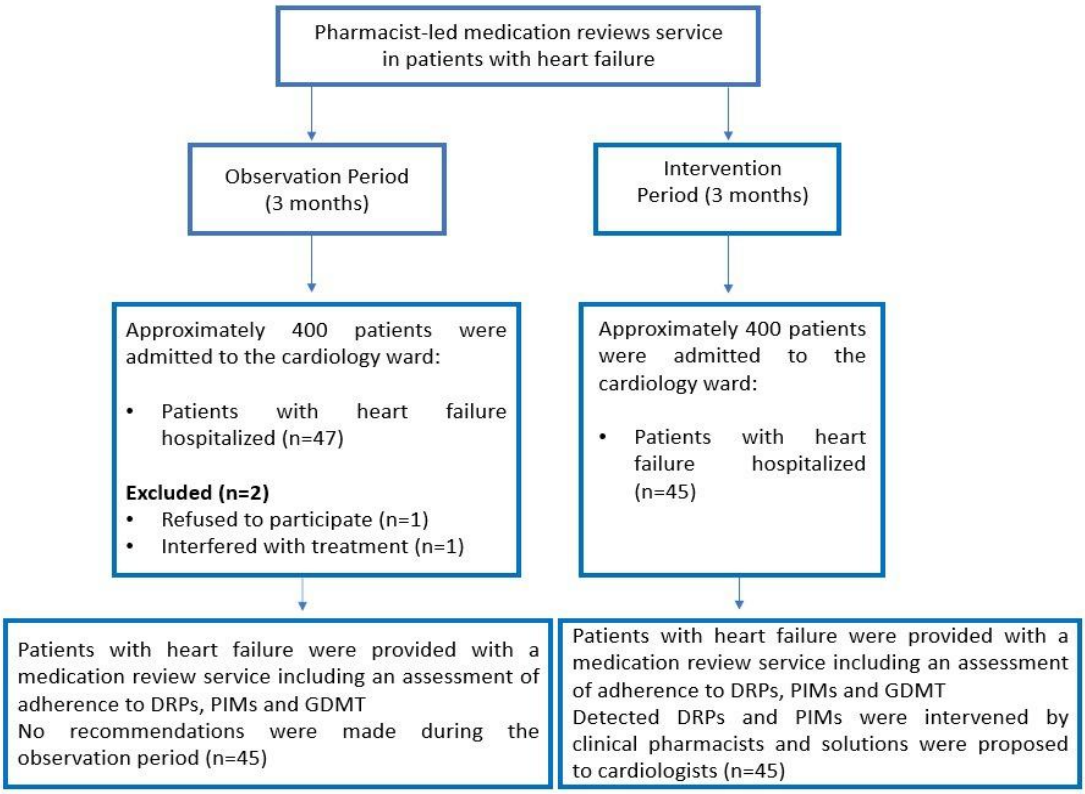

Figure 1. Flowchart for the observation and intervention period of the study

Outcome Measures

Our primary outcome in the medicine review service offered by clinical pharmacists is to determine the observed DRPs in patients with HF and to prevent and resolve these DRPs by consensus with cardiologists. The secondary outcome of our study is to determine the prescribing rates of the medication groups that should be prescribed to patients with HF according to GDMT, to increase these rates by the recommendations provided by the clinical pharmacist, and to detect and reduce PIM according to Beers criteria® in patients over the age of 65. The total and per capita number of DRPs and the number of PIMs according to Beers criteria®, the number of recommendations presented and accepted by physicians, and the prescription rates of medication groups are among the outcome measures of our study.

Data Analysis

All data from the study were analyzed using the Statistical Package for Social Sciences (SPSS) for Windows 23.0 software. Chi-square analysis and Fisher's exact test were used for the analysis of categorical variables. For comparisons of quantitative data between the observation and intervention groups, the Student's t-test was used for normally distributed data, and the Mann–Whitney U test was applied for non-normally distributed data. The change in the prescription rates of medications prescribed

for HF before and after the recommendation was determined using McNemar's analysis. Data were considered statistically significant in all analyses at a *p*-value < 0.05 in the 95% confidence interval.

RESULT AND DISCUSSION

A total of 90 patients were included, 45 in each period. The mean age of all patients was 68.26 ± 11.22 (41-89) years. Fifty-nine (65.6%; 59/90) patients were male. The characteristics of the patients in both periods are shown in Table 1.

Table 1. Patient characteristics

Characteristic variables	**Observation period (n=45)**	**Intervention period (n=45)**	***P* value**
Age (year)	71.1 ± 11.3 Max-min (41-89)	65.4 ± 10.5 Max-min (43-89)	**0.016****
Height (cm)	170 IQR (160-175)	170 IQR (160-175)	0.758*
Weight (kg)	77 IQR (68,5-85)	77 IQR (68-83)	0.878*
Body weight index (kg/m^2)	26.4 IQR (23.6-29.8)	26.4 IQR (24.9-28.3)	0.879**
Gender n, (%) Female Male	 16 (35.6%) 29 (64.4%)	 15 (33.3%) 30 (66.7%)	1.000***
Educational status n, (%) No education Primary school Middle school High school University	 3 (6.7%) 25 (55.6%) 7 (15.6%) 7 (15.6%) 0 (0%)	 3 (6.7%) 28(62.2%) 1 (2.2%) 5 (11.1%) 1 (2.2%)	0.213***
History of cigarette use n, (%) Yes No	 8 (19.0%) 34 (81.0%)	 12 (28.5%) 30 (71.5%)	0.443***
History of alcohol use n, (%) Yes No	 3 (7.1%) 39 (92.9%)	 2 (4.8%) 40 (95.2%)	1.000***
Heart failure class of patients according to LVEF n, (%) HFpEF HFmrEF HFrEF	 6 (13.6%) 8 (18.2%) 30 (68.2%)	 5 (11.6%) 11 (25.6%) 27 (62.8%)	0.701***
Comorbidities Hypertension Hyperlipidemia Coronary artery disease Myocardial infarction	 25 (55.6%) 4 (8.9%) 22 (48.9%) 5 (11.1%)	 22 (48.9%) 5 (11.1%) 20 (44.4%) 19 (42.2%)	 0.673*** 1.000*** 0.833*** **0.020*****
The number of comorbidities	3 IQR (2-4)	3 IQR (2-4)	0.532*

LVEF: Left ventricular ejection fraction, HFpEF: Heart failure with preserved ejection fraction, HFmrEF: Heart failure with mildly reduced ejection fraction, HFrEF: Heart failure with reduced ejection fraction

Mann–Whitney U test*, Student's t test**, chi-square test***

$p < 0.05$ indicates statistical significance.

$p < 0.001$ indicates high statistical significance. IQR: Interquartile range

Table 1 (*continue*). Patient characteristics

Characteristic variables	Observation period (n=45)	Intervention period (n=45)	*P* value
Use of medication			
Diuretics	24 (53.3%)	19 (42.2%)	0.399***
Beta-blocker	39 (86.6%)	41 (91.1%)	0.737***
Angiotensin-converting enzyme inhibitor (ACEi)	24 (53.3%)	25 (55.6%)	1.000***
Angiotensin receptor blocker (ARB)	3 (6.7%)	4 (8.9%)	1.000***
Angiotensin receptor-neprilysin inhibitor (ARNI)	9 (20.0%)	3 (6.7%)	0.121***
Mineralocorticoid receptor antagonists (MRA)	20 (44.4%)	16 (35.6%)	0.519***
Sodium-glucose cotransporter receptor 2 inhibitor (SGLT2i)	9 (20.0%)	10 (22.2%)	1.000***
The number of drugs	9 IQR (7-10)	8 IQR (7-10)	0.788*

LVEF: Left ventricular ejection fraction, HFpEF: Heart failure with preserved ejection fraction, HFmrEF: Heart failure with mildly reduced ejection fraction, HFrEF: Heart failure with reduced ejection fraction
Mann–Whitney U test*, Student's t test**, chi-square test***
$p < 0.05$ indicates statistical significance.
$p < 0.001$ indicates high statistical significance. IQR: Interquartile range

Drug-Related Problems (DRPs)

A total of 162 DRPs were detected in 90 patients, 79 in the intervention period and 83 in the observation period. Eighty-six patients (95.5%) had at least one DRP. During the intervention period, 79 recommendations were made by clinical pharmacists to cardiologists, of which 69 (87.3%) were accepted and 50 (63.3%) were implemented. The median number of DRPs detected per patient in the intervention period decreased from 2 IQR (1-2) to 1 IQR (0-1) ($p < 0.001$). The distributions of the relationships detected during the observation and intervention periods according to DRP class are shown in Table 2 and Table 3.

Prescription Rates of Medications

β blockers, ARNIs, ACEis/ARBs, MRAs, SGLT2is, and diuretics are among the groups of drugs prescribed for the treatment of HF. The frequencies of the medication groups found in the orders of 90 patients included in the study were as follows: β blockers (80/90; 88.9%), ARNI (12/90; 13.3%), ACEi (49/90; 54.4%), ARB (7/90; 7.8%), MRA (36/90; 40%), SGLT2i (19/90; 21.1%), and diuretics (43/90; 47.8%). The drug prescription rates for the intervention period are shown in Table 4.

Table 2. The number of DRPs detected during the observation and intervention periods by DRP class

DRPs detected according to Hepler-Strand's DRPs classification system	Observation period n (%)	Intervention period n (%)	*P* value
Drug use without an indication	2 (2.41)	2 (2.53)	1.000
Untreated indication	50 (60.24)	57 (72.15)	0.377
Subtherapeutic dosage	8 (9.64)	3 (3.80)	0.110
Overdosage	3 (3.61)	3 (3.80)	0.669
Improper drug selection	7 (8.43)	9 (11.40)	0.583
Failure to receive drugs	9 (10.84)	1 (1.26)	**0.014***
Adverse drug reactions	0 (0)	1 (1.26)	0.317
Drug interactions	4 (4.82)	3 (3.80)	0.696

Mann–Whitney U test; *$p < 0.05$ indicates statistical significance

Table 3. The number of DRPs detected before and after recommendation according to DRP class

DRPs detected according to Hepler-Strand's DRPs classification system	Intervention period		*P* value
	Before the recommendation, n (%)	After the recommendation, n (%)	
Drug use without an indication	2 (2.53)	1 (3.45)	0.317
Untreated indication	57 (72.15)	26 (89.65)	**< 0.001****
Subtherapeutic dosage	3 (3.80)	1 (3.45)	0.157
Overdosage	3 (3.80)	0 (0)	0.102
Improper drug selection	9 (11.40)	1 (3.45)	**0.005***
Failure to receive drugs	1 (1.26)	0 (0)	0.317
Adverse drug reactions	1 (1.26)	0 (0)	0.317
Drug interactions	3 (3.80)	0 (0)	0.083

*Wilcoxon t test, $p < 0.05$ indicates statistical significance
**Wilcoxon t test, $p < 0.001$ indicates high statistical significance

Potentially Inappropriate Medications (PIMs)

There were 60 geriatric patients in the observation (n=31) and intervention (n=29) periods. A total of 63 PIMs were identified according to the Beers Criteria®, including at least one PIM in 39 patients (65%) during the observation and intervention period. Medications causing PIMs detected in geriatric patients with HF during the intervention period: Diuretics (12; 44.2%), SGLT2is (6; 22.2%), antipsychotics (2; 7.4%), antidepressants (2; 7.4%), antiplatelet (1; 3.7%), anticoagulant (1; 3.7%), digoxin (1; 3.7%), cilostazol (1; 3.7%), and hyoscine n-butylbromide (1; 3.7%). After the recommendations were presented during the intervention period, there was no significant change in the number of inappropriate criteria according to Beers® (from 27 to 29 $p > 0.05$).

In this study, we evaluated the impact of a medication review service provided by clinical pharmacists on identifying, preventing, and resolving PIMs and DRPs observed in patients with HF.

The characteristics of the patients, except for age, were similar during both the observation and intervention periods. A difference was observed because the patients hospitalized in the cardiology ward during the intervention period were younger than those in the observation period. The patients with HF included in the study all had polypharmacy, as they were taking medications that both affected mortality and treated comorbidities. According to Goyal et al., polypharmacy is observed in at least 75% of

outpatients with HF, and at least 25% are taking 10 medications. It was reported that 96% of HF patients used at least 5 medications after discharge, and 57% used at least 10 medications [19-21].

Table 4. Prescription rates of medication groups prescribed for the treatment of heart failure before and after the recommendation

Groups of medication prescribed for the treatment of heart failure	Intervention period		*P* value
	Before the recommendation, n (%)	After the recommendation, n (%)	
Diuretics	19 (42.2)	19 (42.2)	1.000
β blocker	41 (91.1)	42 (93.3)	1.000
Angiotensin-converting enzyme inhibitor (ACEi)	25 (55.6)	30 (66.7)	0.125
Angiotensin receptor blocker (ARB)	4 (8.9)	3 (6.7)	1.000
Angiotensin receptor-neprilysin inhibitor (ARNI)	3 (6.7)	4 (8.9)	1.000
Mineralocorticoid receptor antagonist (MRA)	16 (35.6)	26 (57.8)	**0.006***
Sodium-glucose cotransporter receptor 2 inhibitor (SGLT2i)	10 (22.2)	22 (48.9)	**< 0.001****

McNemar analysis; * $p < 0.05$ indicates statistical significance
** $p < 0.001$ indicates high statistical significance

Hypertension and coronary artery disease were among the most common comorbidities in patients with HF. However, there was no significant difference in these comorbidities between the observation and intervention periods, whereas the number of patients with a history of myocardial infarction was significantly higher during the advice period. According to Jaber et al., hypertension (78.1%), coronary artery disease (69.8%), and diabetes (43.3%) were among the most common comorbidities associated with HF [22].

In studies conducted with patients with HF, it has been reported that the number of DRPs per patient varies between 1-2. The numbers of DRPs and the most frequently observed DRP classes vary among reported studies because DRPs are detected by different methods. The median value of DRP per patient in patients with HF who received medication review services by clinical pharmacists in the pre-discharge period was 2 IQR (1-2), similar to the literature [23-26]. The difference between the median DRP value per patient in the observation period and the before-recommendation period of the intervention period was not significant (1 IQR(1-3); 2 IQR(1-2) $p > 0.05$). The high number of DRPs supports the need for a clinical pharmacist in the healthcare team of patients with HF. According to the literature, DRPs are most commonly observed during the prescribing process and the most common DRP identified during this process is the untreated indication. During our study, the most common DRP in patients was an untreated indication (66.05%) and this supports the literature [13,24]. DRP categories other than the untreated indication did not differ for the observation period and before the recommendation intervention period. The medication group that caused this DRP most frequently was SGLT2i, which cardiologists hesitated to prescribe due to reimbursement conditions.

DRP was detected during the observation and intervention periods, and DRP numbers were compared in studies in the literature, but after the recommendations were presented to the physicians, DRP control could not be performed due to insufficient time spent in the clinical environment and the implementation rate of the recommendations could not be calculated. In our study, the acceptance rate of the recommendations as well as the implementation rate were determined. In our study, the

acceptance and implementation rate of the recommendations were also determined. In the studies, the acceptance rate of recommendations to cardiologists was at least 70% and more than 90% [25-27]. Similarly, 87.3% of the recommendations presented during the intervention period were accepted and 63.3% were implemented. The high acceptance rate of clinical pharmacists' recommendations regarding HF treatment indicates their critical role in optimizing HF treatment. Reimbursement conditions of the drugs (65.52%), hypotension (10.34%), hyponatremia (6.9%), other reasons (6.88%), and high bleeding risk (3.44%) were among the reasons for the recommendations that could not be implemented.

The secondary outcome of our study is the provision of appropriate treatment to patients with HF according to the GDMT through the drug review service provided by clinical pharmacists. Although ACEis/ARBs, β-blockers, and MRAs have been the first-line treatments for patients with HF, ARNIs, and SGLT2is have replaced other drugs in the current treatment of HF because of the evidence that these novel medications reduce hospitalization and mortality rates in patients. According to the '2023 Focused Update of the 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure', SGLT2is, whose effect on hospitalization and mortality was demonstrated in the EMPEROR-Preserved study (ClinicalTrials.gov number, NCT03057951), should be prescribed to all patients with HF, regardless of class [28-30]. Patil et al. (2022), have shown a significant increase in ARNI (from 22.5% to 48.8%), MRA (from 22.5% to 38.8%), and SGLT2i (from 7.5% to 32.5%) prescribing rates as a result of optimization service according to GDMT offered to patients with HF (p<0.001). According to Campbell et al. (2024) in the study, ACEi, ARB or ARNI (from 22% to 92%); beta-blockers (from 72% to 92%); MRA (from 54% to 88%); and SGLT2i (from 67% to 94%) the rate of prescribing inhibitors has increased (p<0.001) [5,13,31]. Within the scope of the medication review service, the prescription rates of MRA (from 35.6% to 57.8%, $p < 0.05$) and SGLT2i (from 22.2% to 48.9%, $p < 0.001$) in orders issued according to GDMT increased significantly compared to the recommendations of clinical pharmacists. Although SGLT2i like ARNI, is not reimbursed, the prescription rate of SGLT2i can be increased with more affordable equivalent drugs in the market, while no significant change was observed in the prescription rate of ARNI. Despite higher rates of prescription at discharge, β-blockers, ACEs/ARBs, and MRAs are under-prescribed in many patients and are the most common drug groups causing DRP. However, SGLT2i was not evaluated in these studies [15,32].

In the study by Jaber et al., the prevalence of PIM in geriatric patients with HF was found to be 61.1%, and the main drugs causing PIM were proton pump inhibitors (PPIs) and amiodarone [22]. In this study, the prevalence of PIM prescriptions according to the Beers Criteria® in geriatric patients with HF was 65%. Of the PIMs, 23 (85.19%) were PIMs that should be used with caution in geriatric adults, 3 (11.11%) were PIMs used in geriatric adults, and 1 (3.7%) was PIM used in geriatric adults due to drug-disease interactions that may exacerbate the disease or syndrome. Furosemide (12; 44.4%), dapagliflozin (4; 14.8%) and empagliflozin (2; 7.4%), quetiapine (2; 7.4%), sertraline (1; 3.7%), citalopram (1; 3.7%) and ticagrelor (1; 3.7%) were used by patients during the pre-recommendation intervention period and should be used with caution in geriatric adults according to 2023 Beers Criteria®. For medications in this group, other than ticagrelor, there is only a follow-up recommendation. Furosemide was monitored with caution because of the risk of hyponatremia, SGLT2i because of the risk of euglycaemic diabetic ketoacidosis in older adults, and antipsychotics and antidepressants because of the risk of inappropriate ADH release, and these PIMs were not considered DRPs. The Beers Criteria® recommends clopidogrel instead of ticagrelor for the risk of bleeding in adults 75 years and older. This PIM is also viewed as a DRP and the relevant recommendation is presented to physicians. PIMs used in geriatric adults and medications that may exacerbate the disease due to drug-disease interaction were considered improper drug selection from the DRP categories.

The patients' laboratory parameters were monitored during furosemide and SGLT2i use, but no events requiring intervention occurred. Although the number of PIMs detected per patient was similar in the observation and intervention periods, no significant change was observed after the recommendations were presented in the intervention period, and the total number of PIMs increased owing to the increase in SGLT2i prescription rates (total number of PIMs from 27 to 29, $p > 0.05$).

Strengths and Limitations

The study has strengths, including the identification of DRPs through the consensus of two clinical pharmacists and two cardiologists, the identification of DRPs, the presentation of proposed solutions and subsequent implementation rates, and the fact that the prescription rates of SGLT2is, which should be prescribed to all patients with HF regardless of HF class, have not been evaluated in previous studies. However, there are some limitations to our study. First of all, our study was conducted in a single center with a small sample size. DRPs were detected with the Hepler-Strand DRP classification system. However, the Hepler-Strand classification system does not systematically evaluate the causes and relationship status. The effects of interventions during hospitalization in the cardiology ward on patients' quality of life and the treatment process were not assessed. According to the Beers criteria®, medications requiring caution in older adults were considered as PIMs. Therefore, the number of PIMs was high.

Conclusion

Patients with HF frequently encounter DRPs during hospitalization. The main reason for these DRPs is the low rate of SGLT2i prescription. The fact that SGLT2is are not within the scope of reimbursement for HF indications in our country causes this rate to be low. However, with the consensus of clinical pharmacists and cardiologists, DRPs have decreased and the prescription rates of MRAs and SGLT2is have increased. Clinical pharmacists play a key role in the healthcare process of patients with HF.

Randomized controlled trials with larger samples in which clinical pharmacists are included in the HF multidisciplinary team will further clarify the role of clinical pharmacists and provide updated consensus reports. Future studies should determine the impact of the medication review service provided by clinical pharmacists to patients with HF on economic and clinical outcomes such as mortality and rehospitalization rates.

ACKNOWLEDGMENTS

We would like to thank the physicians and other health professionals in the cardiology service of the hospital where we conducted our study.

AUTHOR CONTRIBUTIONS

Concept: S.U., M.S.; Design: S.U., M.S.; Control: S.U., N.S., M.S., M.S.; Sources: S.U., M.S.; Materials: S.U., N.S., M.S.; Data collection and/or Processing: S.U., N.S., M.S., M.S.; Analysis and/or Interpretation: S.U., M.S.; Literature Review: S.U., M.S.; Manuscript Writing: S.U., M.S.; Critical Review: S.U., N.S., M.S., M.S.; Other:-

CONFLICT OF INTEREST

The authors declare that there is no real, potential, or perceived conflict of interest for this article.

ETHICS COMMITTEE APPROVAL

The study with protocol code 09.2023.866 was approved by the Clinical Research Ethics Committee of Marmara University Faculty of Medicine. This study was conducted in accordance with the Declaration of Helsinki and the Clinical Research Ethics Committee. Written informed consent was obtained from all participants included in this study.

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