Original Article

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Internal Medicine Section

Guideline-Directed Medical Therapy in the Management of Cardiovascular Disease: A Cross-sectional Questionnaire-based Study amongst Indian Healthcare Professionals

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ABSTRACT

Introduction: Guideline-Directed Medical Therapies (GDMT) are evidence-based treatments recommended by clinical practice guidelines for the management of Cardiovascular Diseases (CVDs). While GDMT is foundational for treating Heart Failure (HF), its adoption promotes uniform, evidence-driven practices across various cardiovascular conditions. This therapy includes drug classes such as Beta-Blockers (BB), Angiotensin-Converting Enzyme inhibitors, Angiotensin-Receptor Blockers, and Angiotensin Receptor-Neprilysin Inhibitors (ACEi/ARB/ARNI), Mineralocorticoid Receptor Antagonists (MRAs), and Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2i). Implementing GDMT can enhance cardiac function, improve quality of life and reduce hospitalisation and mortality risks.

Aim: To understand the preferences of drug choice among Indian Healthcare Practitioners (HCPs) regarding the adaptation of GDMT in CVD management.

Materials and Methods: A cross-sectional, questionnaire-based study was conducted in India from December 2022 to March 2023. Participants (n=93) included cardiologists, electrophysiologists and cardiophysicians, who were actively involved in managing CVD. A predefined questionnaire consisting of seven questions, developed from existing literature, guidelines and expert opinions, was used. Responses were digitally analysed, with descriptive statistics presented as numbers and percentages.

Results: For hypertension management in Acute Coronary Syndrome (ACS), telmisartan (60.22%) was the most preferred ARB, followed by metoprolol (48.39%; BB), amlodipine (39.78%; Calcium Channel Blockers [CCB]), and torsemide (32.26%; diuretics). For patients with diabetes and ACS, SGLT2i (89.29%) were favoured. Clopidogrel (56.99%) was the preferred oral antiplatelet drug alongside aspirin in ACS. In Acute Decompensated HF (ADHF), the preferred sequential addition of GDMT includes loop diuretics (44.74%) as the first choice, followed by ARB, SGLT2i, and MRAs as subsequent choices. One in four HF patients was on ARNI (37.36%) and SGLT2i (35.62%), while three in four HF patients were on BB (36.99%) and ACEi/ARBs (34.28%). In HF patients on loop diuretics and MRAs, the preferred doses were torsemide 10 mg with spironolactone 25 mg (57.32%) and torsemide 10 mg with spironolactone 50 mg (37.80%). In addition to symptomatic treatment with loop diuretics in HF patients, 72.50% of HCPs preferred ARNI, and 35.0% preferred ARBs as combination therapy.

Conclusion: ARBs and BBs were preferred for hypertension in ACS, while SGLT2i were favoured for diabetes. Clopidogrel was the most popular P2Y12 inhibitor in ACS. For HF, HCPs favoured sequential therapy, with loop diuretics and ACEi/ARBs as the first and second choices and preferred combinations of ARNI or ARBs with loop diuretics for symptomatic HF.

Keywords: Acute coronary syndrome, Anticoagulant, Antiplatelet, Beta-blockers, Heart failure, Hypertension

INTRODUCTION

The CVD, including ischaemic heart disease, stroke, HF, peripheral arterial disease and various other cardiovascular conditions, stands as the foremost contributor to worldwide mortality [1]. In 2019, India ranked first globally in CVD mortality, accounting for 27.4% of total deaths [2]. The burden of ACS and HF on the Indian healthcare system is substantial, given their significant impact on both morbidity and mortality [3].

The GDMT includes evidence-based treatments recommended by clinical practice guidelines for managing CVD. Indian guidelines recommend the use of GDMT to reduce readmissions for patients with CVD [4], and it serves as the foundation for managing HF with Reduced Ejection Fraction (HFrEF) [5]. Ideally, GDMT entails combining various medications and gradually adjusting to evidence-based target doses [6]. This therapy comprises drug classes, namely, BB, ACEi, ARB, ARNI, MRAs [5], and SGLT2i [6]. The cumulative life-saving effect of these therapies has been proven to become noticeable within weeks [7]. The implementation of GDMT has been shown to enhance cardiac function, improve quality of life and functional status, while also reducing the risks of hospitalisation and mortality [5].

Data from HF and ACS registries, as well as large cohort studies from India, have portrayed wide variations in GDMT usage rates and emphasised the limited utilisation of GDMT, especially ACEi/ARB and BB [3,8-13]. As HCPs increasingly recognise the importance of adhering to these guidelines, the adoption of GDMT has become instrumental in promoting a more uniform and evidence-driven practice across a broader spectrum of cardiovascular conditions, extending beyond HF. In managing CVD through GDMT, the choices made by HCPs regarding drug selection play a pivotal role in determining patient outcomes. Exploring the selection of drugs by

HCPs can offer valuable insights for enhancing cardiovascular care strategies in the Indian context. Moreover, there is a lack of data on the use of GDMT in managing CVD within the Indian healthcare setting. Therefore, the present study aimed to understand the preferences of HCPs regarding drug choice towards the adaptation of GDMT in CVD.

MATERIALS AND METHODS

A cross-sectional, questionnaire-based study was conducted between December 2022 and March 2023 across India. Since it was a survey, ethical approval was not considered; however, the study followed all ethical guidelines.

Inclusion criteria: The target participants were cardiologists, electrophysiologists and cardiophysicians actively involved in managing CVD. They were invited to participate in the survey. Both complete and incomplete survey responses from HCPs were included in the study.

Exclusion criteria: HCPs who do not manage CVD patients and those who were not willing to provide consent were excluded from the study.

Sample size: Sample size calculations was not performed for this survey. This survey aimed to understand the usage of GDMT in CVDs. A questionnaire was prepared and circulated among HCPs. A total of 110 HCPs were approached during meetings and responses were collected.

Study questionnaire: A predefined questionnaire consisting of seven questions was developed based on existing literature, guidelines [6,14,15], and expert opinions for this study. The questionnaire aimed to collect information on various aspects related to the management of CVD, such as the preference of drugs in the management of diabetes and hypertension, the preference of oral anticoagulants and antiplatelet drugs in ACS, the proportion of patients with HF on GDMT therapy, the sequence of adding drugs while implementing GDMT in patients with HF, the preferred dose of torsemide for combination with spironolactone, and the preferred disease-modifying drug to be considered for combination with a loop diuretic [Table/Fig-1]. The participants were asked to respond based on their professional experience and knowledge.

List of questions			
1. What is your drug of choice for hypertension management in patients with coronary artery syndrome? (Please pick either dual OR triple combination; in case of others please specify)			
a. Diuretic i. Torsemide ii. Hydrochlorothiazide iii. Chlorthalidone iv. Others	b. CCB i. Amlodipine ii. Cilnidipine iii. Nifedipine iv. Others	c. ARB/ACEi i. Telmisartan ii. Olmesartan iii. Ramipril iv. Others	d. BBs i. Metoprolol ii. Bisoprolol iii. Carvedilol iv. Nebivolol
2. What is your preference for oral drug for diabetes management in patients with coronary artery syndrome? (Please pick either dual OR triple combination; in case of others please specify)			
a. Metformin i. 500 mg ii. 1000 mg iii. Do not prefer	b. SGLT2i i. Dapagliflozin ii. Empagliflozin iii. Canagliflozin	c. DPP4i i. Sitagliptin ii Vildagliptin iii Linagliptin	d. SU i. Glipizide ii. Glimepiride iii Others
3. What is your preference for oral anticoagulant and antiplatelet drugs in ACS? (Please pick either dual OR triple combination; in case of others please specify)			
a. Aspirin	b. NOACs i. Rivaroxaban ii. Apixaban iii. Dabigatran	c. P2Y12i i. Clopidogrel ii. Prasugrel iii. Ticagrelor	d. VKA i. Warfarin ii. Acenocoumarol iii. Others
4. What is the sequence of drug addition while implementing GDMT in ADHF patient? (Please mention the Number against the class of drugs)			
a. ARNI _____ b. ACEi/ARB _____ c. SGLT2i _____ d. MRA _____ e. Loop diuretic _____ f. BB _____ g. Ivabradine _____			
5. In your clinical practice, how many HF patients are on GDMT therapy?*			
a. MRA i. 1 in 4 ii. 2 in 4 iii. 3 in 4 iv. All	b. SGLT2i i. 1 in 4 ii. 2 in 4 iii. 3 in 4 iv. All	c. ARNI i. 1 in 4 ii. 2 in 4 iii. 3 in 4 iv. All	d. ACEi/ARB i. 1 in 4 ii. 2 in 4 iii. 3 in 4 iv. All	e. BB i. 1 in 4 ii. 2 in 4 iii. 3 in 4 iv. All	f. Loop diuretic i. 1 in 4 ii. 2 in 4 iii. 3 in 4 iv. All
6. When prescribing Torsemide along with Spironolactone, which is most preferred dose of Torsemide with?					
i) Spironolactone 25 mg			ii) Spironolactone 50 mg		
a) 5 mg	b) 10 mg	c) 20 mg	a) 5 mg	b) 10 mg	c) 20 mg
7. In addition to symptomatic treatment with loop diuretics, which disease modifying drug would you like to consider in combination?					
a) ARB: Yes/No – Telmisartan/Valsartan/Losartan/Olmesartan b) ARNI: Yes/No					

[Table/Fig-1]: Study questionnaire.
*1 in 4=25%; 2 in 4=50%; 3 in 4=75%; ACEi: Angiotensin-converting enzyme inhibitor; ACS: Acute coronary syndrome; ADHF: Acute decompensated heart failure; BB: Beta-blocker; CCB: Calcium channel blocker; DPP4i: Dipeptidyl peptidase-4 inhibitor; GDMT: Guideline-directed medical therapy; HF: Heart failure; MRA: Mineralocorticoid receptor antagonist; NOACs: Non-vitamin K antagonist oral anticoagulants; P2Y12I: P2Y12 receptor inhibitor; SGLT2i: Sodium-glucose cotransporter 2 inhibitor; SU: Sulfonylurea; VKA: Vitamin K antagonist

STATISTICAL ANALYSIS

The responses were digitally analysed, and a descriptive analysis was conducted to present the data in numbers and percentages.

RESULTS

A total of 93 HCPs responded to the questionnaire and were included in this study. ARB/ACEi in 91 (97.85%) and BBs in 85 (91.40%) were the most preferred drug classes for the management of hypertension in patients with ACS. Telmisartan was the major preference in 56 (60.22%) among ARBs for the management of hypertension in patients with ACS, followed by metoprolol in 45 (48.39%), amlodipine in 37 (39.78%), and torsemide in 30 (32.26%) among Beta-Blockers (BBs), Calcium Channel Blockers (CCBs), and diuretics, respectively [Table/Fig-2].

Drug of choice	Response of HCPs (%) (N=93)
Diuretics	**76 (81.72)**
Torsemide	30 (32.26)
Hydrochlorothiazide	24 (25.81)
Chlorthalidone	22 (23.66)
Others	0
CCB	**66 (70.97)**
Amlodipine	37 (39.78)
Cilnidipine	28 (30.11)
Nifedipine	1 (1.08)
Others	0
ARB/ACEi	**91 (97.85)**
Telmisartan	56 (60.22)
Olmesartan	8 (8.60)
Ramipril	27 (29.03)
Others	0
Beta-blockers (BB)	**85 (91.40)**
Metoprolol	45 (48.39)
Bisoprolol	25 (26.88)
Carvedilol	15 (16.13)
Nebivolol	0

[Table/Fig-2]: Drug preferences for the management of hypertension in Acute Coronary Syndrome (ACS).
Data presented as n (%); ACEi: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin receptor blockers; CCB: Calcium channel blockers; HCPs: Healthcare practitioners

SGLT2 inhibitors (SGLT2i) in 75 (89.29%) were the most preferred class of antidiabetics for patients with diabetes and ACS, followed by

metformin in 68 (80.95%), dipeptidyl peptidase-4 inhibitors (DPP4i) in 64 (76.19%), and sulfonylureas in 43 (51.19%). For the management of diabetes in patients with ACS, the most preferred drug choice among SGLT2 inhibitors was dapagliflozin in 55 (65.48%), followed by metformin 500 mg in 43 (51.19%) (comparing metformin 500 mg and 1000 mg), sitagliptin in 34 (40.48%) among DPP4i, and glimepiride in 30 (35.71%) among sulfonylureas [Table/Fig-3].

Drug of choice	Response of HCPs (%) (N=84)
Metformin	**68 (80.95)**
500 mg	43 (51.19)
1000 mg	21 (25.00)
Do not prefer	4 (4.76)
SGLT2i	**75 (89.29)**
Dapagliflozin	55 (65.48)
Empagliflozin	19 (22.62)
Canagliflozin	1 (1.19)
DPP4i	**64 (76.19)**
Sitagliptin	34 (40.48)
Vildagliptin	20 (23.81)
Linagliptin	10 (11.90)
SU	**43 (51.19)**
Glipizide	11 (13.10)
Glimepiride	30 (35.71)
Others	2 (2.38)

[Table/Fig-3]: Drug preferences for the management of diabetes in Acute Coronary Syndrome (ACS).
Data presented as n (%); DPP4i: Dipeptidyl peptidase-4 inhibitors; HCPs: Healthcare practitioners; SGLT2i: Sodium-glucose cotransporter 2 inhibitors; SU: Sulfonylurea

In patients with ACS, the most preferred P2Y12 inhibitor, alongside aspirin, was clopidogrel in 53 (56.99%). The preferred Direct Oral Anticoagulants (DOACs) combined with aspirin were rivaroxaban in 39 (41.94%), and the preferred Vitamin K Antagonist (VKA) with aspirin was warfarin in 15 (16.13%) among patients with ACS [Table/Fig-4].

Drug of choice	Response of HCPs (%) (N=93)
Aspirin	**85 (91.39)**
NOACs	**74 (79.57)**
Rivaroxaban	39 (41.94)
Apixaban	30 (32.26)
Dabigatran	5 (5.38)
P2Y12i	**81 (87.10)**
Clopidogrel	53 (56.99)
Prasugrel	3 (3.23)
Ticagrelor	25 (26.88)
VKA	**26 (27.96)**
Warfarin	15 (16.13)
Acenocoumarol	8 (8.60)
Others	3 (3.23)

[Table/Fig-4]: Preference of oral anticoagulant and antiplatelet drugs in Acute Coronary Syndrome (ACS).
Data presented as n (%); HCPs: Healthcare practitioners; NOACs: Non-vitamin K antagonist oral anticoagulants; P2Y12i: Purinergic receptor P2Y; G-protein coupled, 12 protein inhibitors; VKA: Vitamin K antagonists

While implementing GDMT in patients with ADHF, HCPs preferred the sequential addition of GDMT drugs, including a loop diuretic in 28 (43.75%) as the first choice, followed by ACEi/ARB in 21 (37.50%) as the second choice, SGLT2i in 26 (36.11%) as the third choice, and Mineralocorticoid Receptor Antagonist (MRA) in 18 (27.69%) as the fourth choice [Table/Fig-5]. Regarding the role of BBs in GDMT, 14 (21.21%) HCPs ranked it as their first choice, 13 (19.70%) considered it their second choice, and 12 (18.18%) ranked it as their third and fourth choices, respectively [Table/Fig-5]. According to 34 (44.74%) and 26 (35.62%) HCPs, one out of four HF patients was on ARNI and SGLT2i, respectively. A total of 27 (36.99%) and 24 (34.28%) HCPs reported that three out of four HF patients were on BBs and ACEi/ARBs, respectively. Additionally, 24 (34.78%) HCPs responded that half of their HF patients were on loop diuretics [Table/Fig-6].

Drug of choice	Response of HCPs (%)			
	First choice	Second choice	Third choice	Fourth choice
ARNi (n=73)	22 (30.14)	16 (21.92)	7 (9.59)	16 (21.92)
ACEi/ARB (n=56)	17 (30.36)	21 (37.50)	9 (16.07)	4 (7.14)
SGLT2i (n=72)	10 (13.89)	11 (15.28)	26 (36.11)	13 (18.06)
MRA (n=65)	4 (6.15)	6 (9.23)	15 (23.08)	18 (27.69)
Loop diuretic (n=64)	28 (43.75)	8 (12.50)	7 (10.94)	6 (9.38)
Beta blocker (n=66)	14 (21.21)	13 (19.70)	12 (18.18)	12 (18.18)
Ivabradine (n=45)	1 (2.22)	6 (13.33)	3 (6.67)	5 (11.11)

[Table/Fig-5]: Sequence of drug addition in Guideline-Directed Medical Therapy (GDMT) implementation for Acute Decompensated Heart Failure (ADHF).
Data presented as n (%) and has captured in this table include the most commonly selected first four choices; ACEi: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin-receptor blockers; ARNI: Angiotensin receptor-neprilysin inhibitors; HCPs: Healthcare practitioners; MRA: Mineralocorticoid receptor antagonist; SGLT2i: Sodium-glucose cotransporter 2 inhibitors

Drug of choice	Response of HCPs (%)			
	1 in 4	2 in 4	3 in 4	All
MRA (N=73)	22 (30.14)	27 (36.99)	10 (13.70)	14 (19.17)
SGLT2i (N=73)	26 (35.62)	23 (31.50)	12 (16.44)	12 (16.44)
ARNI (N=76)	34 (44.74)	25 (32.89)	9 (11.84)	8 (10.53)
ACEi/ARB (N=70)	12 (17.14)	18 (25.71)	24 (34.28)	16 (22.85)
Beta-blocker (BB) (N=73)	7 (9.58)	15 (20.55)	27 (36.99)	24 (32.88)
Loop diuretic (N=69)	10 (14.49)	24 (34.78)	15 (21.74)	20 (28.99)

[Table/Fig-6]: Utilisation of Guideline-Directed Medical Therapy (GDMT) in patients with Heart Failure (HF).
Data presented as n (%); ACEi: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin-receptor blockers; ARNI: Angiotensin receptor-neprilysin inhibitors; HCPs: Healthcare practitioners; MRA: Mineralocorticoid receptor antagonist; SGLT2i: Sodium-glucose cotransporter 2 inhibitors

According to the majority of HCPs, torsemide 10 mg was the most preferred dosage when prescribed in combination with spironolactone 25 mg in 47 (57.32%) and spironolactone 50 mg in 31 (37.80%) [Table/Fig-7].

Combination	Response of HCPs (%) [N=82*]
Spironolactone 25 mg with torsemide dose	
5 mg	24 (29.27)
10 mg	47 (57.32)
20 mg	7 (8.54)
Spironolactone 50 mg Torsemide dose	
5 mg	5 (6.10)
10 mg	31 (37.80)
20 mg	13 (15.85)

[Table/Fig-7]: Preferred torsemide dosage for combination with spironolactone.
Data presented as n (%); *Response received from only 82 HCPs for this question; HCPs: Healthcare practitioners

In addition to symptomatic HF patients treated with loop diuretics, 58 (72.50%) physicians preferred ARNI, and 28 (35%) preferred telmisartan among ARBs for combination therapy with loop diuretics, followed by valsartan (16.25%), losartan (5.00%), and olmesartan (1.25%), according to 46 HCP responses [Table/Fig-8].

Drug of choice	Response of HCPs (%) (N=80*)	
	Yes	No
ARB	**n=46**	
Telmisartan	28 (35.00)	-
Valsartan	13 (16.25)	-
Losartan	4 (5.00)	-
Olmesartan	1 (1.25)	-
ARNI	**58 (72.50)**	**1 (1.25)**

[Table/Fig-8]: Preference of drug in combination with loop diuretics for treatment of Heart Failure (HF).
Data presented as n (%); *Response received from only 80 HCPs for this question; ARB: Angiotensin-receptor blockers; ARNI: Angiotensin receptor-neprilysin inhibitors; HCPs: Healthcare practitioners

DISCUSSION

The present study represents the drug preferences of Indian HCPs regarding the adoption of GDMT in CVD. A clear preference among HCPs for well-established medications, such as ARBs/ACEi and BBs, was observed, along with a noticeable underutilisation of therapeutic alternatives, such as ARNIs and SGLT2is, in the Indian healthcare landscape.

For hypertension control in patients with ACS, telmisartan emerged as the most commonly chosen ARB, while metoprolol was the preferred BB, amlodipine was the favoured CCB, and torsemide was the chosen diuretic. For the management of ADHF, HCPs indicated that the sequential addition of GDMT can begin with a loop diuretic as the initial choice, followed by an ARB as the second choice, SGLT2i as the third choice, and MRAs as the fourth choice.

The present study revealed that ARB/ACEi and BB were the most preferred drug classes by Indian HCPs for the management of hypertension in patients with ACS. This observation was in accordance with the recent guidelines on hypertension management [16-18]. An Australian registry demonstrated high (80-87%) usage of ACEi/ARB, which was associated with a substantial long-term survival advantage in patients who underwent Percutaneous Coronary Intervention (PCI) for St-Elevated Myocardial Infarction (STEMI) or non-STEMI (NSTEMI), regardless of their initial left ventricular function [19]. The Kerala ACS registry reported a 62.7% usage of BBs and a 25.5% usage of ACEi/ARBs in patients with ACS after discharge [20]. In the ACS: Quality Improvement in Kerala (ACS QUIK) study, BBs were part of the optimal in-hospital and discharge medications [8]. In the CREATE registry, more than 50% of patients were on BBs, lipid-lowering drugs, and ACEi or ARBs during hospitalisations [9]. Overall, these findings suggest the suboptimal use of guideline-recommended therapy in the management of ACS and variation in the usage rates of ACEi/ARB and BBs across India.

Among ARBs, HCPs preferred telmisartan for the management of hypertension in patients with ACS. This finding aligns with real-world studies [21-23], which reveal that Indian physicians favour telmisartan over other ARBs for hypertension with co-morbidities. For BBs and CCBs, metoprolol and amlodipine were the primary choices, respectively. A nationwide survey indicated that S-metoprolol was the most preferred BB for patients with hypertension and sympathetic overdrive [24]. Similarly, an electronic medical records study reported that amlodipine provided better blood pressure reduction at lower doses and remained a favoured CCB despite newer alternatives [25].

In the present study, 65.48% of HCPs preferred dapagliflozin among SGLT2 inhibitors (SGLT2i) for the management of diabetes in patients with ACS. In patients with type 2 diabetes who had or were at risk for atherosclerotic CVD, treatment with dapagliflozin resulted in a lower rate of cardiovascular death or hospitalisation for heart failure [26]. Additional studies, such as the DAPA HF trial [27] and the DELIVER trial [28], reported the cardioprotective effects of dapagliflozin in patients with and without diabetes, as well as in patients with reduced or preserved ejection fraction, respectively. The American Diabetes Association (ADA) 2024 guidelines also recommend SGLT2i due to their efficacy in reducing the risk of composite Major Adverse Cardiovascular Events (MACE), cardiovascular death, all-cause mortality, myocardial infarction, hypertensive heart failure, and renal outcomes in individuals with type 2 diabetes who have established or high-risk of CVD [29].

In this study, clopidogrel was the preferred antiplatelet drug among P2Y12 inhibitors when used alongside aspirin in ACS. This aligns with a cross-sectional survey of Indian cardiologists, which expressed a strong preference for dual antiplatelet therapy consisting of aspirin plus clopidogrel (100%). Both clopidogrel (47%) and ticagrelor (51%) were favoured among P2Y12 inhibitors [30]. The Tamil Nadu ST-Segment Elevation Myocardial Infarction (TN-STEMI) program indicated that aspirin and clopidogrel were prescribed in more than 55% of the patient population [10]. Furthermore, the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial also supported the benefits of combining aspirin and clopidogrel in reducing cardiovascular death, myocardial infarction, or stroke, regardless of aspirin dosage [31]. According to the 2020 American College of Cardiology (ACC) expert consensus pathway for anticoagulant and antiplatelet therapy, clopidogrel is the recommended antiplatelet agent for most patients when combined with an anticoagulant [32].

Among oral anticoagulants, the majority of HCPs preferred rivaroxaban (a direct oral anticoagulant, or DOAC) with aspirin. Landmark trials reported that rivaroxaban reduced the risk of cardiovascular death, myocardial infarction, or stroke in patients with a recent ACS. However, it increased the risk of Thrombolysis In Myocardial Infarction (TIMI) major bleeding and intracranial haemorrhage, without a significant increase in fatal bleeding [33]. This led to the approval of rivaroxaban (2.5 mg twice daily) for Non-ST-segment Elevation Myocardial Infarction (NSTEMI) and ST-segment Elevation Myocardial Infarction (STEMI) patients after the acute phase, alongside aspirin and clopidogrel, according to the 2016 European Society of Cardiology (ESC) guidelines [34].

The conventional approach to implementing GDMT involves initiating the four drug classes in the sequential order in which they were incorporated into the guidelines. This entails starting with ACEi, then proceeding to BBs, followed by MRA, changing from ACEi to ARNI, and finally initiating sodium-glucose co-transporter-2 inhibitors (SGLT2i) [7].

In implementing GDMT for HF, HCPs preferred a sequence starting with loop diuretics, followed by ACEi or ARB or ARNI as second-line drugs, SGLT2i as third-line agents, and MRA as fourth-line agents in the current study. Similarly, the Heart Failure Society of America (HFSA) [35] guidelines suggest initiating treatment with intravenous loop diuretics for patients with ADHF and fluid overload. However, in cases of cardiogenic shock or symptomatic hypotension, temporary discontinuation of an ACEi/ARB or BB may be required. The ACEi/ARB and MRA can be temporarily discontinued in cases of renal dysfunction, particularly when oliguria and/or hyperkalaemia are present [36]. While BBs are contraindicated during ADHF due to their negative inotropic effects, initiating a low dose before discharge in euvolemic patients can improve outcomes [37], as supported by evidence showing benefits from careful initiation in stable conditions.

According to the majority of HCPs, BBs and ACEi/ARB were prescribed to 75% of patients with HF. Subsequently, 50% of patients with HF were on MRA and loop diuretics. However, only 25% of HF patients were prescribed ARNI and SGLT2i, suggesting potential underutilisation of GDMT in patients with HF.

The ESH 2023 guidelines strongly recommend SGLT2i and ARNI for hypertension in patients with heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction

(HFpEF) [16]. The 2022 AHA/ACC/HFSA guidelines [38] also strongly recommend SGLT2i and ARNI in the management of patients with HFrEF and provide a class 2A recommendation for HF with mildly reduced ejection fraction (HFmrEF) and HFpEF [16].

Similar to the present study, an analysis of real-world data reported that the use of ARNI and SGLT2i in patients with atrial fibrillation and HF is suboptimal. The authors noted that the low frequency of ARNI and SGLT2i use underscores existing gaps in the utilisation of GDMT among patients with HF [39]. Evidence from Indian registries of Cardiovascular Diseases (CVDs) also highlighted the suboptimal utilisation of other pillars of GDMT in HF, including BBs, ACEi/ARB, and MRAs [11-13,40].

Observations from a global registry (REPORT-HF) confirmed the low utilisation of GDMT (ACEi/ARB, MRA, and BBs), with approximately 34% of the patient population receiving GDMT. The authors also emphasised that the rates of GDMT underutilisation in developing countries were worse compared to high-income countries, at discharge (19% vs. 41%) and at six-month follow-up (15% vs. 37%) [41].

In the present study, torsemide 10 mg was the most preferred dosage when used along with both spironolactone 25 mg and 50 mg. The 2022 ACC/AHA and ESH 2023 guidelines indicate the use of oral loop diuretics, such as torsemide, to alleviate congestion, improve symptoms, prevent worsening of HF, enhance exercise capacity, and reduce the risk of HF hospitalisations (Class 1B) [16,38]. An expert opinion from India on the optimal use of torsemide in HF patients with or without renal impairment suggested considering torsemide therapy for patients at high-risk of hospitalisation for HF, for post-discharge ADHF patients who exhibit more severe symptoms, have a history of HF hospitalisation, or have renal impairment [42].

Spironolactone is a MRA indicated for the treatment of heart failure with reduced ejection fraction (HFrEF) in patients with New York Heart Association (NYHA) class II-IV (Class 1A), and for resistant hypertension (Class 2B) at maximum daily dosages of 50 mg and 100 mg, respectively [38,43]. It has also been indicated for the management of resistant hypertension in the lower spectrum of heart failure with preserved ejection fraction (HFpEF) (Class 2B) [16].

Currently, ARNI is recommended to enhance the effectiveness of Renin-Angiotensin-Aldosterone System (RAAS) blockers in HF. ARNI demonstrates superiority over ACEi or ARB alone, even when combined with diuretics. This superiority is attributed to neprilysin inhibition, which establishes a physiological "sequential nephron blockade," further strengthened by the concurrent administration of diuretics (loop diuretics or thiazides) or an MRA [44]. The post-hoc analysis of a landmark trial revealed that the use of sacubitril-valsartan significantly reduces the need for loop diuretics [45]. Additionally, the physiological nephron blockade by natriuretic peptides does not cause typical diuretic side effects, such as hyperuricemia or hyperkalaemia [44]. HCPs preferred ARNI as an additional treatment in combination with a loop diuretic. However, there is a paucity of data regarding the use of ARNI in combination with a loop diuretic for the treatment of HF, implying that this combination is innovative and that further studies are required.

Limitation(s)

This study had certain limitations. First, the data were collected through a self-report questionnaire, which may be subject to recall bias or social desirability bias. Second, the study sample consisted of HCPs from specific specialties in India, which may limit the generalisability of the findings to other healthcare settings or countries. Finally, as this is a first-of-its-kind cross-sectional observational study from India, readers need to consider the nature and design of the study while interpreting the data for general use. Furthermore, a causal relationship cannot be established based on this study's findings.

CONCLUSION(S)

This study highlights the prescribing preferences of HCPs in the management of CVD. ARBs and BBs were the most preferred drug classes for hypertension in ACS. SGLT2i were the preferred antidiabetic agents, while clopidogrel emerged as the most popular P2Y12 inhibitor for patients with ACS. For HF, HCPs preferred sequential drug therapy, with loop diuretics and ACE inhibitors/ARBs as the first and second choices. The majority of HCPs also preferred the combination of ARNI or ARBs with loop diuretics for patients with symptomatic HF. These findings offer valuable insights into clinical practices and medication preferences among HCPs, contributing to a better understanding of treatment trends in different patient populations. However, Indian HCPs are still adapting to GDMT to improve CVD outcomes.

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