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Original Research

Prescribing pattern, appropriateness, and factors influencing medication use in heart failure patients with reduced ejection fraction at a private tertiary hospital in Malaysia

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Abstract

Background: Heart Failure with Reduced Ejection Fraction (HFrEF) is a prevalent and serious medical condition worldwide. It affects millions of people and contributes significantly to morbidity and mortality. Inappropriate use of the medications may lead to adverse health outcomes and treatment failure. **Objectives:** This study aimed to assess prescribing patterns, the prevalence of potentially inappropriate medications (PIMs), the proportion of patients receiving the target guideline-directed medical therapy (GDMT) dose, and factors associated with suboptimal dosing in patients with HFrEF at a private tertiary care hospital in Malaysia. **Methodology:** This retrospective observational study involved 118 Malaysian adult patients with HFrEF who attended at least two outpatient cardiology appointments at the study hospital. The study reviewed prescriptions to identify drug prescribing patterns, GDMT use, target dose attainment, and prescribing of PIM. **Results:** The cohort was primarily comprised of Chinese individuals (84.80%) and males (78.80%), with a mean age of 58.7 years. The majority of patients (51.70%) received a combination of three GDMT drugs. Only 23.70% of patients were prescribed all four GDMT drugs, with 82.14% of these patients achieving at least one drug at the target dose. The prescribing rates of Renin-Angiotensin-Aldosterone System (RAAS) inhibitors, beta-blockers, mineralocorticoid receptor antagonists, and Sodium-Glucose Cotransporter-2 (SGLT-2) inhibitors were 98.31%, 72.97%, 48.31%, and 78.81%, respectively. The attainment of target doses was low, with only 11.21% reaching the target for RAAS inhibitors, 2.32% for beta-blockers, and 1.89% for MRAs. The study indicated no significant association between target dose attainment and clinical factors, except for beta-blockers in atrial fibrillation and SGLT-2 inhibitors in diabetes mellitus. Additionally, 4.24% of patients were prescribed PIM. **Conclusion:** Both adequate prescribing rates and target dose attainment of GDMT remain challenging in clinical practice, underscoring the need for strategies to improve adherence and enhance patient outcomes.

Keywords: Adherence, ejection fraction, heart failure, inappropriate medication, medical therapy, target dose

INTRODUCTION

Heart failure (HF) is a complex clinical syndrome that arises from structural and/or functional abnormalities within the heart, confirmed through elevated natriuretic peptides and/or objective evidence of pulmonary or systemic congestion[1,2]. In Malaysia, the most commonly observed phenotype is HFrEF.[2]

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HFrEF is defined as HF with a left ventricular ejection fraction of ≤40%[1-3]. Chronic HF (CHF) is a major public health problem worldwide due to its high prevalence and substantial financial impact on healthcare systems. Moreover, it is associated with increased morbidity and mortality rates, diminished functional capacity, and reduced quality of life.

Over the recent decades, several drug classes have demonstrated significant efficacy in reducing morbidity and mortality among HFrEF. These drugs, collectively known as GDMT, include angiotensin-converting enzyme (ACE) inhibitors/ angiotensin receptor blockers (ARBs)/ angiotensin receptor-neprilysin inhibitors (ARNI), beta-blockers, mineralocorticoid receptor antagonists, and sodium-glucose co-transporter 2 (SGLT-2) inhibitors[1–3]. Studies consistently demonstrate that the optimal use of GDMT provides prognostic and survival benefits, characterized by improved functional capacity, symptom reduction, decreased mortality, and a lower hospitalization risk[4–7]. Despite robust evidence and strong endorsements, the actual use of GDMT remains suboptimal, evidenced by a high underprescribing rate and a low proportion of patients achieving target doses[8–11]. In Malaysia, there is a lack of recent studies assessing the prescribing patterns and prescribers' adherence to the latest guideline recommendations for HF treatment, particularly on the use of ARNI and SGLT-2 inhibitors.

In addition to optimizing GDMT, the avoidance of PIMs is critical in managing patients with HFrEF, as they can

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exacerbate symptoms and lead to hospitalization. Certain medications are found to be contraindicated or harmful to HF patients. Nevertheless, the unintentional prescribing of these medications and failure to deprescribe them remain a persistent challenge in real-world clinical practice. Despite growing awareness of the risks associated with prescribing PIMs to HFrEF patients, there remains a notable gap in understanding the prevalence of such prescribing practices in Malaysian private hospital settings. The prescribing practices in private hospital settings in Malaysia significantly vary from those in public or government hospital settings due to a wider choice of medications and instant availability of life-saving medications.

Although the Malaysian National Heart Association revised its clinical guideline on the management of HF in 2023, discrepancies are believed to exist between recommendations and actual clinical practice in private hospital settings. Currently, there is a lack of local studies analysing the prescribing patterns for HF management and the compliance of Malaysian physicians with this guideline. Therefore, a study was conducted to assess the prescribing patterns among patients with HFrEF, determine the prevalence of PIMs, identify the proportion of HFrEF patients receiving the recommended target GDMT dose, and factors associated with the suboptimal dosing of GDMT for HFrEF at a private tertiary care hospital in Malaysia.

METHODS

Study design, population, and selection criteria

A retrospective, non-interventional observational study was conducted from September 2023 to August 2024 at a private tertiary hospital located in Kuala Lumpur, Malaysia. Malaysian patients aged 18 years and older, diagnosed with HFrEF, regardless of their New York Heart Association functional classification, who met the criteria for the use of each GDMT medication with no contraindications, and who attended at least two visits at the facility's outpatient cardiology clinics, were identified and screened from the facility's electronic hospital information system (eHIS) and included in the study.

However, patients diagnosed with acute de-novo cardiac failure with known precipitating factors, pregnant women, and patients with congenital cardiomyopathy were excluded from the study. These groups were excluded because they have distinct treatment strategies and underlying pathophysiology that differ from the general HF population. Acute de-novo cardiac failure often requires acute management strategies that differ significantly from chronic HFrEF treatment, which could confound the evaluation of long-term prescribing patterns of GDMT. Pregnant women were excluded because many GDMT drugs are contraindicated during pregnancy, necessitating different treatment approaches. Additionally, congenital cardiomyopathy was excluded as it represents a different pathophysiological entity from acquired HFrEF, often requiring specialized management. By excluding these subgroups of patients, the study aimed to ensure that the findings more accurately represent the general aetiology and management of CHF in Malaysia, thereby enhancing the relevance and applicability of the results to the local patient population.

A total of 118 patients were included in the study, based on the number of outpatient visits (n=239,602) documented at the facility during the study period and the reported prevalence of HF in Malaysia (6.7%).

Data collection and screening

The data were collected from the facility's eHIS and recorded in a structured data collection form. Considering that GDMT often involves dose titration to achieve the maximally tolerable dose, all prescriptions from the cardiology clinics within the study period were recorded to observe whether dosage adjustments are ongoing or if a stable dose has been established. However, the most recent prescription was used for the analysis of prescribing patterns and dose comparison, assuming it represents the latest treatment plan.

The medication record of each patient was screened to identify the eligibility criteria and absolute contraindications associated with each GDMT medication outlined by the 2021 ESC guideline on HF[3]. The prescribed dose was compared with the recommended target doses[1-3,12]. Patients were then categorised into one of five groups based on the prescribed dose: (1) patients not receiving medication due to contraindication or adverse drug reaction; (2) eligible patients not receiving medication; (3) eligible patients treated with <50% of the target dose; (4) eligible patients treated with 50% - <100% of the target dose and (5) eligible patients treated with ≥ 100% of the target dose.

The prescriptions were also reviewed using the 11-item Consensus PIMS in HF list to identify the use of PIMS among the subjects[13]. All medications prescribed by any prescriber for regular use during the study period, with a duration of at least one week, were documented in the data collection form. This approach ensured that all relevant medications, regardless of the prescribers' specialty, were evaluated for their appropriateness. On the other hand, medications prescribed on an "as required" basis or for durations less than one week were excluded from the assessment for potentially inappropriate medicines. The study protocol was approved by the IMU Joint Committee on Research & Ethics (Approval Number: MPP 1-2023(06)) and the SREC (Approval Number: 019/2023/IND/ER). Informed consent was not required for this study as it involved retrospective data collection from the eHIS without active intervention in the subjects' medical treatment plan. The study strictly adhered to the principles stated in the 'Declaration of Helsinki'.

Statistical analysis

Data was statistically analysed using IBM SPSS Statistics for Windows Version 29 (SPSS Inc., Chicago, Illinois). Categorical variables were presented as frequency and percentage, while continuous variables were assessed for normality using the Kolmogorov-Smirnov test and expressed as mean ± standard deviation or median with interquartile range. The proportion of patients receiving specific medications, potentially

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inappropriate medications, and the recommended target doses of GDMT were presented as frequency and percentage.

Univariate analysis was conducted to identify potential predictors of suboptimal doses of GDMT. The factors evaluated included age, gender, body mass index (BMI), left ventricular ejection fraction, NYHA functional classification, estimated glomerular filtration rate (eGFR), use of loop diuretics, and comorbidities. Variables with a p-value of <0.05 underwent further analysis using multivariate logistic regression. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographic and clinical characteristics of the patients

A total of 118 patients diagnosed with HFrEF were included in this study. The majority of patients were male (78.80%), Chinese (84.80%), with a mean age of 58.70 years. The median body weight and body mass index were 68.36 kg and 25.68 kg/m^2, respectively. Notably, 45.76% of the patients were pre-obese, while 37.30% were obese. Common comorbidities included coronary artery disease (59.32%), dyslipidaemia (54.24%), hypertension (43.22%), diabetes mellitus (43.22%), and atrial fibrillation (25.42%).

The median left ventricular ejection fraction was 34.00%, and the mean N-terminal prohormone of brain natriuretic peptide (NT-proBNP) level was 1517.20 pg/ml. Analysis of the renal profile revealed a median serum creatinine of 92.00 mmol/L and a mean estimated glomerular filtration rate (eGFR) of 69.58 mL/min/1.73 m², with 51.39% of the patients identified as being at chronic kidney disease stage 2. Around 84.72% of patients had a total cholesterol level of ≤ 5.2 mmol/L, and 33.90% had an HbA1c level of ≥ 6.3%, indicating higher cholesterol and diabetes mellitus, respectively. The demographic and clinical characteristics of the study population are summarised in Table 1.

Types of medications prescribed at the last clinic review

The most commonly prescribed drug classes were RAAS inhibitors (98.31%), statins (87.29%), SGLT-2 inhibitors (78.81%), antiplatelets (72.88%), and MRA (44.92%). Among the 118 patients, the most frequently prescribed GDMT drug was the angiotensin receptor-neprilysin inhibitor, sacubitril-valsartan, with 115 patients (97.46%) followed by bisoprolol, a GDMT beta-blocker, to 75.42% of the cohort. In terms of lipid management, three types of drugs were used. Among statins, rosuvastatin and atorvastatin were the most commonly prescribed lipid-lowering medications in 44.07% and 43.22% of the patients, respectively. Metformin, a biguanide, was the primary anti-diabetic medication, prescribed to 16.95% of patients in this study. For the management of hypertension, nebivolol, a non-GDMT beta-blocker, was prescribed to 11.02% of the patients. Furosemide was prescribed to about one-third (33.05%) of the patients to reduce fluid buildup. Ivabradine, an anti-angina agent, was prescribed to a quarter (25.42%) of the patients. Rivaroxaban was the most commonly prescribed anticoagulant, given to 13.56% of the patients. Allopurinol, an anti-hyperuricaemic agent, was prescribed to 6.78% of patients. The details are presented in Table 2.

Table 1. Patient baseline characteristics (N = 118)

Variables	Frequency, n (%)
Demographics	
Gender	
Male	93 (78.80%)
Female	25 (21.20%)
Ethnicity	
Chinese	100 (84.80%)
Indian	8 (6.80%)
Malay	6 (5.00%)
Others	4 (3.40%)
Age (years), mean ± SD	58.70 ± 12.72
Body weight (kg), median (IQR)	68.36 (62.05 – 83.53)
Height (cm), mean ± SD	163.91 ± 9.31
Body mass index (kg/m^2), median (IQR)	25.68 (22.93 – 28.29)
Underweight (<18.5 kg/m^2)	2 (1.69 %)
Normal (18.5 – 22.9 kg/m^2)	18 (15.25 %)
Pre-obese/ Overweight (23.0 – 27.4 kg/m^2)	54 (45.76 %)
Obese (≥ 27.5 kg/m^2)	44 (37.30 %)
Comorbidity	
Coronary Artery Disease	70 (59.32 %)

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Dyslipidemia	64 (54.24 %)
Hypertension	51 (43.22 %)
Diabetes mellitus	38 (32.20 %)
Atrial fibrillation	30 (25.42 %)
Chronic kidney disease	13 (11.02 %)
Stroke/ Transient ischaemic attack	11 (9.32 %)
Gout	10 (8.47 %)
Deep vein thrombosis/ Pulmonary embolism	2 (1.69 %)
Hyperthyroidism	1 (0.85 %)
Parkinson's disease	1 (0.85 %)
Left ventricular ejection fraction (%), median (IQR)	34.00 (28.00 – 37.00)
Blood investigation	
Sodium level (mmol/L), median (IQR)	141.00 (139.00 – 142.00)
Potassium level (mmol/L), median (IQR)	4.20 (3.85 – 4.50)
Serum creatinine (mmol/L), median (IQR)	92.00 (80.50 – 107.00)
eGFR (mL/min/1.73 m²), mean ± SD	69.58 ± 20.59
Stage 1 (≥ 90 mL/min/1.73 m²)	16 (13.89 %)
Stage 2 (60 – 89 mL/min/1.73 m²)	61 (51.39 %)
Stage 3 (30 – 59 mL/min/1.73 m²)	34 (29.17 %)
Stage 4 (15 – 29 mL/min/1.73 m²)	-
Stage 5 (< 15 mL/min/1.73 m²)	7 (5.56 %)
NT-proBNP (pg/ml), median (IQR)	1517.20 (759.90 – 5620.68)
Total cholesterol (mmol/L), mean ± SD	3.81 ± 0.60
Total cholesterol ≤ 5.2 mmol/L	100 (84.72%)
Total cholesterol > 5.2 mmol/L	18 (15.28%)
High-density lipoprotein (mmol/L), median (IQR)	1.12 ± 0.30
Low-density lipoprotein (mmol/L), median (IQR)	2.04 ± 0.66
Triglyceride (mmol/L), median (IQR)	1.34 (0.97-1.89)
Haemoglobin A1c (%), mean ± SD	5.72 ± 0.48
Non-diabetic (<5.7%)	41 (34.75 %)
Pre-diabetes (5.7 - < 6.3%)	37 (31.35 %)
Diabetes mellitus (≥ 6.3%)	40 (33.90 %)

Table 2. Types of medications prescribed at the last clinic review (N=118)

Drug class	Drugs	Frequency, n (%)
GDMT for heart failure		
ARNI	Sacubitril/Valsartan	115 (97.46)
ARB	Valsartan	1 (0.85)
GDMT beta-blockers	Bisoprolol	86 (72.88)
MRA	Spironolactone	53 (44.92)
SGLT-2 inhibitors	Dapagliflozin	54 (45.76)
	Empagliflozin	39 (33.05)
Anti-hypertensive medications		
Diuretics	Furosemide	39 (33.05)
	Bumetanide	3 (2.54)

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Non-GDMT beta-blocker	Nebivolol	13 (11.02)
Non-dihydropyridine calcium channel blocker	Amlodipine	5 (4.24)
	Felodipine	3 (2.54)
Anti-diabetic medications		
Biguanide	Metformin	20 (16.95)
Sulphonylurea	Gliclazide	5 (4.24)
Dipeptidyl peptidase-4 inhibitors	Sitagliptin	5 (4.24)
	Vildagliptin	5 (4.24)
	Linagliptin	3 (2.54)
Insulin	Degludec + Aspart (Ryzodeg®)	3 (2.54)
	Aspart (NovoRapid®)	2 (1.69)
	Glargine (Lantus®)	2 (1.69)
Lipid-lowering drugs		
Statin	Rosuvastatin	52 (44.07)
	Atorvastatin	51 (43.22)
Fibrate	Fenofibrate	5 (4.24)
Cholesterol absorption inhibitor	Ezetimibe	11 (9.32)
Antiarrhythmic drugs	Amiodarone	7 (5.93)
	Digoxin	7 (5.93)
Antiplatelets	Clopidogrel	35 (29.66)
	Aspirin + Glycine	31 (26.27)
	Aspirin + Clopidogrel	11 (9.32)
	Ticagrelor	8 (6.79)
	Cilostazol	1 (0.85)
Anticoagulants	Rivaroxaban	16 (13.56)
	Apixaban	10 (8.47)
	Dabigatran	5 (4.24)
	Edoxaban	3 (2.54)
	Warfarin	1 (0.85)
Anti-angina drugs	Ivabradine	30 (25.42)
	Trimetazidine	16 (13.56)
	Ranolazine	2 (1.69)
Proton pump inhibitors	Pantoprazole	26 (22.03)
	Esomeprazole	15 (12.71)
Anti-hyperuricaemic drugs	Allopurinol	8 (6.78)
	Benzbromarone	1 (0.85)
Antithyroid drugs	Carbimazole	1 (0.85)

ARNI- angiotensin receptor-neprilysin inhibitor, ARB- Angiotensin II Receptor Blockers, MAR - Mineralocorticoid Receptor Antagonists, GDMT - Guideline-Directed Medical Therapy

GDMT drugs prescribed for patients with HFrEF

GDMT for HFrEF comprises a combination of medications including RAAS inhibitors, beta-blockers, MRAs, and SGLT-2 inhibitors. In this study, the majority (51.70%) of patients received a combination of three GDMT drugs. The most frequently prescribed regimen among these patients was a combination of a RAAS inhibitor, beta-blocker, and SGLT-2 inhibitor, accounting for 65.71% of the patients. This was followed by the combination of a RAAS inhibitor, MRA, and an SGLT-2 inhibitor, prescribed to 22.86% of the patients (Table 3). A total of 23.70% of patients were prescribed all four GDMT drugs. Among these patients, 82.14% received one GDMT drug at the target dose, 14.29% received two GDMT drugs at the target dose, and 3.57% received three GDMT drugs at the target dose. Notably, none of the patients received all four GDMT drugs at their target doses.

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Table 3. Number of GDMTs prescribed at the last clinic review (N = 118)

Number of GDMT drugs prescribed	Frequency, n (%)
One GDMT drug	3 (2.50)
RAAS inhibitor	3 (100.00)
Two GDMT drugs	26 (22.10)
RAAS inhibitor and beta-blocker	13 (50.00)
RAAS inhibitor and SGLT-2 inhibitor	9 (34.61)
RAAS inhibitor and MRA	4 (15.39)
Three GDMT drugs	61 (51.70)
RAAS inhibitor, beta-blocker, and SGLT-2 inhibitor	40 (65.71)
RAAS inhibitor, MRA, and SGLT-2 inhibitor	13 (22.86)
RAAS inhibitor, beta-blocker, and MRA	5 (6.56)
Beta-blocker, MRA, and SGLT-2 inhibitor	3 (4.92)
Four GDMT drugs	28 (23.70)
RAAS inhibitor, beta-blocker, MRA, and SGLT-2 inhibitor	28 (100.00)

Around 22.00% of the patients were receiving only two GDMT drugs, with 50.00% on a combination of an RAAS inhibitor and a beta-blocker. Among the study population, 2.50% of patients were prescribed a single GDMT, all of which were RAAS inhibitors. These findings highlight the current prescribing patterns of GDMT in patients with HFrEF, indicating suboptimal adherence to clinical guidelines in the local private clinical setting. The distribution of the number of GDMT drugs prescribed at the last clinic review is presented in Table 3.

Distribution of GDMT drugs prescribed at target doses

In this study, most patients were prescribed suboptimal doses of GDMTs, except for SGLT-2 inhibitors, which were consistently prescribed at their target dose. Around 97.46% of patients were prescribed ARNI. Despite the high prescribing rate, only 11.30% of these patients were receiving the target dose. The majority (50.44%) were prescribed a dose that was less than 50% of the target dose, while 38.26% received at least 50% of the target dose.

In contrast, the use of angiotensin receptor blockers (ARBs) was notably rare, with only one patient (0.85%) on this drug, and this patient was receiving a dose that was less than 50% of the target dose. Beta-blockers were prescribed to 77.97% of the patients, of which only 2.17% reached the target dose, and 6.53% discontinued the medication due to bradycardia (50.00%) and hypotension (33.33%). Failing to reach the target dose could potentially increase the risk of mortality and rehospitalization, preventing patients from experiencing desired hemodynamic improvements like an increase in ejection fraction or a decrease in end-systolic volume.

MRA was prescribed to 48.31% of the patients. Among those on MRA, only 1.75% were at the target dose. Discontinuation of MRA treatment was observed in 7.01% of the patients, with two cases having no documented reason, one due to hypotension and one due to hyperkalaemia. Regarding SGLT-2 inhibitors, 78.81% of the patients were receiving this drug, and all patients prescribed these drugs received the target dose. The overview of the proportion of patients receiving GDMT drugs at target doses is presented in Table 4.

Factors associated with suboptimal GDMT therapy

The association between various clinical factors and suboptimal GDMT for HFrEF was assessed using univariate and multivariate analyses. For both RAAS inhibitors and MRA, none of the factors examined—including age, gender, BMI, LVEF, eGFR, use of loop diuretics, coronary artery disease, hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, or atrial fibrillation—showed a significant association with suboptimal therapy. In contrast, for beta-blockers, atrial fibrillation was found to be significantly associated with suboptimal dosing in both univariate (OR: 2.646; 95% CI: 1.080 – 6.845; p=0.032) and multivariate analyses (OR: 3.286; 95% CI: 1.246 – 8.663; p=0.016). For SGLT-2 inhibitors, diabetes mellitus was significantly associated with suboptimal dosing, as indicated by both univariate (OR: 3.025; 95% CI: 1.006 – 9.097;

Table 4. Proportion of patients receiving GDMT at target doses (N=118)

GDMT drugs prescribed	Frequency, n (%)
Angiotensin receptor/ neprilysin inhibitor	
Not receiving an ARNI	2 (1.69%)
Receiving an ARNI	115 (97.46%)
At target dose	13 (11.30%)
≥50% of target dose	44 (38.26%)
<50% of target dose	58 (50.44%)
Angiotensin receptor blockers	
Receiving an ARB	1 (0.85%)
<50% of target dose	1 (100.00%)
Beta-blockers	
Not receiving a beta-blocker	26 (22.03%)
Receiving a beta-blocker	92 (77.97%)
At target dose	2 (2.17%)
≥50% of target dose	13 (14.13%)
<50% of target dose	71 (77.17%)
Discontinued	6 (6.53%)
Mineralocorticoid receptor antagonists	
Not receiving a MRA	61 (51.69%)
Receiving a MRA	57 (48.31%)
At target dose	1 (1.75%)
≥50% of target dose	31 (54.39%)
<50% of target dose	21 (36.85%)
Discontinued	4 (7.01%)
Sodium-glucose cotransporter-2 inhibitors	
Not receiving an SGLT2 inhibitor	25 (21.19%)
Receiving an SGLT2 inhibitor	93 (78.81%)
At target dose	93 (100.00%)

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p=0.032) and multivariate analyses (OR: 2.960; 95% CI: 1.164 – 7.520; p=0.023). The details are presented in Table 5.

Proportion of patients who receive PIMHF

Out of the 118 patients in this study, 5 patients (4.24%) were identified as having been prescribed PIMHF. The most commonly prescribed drug class was NSAIDs, with celecoxib being the most frequently prescribed (n=3; 2.54%), followed by etoricoxib (n=2; 1.69%). These NSAIDs were mainly prescribed for their analgesic and anti-inflammatory properties, as they were all prescribed during orthopaedic clinic visits.

Table 5: Association between patient-level factors and target dose attainment rate of GDMT

	Univariate	
	OR (95% CI)	**p-value**
Renin-angiotensin-aldosterone system inhibitor		
Age	1.067 (0.965 – 1.180)	0.603
Gender	0.146 (0.013 – 1.676)	0.140
BMI	0.999 (0.454 – 2.196)	0.530
LVEF	0.806 (0.499 – 1.303)	0.499
eGFR	1.014 (0.958 – 1.073)	0.803
Use of loop diuretic	0.938 (0.082 – 1.659)	0.962
Diabetes mellitus	0.902 (0.079 – 1.257)	0.919
Hypertension	2.792 (0.246 – 3.675)	0.701
Chronic kidney disease	4.292 (0.362 – 5.930)	0.700
Coronary artery disease	1.594 (0.141 – 2.876)	0.700
Dyslipidemia	1.333 (0.117 – 2.136)	0.950
Atrial fibrillation	2.917 (0.247 – 3.446)	0.700
Beta-blocker		
Age	1.014 (0.977 – 1.053)	0.700
Gender	0.626 (0.223 – 1.759)	0.372
BMI	1.120 (0.783 – 1.601)	0.633
LVEF	0.994 (0.924 – 1.070)	0.896
eGFR	1.006 (0.980 – 1.032)	0.707
Use of loop diuretic	1.181 (0.548 – 2.546)	0.670
Diabetes mellitus	0.908 (0.406 – 2.031)	0.819
Hypertension	0.870 (0.417 – 1.815)	0.707
Chronic kidney disease	1.313 (0.405 – 4.256)	0.800
Coronary artery disease	1.053 (0.507 – 2.185)	0.871
Dyslipidemia	1.211 (0.584 – 2.510)	0.617
Atrial fibrillation	2.646 (1.080 – 6.485)	0.032
Mineralocorticoid receptor antagonists		
Age	1.007 (0.971 – 1.045)	0.707
Gender	1.360 (0.511 – 3.619)	0.533
BMI	0.916 (0.645 – 1.301)	0.606
LVEF	1.042 (0.970 – 1.109)	0.803
eGFR	1.002 (0.981 – 1.024)	0.910
Use of loop diuretic	1.101 (0.549 – 2.210)	0.800
Diabetes mellitus	0.821 (0.403 – 1.671)	0.600
Hypertension	1.188 (0.604 – 2.337)	0.707
Chronic kidney disease	1.953 (0.637 – 5.991)	0.900
Coronary artery disease	0.908 (0.447 – 1.844)	0.800

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Dyslipidemia	1.542 (0.763 – 3.116)	0.707
Atrial fibrillation	1.263 (0.604 – 2.542)	0.600
Sodium-glucose cotransporter-2 inhibitors		
Age	0.856 (0.656 – 1.119)	0.890
Gender	0.358 (0.023 – 5.667)	0.810
BMI	0.783 (0.316 – 1.938)	0.700
LVEF	1.066 (0.917 – 1.238)	0.856
eGFR	0.966 (0.811 – 1.151)	0.870
Use of loop diuretic	0.865 (0.222 – 3.366)	0.890
Diabetes mellitus	3.025 (1.006 – 9.097)	0.032
Hypertension	1.011 (0.312 – 3.279)	0.990
Chronic kidney disease	1.546 (0.360 – 6.631)	0.870
Coronary artery disease	1.316 (0.311 – 5.565)	0.990
Dyslipidemia	0.568 (0.146 – 2.207)	0.700
Atrial fibrillation	1.080 (0.307 – 3.798)	0.810

DISCUSSION

The demographic analysis of the current study population shows a mean age of 58.70 years, which is in line with the Malaysian Heart Failure Registry's reported mean age of 60.17 years. This finding is consistent with results from other local studies in Malaysia. For instance, the National Heart Institution (NHI) reported a mean age of 62 years, Sarawak General Hospital found a mean age of 59, Hospital Sungai Buloh reported a mean age of 63.4, Universiti Teknologi MARA Sungai Buloh recorded a mean age of 58.64, and another study at the NHI reported a mean age of 61 years[12,14-17]. These findings collectively suggest that HF patients in Malaysia are relatively younger.

The current study found a high prevalence of HFrEF in males, consistent with previous local studies[12,14,17,18]. This aligns with findings from other countries such as Korea (53.2%), China (60.8%), Japan (58.0%), Taiwan (72%), and Italy (60.2%)[19-23]. The study also showed a high prevalence of HF in Chinese patients (84.8%), which is likely attributed to the private hospital setting. A study reported that non-Malays prefer private outpatient services over Malays[24]. Since the Chinese make up the second largest ethnic group in Malaysia and are mostly in urban areas where private healthcare is more accessible, this demographic trend likely explains why the Chinese population uses private healthcare services more than Malays[24].

In the current study, a significant proportion of individuals were either overweight or obese. This prevalence surpasses the findings of the National Health and Morbidity Survey 2023, which reported a 53.5% prevalence of overweight and obesity among Malaysian adults[25]. The relationship between obesity and HF is well-documented and multifaceted. Obesity is recognised as a significant risk factor for HF due to its strong association with hypertension, cardiovascular disease, and left ventricular hypertrophy. The Framingham Heart Study found that the incidence of HF increased by 5% in men and 7% in women for every 1-unit rise in BMI[26].

Among the current study population, the most common comorbidities were coronary artery disease, dyslipidemia, hypertension, and diabetes mellitus. This finding aligns with the ASIAN-HF registry, which characterised Malaysia by a high prevalence of metabolic patterns (characterised by obesity, hypertension, and diabetes) and ischaemic patterns (characterised by coronary artery disease and ischemic aetiology)[10]. This observation is supported by local studies, which frequently report ischaemic heart disease, diabetes, and hypertension as common comorbidities among the local population with HFrEF. Interestingly, the present study had a lower prevalence of hypertension, diabetes mellitus, and chronic kidney disease compared to other local studies[14–18]. However, the prevalence of coronary artery disease in the present study population is notably higher than that reported in other Asian countries, such as Japan (39%), Korea (19%), and China (17%)[27]. Although the specific aetiology of HF in the cohort was not documented, the high prevalence of ischemic risk factors, such as coronary artery disease, dyslipidemia, diabetes, and hypertension, strongly suggests an ischemic origin. Furthermore, the high prescribing rates of statins and antiplatelets in the present study further support this theory. This disparity underscores the significant burden of ischemic heart disease in the Malaysian population, contributing to the overall incidence of HF.

In this study, only one-fifth of the subjects were prescribed all four GDMT drugs. This finding is notably lower than the earlier study, which reported 49.5%[17]. This discrepancy may be attributed to differences in clinical settings. Raja Shariff's study was conducted in a multidisciplinary team heart failure (MDT-HF) clinic within a cardiac tertiary centre, whereas our study involved outpatient cardiology clinics led by cardiologists. The benefits of a multidisciplinary approach in HF management are well-documented, with MDT-HF clinics often demonstrating superior care and better treatment optimisation. The success of these clinics can be attributed to several factors, including more frequent follow-up appointments, which allow for

timely adjustments of medication, close monitoring of patient symptoms, and ongoing education about HF management. Patients in MDT-HF clinics typically experience better outcomes, such as improved symptoms and functional capacity, as well as lower rates of hospitalization and mortality due to HF[28–30].

A key component of the MDT-HF clinic model is the involvement of pharmacists, whose role in HF management is increasingly recognised. Pharmacists provide valuable expertise in drug selection, titration, and monitoring, and their involvement has been shown to increase the rates of GDMT prescribing and optimization[31]. A study showed that pharmacist-led HF medication titration clinics have significantly increased the proportion of patients on quadruple and triple GDMT. This has led to a significant reduction in the combined HF-related hospitalizations and emergency department visits at 90 days post-enrolment[32]. Additionally, pharmacists contribute to improved medication adherence and provide counseling on both pharmacological and non-pharmacological aspects of HF care[30,31]. Another study showed that pharmacist involvement improved patients' adherence to self-care[32]. Given these findings, there is a clear opportunity to enhance HF management in our facility by integrating pharmacists into the care team. Their involvement could help bridge the gap in GDMT adherence and contribute to better outcomes for our patients.

In terms of the GDMT drug class, the prescribing rate of RAAS inhibitors in our study was higher than the rates reported in previous studies, which ranged from 40.0% to 92.9%[8–10,14–18,33–36]. Similarly, the usage of ARNIs in our study surpasses the rates reported in local studies, which found only 15.7% and 85.5%[15,18]. The prescribing rate of SGLT-2 inhibitors in our study was also higher compared to the previous study, which reported 56.5%[17]. However, it is important to note that the study period of the previous research spanned from 2019 to 2023, during which the approval of dapagliflozin and empagliflozin by Malaysia's National Pharmaceutical Regulatory Agency (NPRA) for HF management occurred in 2021 and 2022, respectively. This likely explains the lower utilisation of SGLT-2 inhibitors in their study. The higher prescribing rates of ARNIs and SGLT-2 inhibitors in our study suggest that our physicians are closely adhering to GDMT recommendations, particularly regarding drug selection. On the other hand, the prescribing rates of beta-blockers and MRAs in our study were comparable to those reported in previous studies, where beta-blocker use ranged from 38.1% to 92.7%, and MRA use ranged from 18.0% to 94.0%[8–10,14–18,33–36].

The proportion of patients who achieved the target dose of GDMT drugs indicates that the percentage of patients reaching the target dose for each drug class is lower than previously reported in other studies[8-10]. This highlights that the medication regimens for the current study subjects were not optimally titrated, emphasizing a significant gap in achieving optimal GDMT in our patients. This study demonstrates that suboptimal adherence to GDMT continues to be a significant challenge in the management of HF in Malaysia.

The univariate analysis revealed that there was no significant association between target dose attainment rates of GDMT drugs and the majority of clinical factors, except for beta-blockers in patients with atrial fibrillation and SGLT-2 inhibitors in patients with diabetes mellitus. These exceptions can be explained by the additional clinical indications for beta-blockers in the management of atrial fibrillation and SGLT-2 inhibitors in the treatment of diabetes mellitus. The lack of significant associations between target dose attainment rates and most patient-level factors highlights a concerning issue: the gaps in adherence to GDMT observed in our setting are predominantly attributable to clinical inertia rather than physiological limitations[37–42].

The prevalence of PIMHF use identified using the St. Vincent criteria in our study was very low. This prevalence is notably lower than the rates reported in similar studies conducted in Thailand and Ireland, which found a prevalence of 23.76% and 28.0%, respectively, using the same criteria[43,44]. This discrepancy may be attributed to the smaller sample size in this study. Among the PIMHF drug classes, non-steroidal anti-inflammatory drugs (NSAIDs) were the most commonly prescribed, with celecoxib being the most frequently prescribed (2.54%), followed by etoricoxib (1.69%). This finding differs from the results of an earlier study, which identified non-dihydropyridine calcium channel blockers as the most commonly prescribed PIMHF[44]. In contrast, a reported oral corticosteroids as the most frequently prescribed PIMHF, followed by NSAIDs[43].

NSAIDs are frequently prescribed for their analgesic and anti-inflammatory properties. However, their use in patients with HF is associated with significant risks, as they have been shown to exacerbate HF. Several studies have found a strong association between NSAID use and an increased risk of HF exacerbations[45–48]. A case-control study in four European countries found a 19% rise in hospital admissions for HF after NSAID use[45]. Other studies have shown significant impacts on cardiovascular health and disease outcomes, as well as increased risk of death[47], and hospitalization for HF patients in Japan[47,48].

In light of this robust body of evidence, current clinical guidelines strongly discourage the use of NSAIDs in patients with HFrEF due to the heightened risk of HF exacerbation and hospitalization. To mitigate the associated risks, clinicians should carefully evaluate the necessity of NSAIDs in HF patients and consider safer therapeutic options[49,50].

This study has several limitations. Firstly, the findings cannot be generalised to the entire Malaysian population due to its single-center design and small sample size. Additionally, as the current study was conducted in a private hospital setting, the results may not be directly applicable to government healthcare settings, where both settings have distinct factors that influence treatment decisions. Furthermore, this study only included patients with HFrEF, limiting its applicability to the broader spectrum of HF. The use of convenience sampling may introduce selection bias in this study, which may have affected the representativeness of the sample. The prescribing patterns observed in outpatients, who are typically more clinically stable, may differ from those in inpatients.

As a retrospective study, the analysis relied heavily on the completeness and quality of the available documentation. Furthermore, the present study was not designed to evaluate outcomes; hence, we were unable to evaluate the impact of prescribers' low adherence to guidelines on patient outcomes such as hospitalization, disease prognosis, and mortality.

CONCLUSION

The current study found that there is a concerning low adherence by prescribers to GDMT recommendations. Less than a quarter of patients were prescribed all four GDMT drugs at the target dose. This highlights the critical need for improved adherence to heart failure treatment guidelines in private hospital settings to optimize patient outcomes. Enhanced efforts to ensure that patients receive the full benefits of GDMT, including the achievement of target doses, are essential for improving the quality of care and outcomes for heart failure patients.

AUTHORS CONTRIBUTION

All authors contributed substantially to the design and/or planning of the study; in obtaining, analyzing, and interpreting data; in writing and critical review; and approved the final version to be published.

CONFLICT OF INTEREST

No potential conflict of interest was reported by the author(s).

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