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Original Research Article

Real-world, in-clinic challenges and opportunities in the management of heart failure patients with dyslipidaemia: comprehensive experiences by healthcare professionals

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ABSTRACT

Background: Dyslipidemia is a significant modifiable risk factor for cardiovascular disease (CVD), particularly in Asian Indians, who exhibit a distinctive lipid profile. Effective management is critical in heart failure (HF) patients to mitigate CVD risk.
Methods: This cross-sectional, observational study, the Dyslipidemia and Heart Failure Survey, was conducted across India from July to September 2023. It involved 325 healthcare professionals (HCPs) specializing in HF management. Data were collected using a structured questionnaire addressing lipid parameter assessment, ARNi (sacubitril/valsartan) therapy and its integration into HF management.
Results: Among the HCPs, 49% emphasized addressing all lipid parameters, including HDL, LDL, triglycerides and non-HDL, with LDL cholesterol identified as the primary therapeutic target. Statins were the most commonly prescribed lipid-lowering agents. For de novo heart failure with reduced ejection fraction (HFrEF) patients, 55% of HCPs preferred ARNi over ACE inhibitors or ARBs. However, HCP practices vary widely regarding adherence to ACC/AHA guidelines for stage C HFrEF, with 145 (45%) fully compliant and 136 (42%) selectively advising ARNi for specific subsets. Barriers to ARNi usage included concerns about hyperkalemia and angioedema. Despite these challenges, many HCPs expressed optimism about ARNi's potential to improve ejection fraction, underscoring the need for a tailored, patient-specific approach to its application.
Conclusions: The study highlights current practices and challenges in managing dyslipidemia and HF among Indian HCPs. It represents the need for improved adoption of ARNi therapy and targeted interventions to address barriers, paving the way for better outcomes in HF management.

Keywords: ARNi therapy, Cardiovascular disease, Dyslipidemia, Heart failure, India

INTRODUCTION

Dyslipidemia is a recognized contributor that is closely linked to the pathophysiology of CVD and is a crucial independent modifiable risk factor for CVD. Asian Indians are known to have a unique pattern of dyslipidemia with deviations in lipid levels, encompassing elevated total cholesterol (TC), elevated low-density lipoprotein cholesterol (LDL-c), increased triglycerides (TG) or decreased high-density lipoprotein cholesterol (HDL-c).[1,2] The prevalence of dyslipidemia varies with age, gender, residence region and socioeconomic status.[3] The recent nationwide ICMR-INDIAB study, regarded as the most comprehensive cardiovascular risk factor assessment in India, revealed the following prevalence rates for different dyslipidemias, hypercholesterolemia (≥200 mg/dl) at 24.0%, high LDL cholesterol (>130 mg/dl) at 20.9%, low

HDL cholesterol at 66.9% and hypertriglyceridemia at 32.1%.[4,5]

The importance of addressing metabolic risk and cardiac lipotoxicity in heart failure, particularly related to diastolic dysfunction, is acknowledged. Hence, managing dyslipidemia should be a fundamental aspect of cardiovascular prevention strategies, focusing primarily on individuals at higher risk to maximize benefits.[6,7] Lipid levels are complexly regulated and influenced by several pathways affected by neprilysin, a ubiquitous endopeptidase responsible for the breakdown of many vasoactive peptides.[8] Pathways relevant to neprilysin inhibition and lipid metabolism include insulin and sympathetic and natriuretic peptide (NP) activity.[9]

Sacubitril/valsartan is a combination medication prescribed for heart failure, combining sacubitril (a neprilysin inhibitor) and valsartan (an angiotensin II receptor blocker) to reduce strain on the heart.[10] They simultaneously inhibit the degradation of atrial and brain natriuretic peptides, thereby exerting multifaceted neurohormonal effects via vasodilation and natriuresis to afford additional cardiovascular benefits and therefore may significantly alter lipid levels through these common pathways.[11] In 2020, the FDA extended the approved use of ARNI (Angiotensin-Receptor Neprilysin Inhibitor) is to include certain patients with heart failure and an ejection fraction (EF) above 40%, marking the first medication to receive approval for this particular indication.[12] The American College of Cardiology Foundation (ACCF)/ Heart Failure Society of America (HFSA) guidelines strongly recommend ARNi with a Class 1A designation, while the European Society of Cardiology (ESC) guidelines provide it with a 1B recommendation.[13]

Despite recommendations for the use of ARNi in heart failure guidelines and expanding indications, the widespread incorporation of the drug into clinical practice seems to be limited. A better understanding of current ARNi use may help elucidate potential barriers to its use.[12]

The present study called "Dyslipidemia and Heart Failure Survey", was conducted to understand Health care professional (HCPs)' clinical practices, preferences and challenges in heart failure patients with dyslipidemia. This questionnaire-based survey was carried out across India with the primary goal of investigating perspectives on the in-clinic diagnosis and management of heart failure patients with dyslipidemia; by including a large and diverse sample, the survey aimed to capture a wide range of responses, thereby minimizing bias and increasing the relevance of the findings.

METHODS

Survey design and participants

This was a cross-sectional, observational approach through a questionnaire-based survey conducted nationwide in India from 20th July to 20th Sept. 2023. The methodology involved a structured questionnaire for in-depth one-on-one conversations with HCPs via personal interviews. A significant sample size of 325 participants was included to ensure the robustness and statistical validity of the survey's conclusions. The survey utilized an electronic survey format via the FastSigns Questionnaire platform comprising 15 questions. This standardized approach facilitated a uniform data collection process, bolstering the research findings' credibility and reliability. In this study, doctors with an MD, DM (cardiology) degree or expertise treating patients with heart problems are referred to as "health care professionals". The inclusion criteria for the survey participants were practicing physicians actively involved in managing patients with heart failure, dyslipidemia, hypertension and associated comorbidities. Physicians who were not directly involved in the management of these conditions or had limited experience in prescribing ARNi or lipid-lowering therapies were excluded. Additionally, healthcare professionals without the willingness or ability to provide informed responses during the structured interviews were not considered for the study.

Survey outcomes

The initial four questions inquired about the essentiality of ARNi therapy in managing heart failure and sought to identify the relevant lipid parameters such as HDL cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides. Subsequently, the following six questions delved into clinical practices, exploring HCPs preferences for ARNi in HFrEF patients based on various guidelines, including ACC/AHA.

The final five questions centered on the safety aspects of ARNi therapy, covering topics such as the average improvement in ejection fraction among HFrEF patients, occurrences of angioedema associated with ARNi therapy, instances of hyperkalemia in heart failure patients, participation in research or clinical trials and other medications recommended for combination therapy.

Data analysis

Upon completion of the data collection phase, the amassed information was meticulously entered and organized using Microsoft Excel 2013. This software was employed to analyze the responses to the 10 survey questions. Subsequently, the detailed data analysis was performed using descriptive statistics.

RESULTS

Results revealed that 158 (49%) HCPs advocate addressing all listed lipid parameters, highlighting a comprehensive approach. Notably, 130 (40%) HCPs prioritize LDL cholesterol as the primary target, underscoring its crucial role in managing dyslipidemia, while HDL and non-HDL cholesterol are less frequently

selected (Figure 1a). The majority of HCPs (312) prefer prescribing statins as the primary choice, emphasizing their pivotal role. In contrast, only one HCP indicated bile acid sequestrants as their most frequently prescribed lipid-lowering medication (Figure 1b).

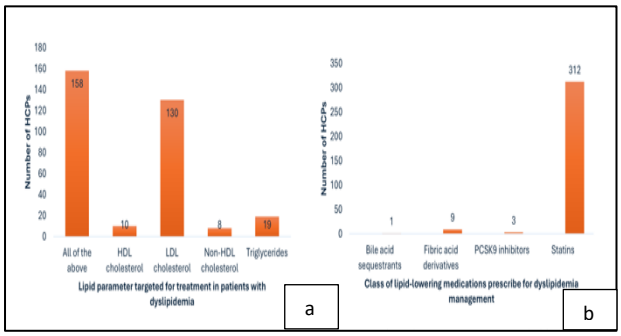

Figure 1 (a and b): HDL and non-HDL cholesterol.

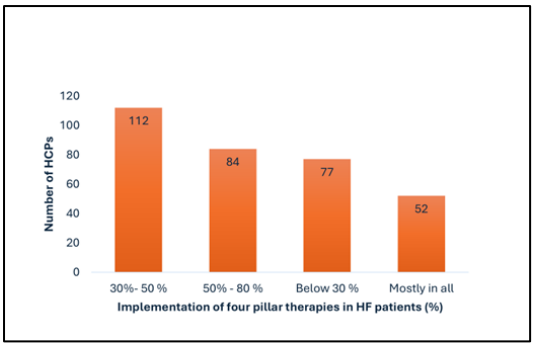

Figure 2: HCPs initiated all four pillar therapies in nearly all cases.

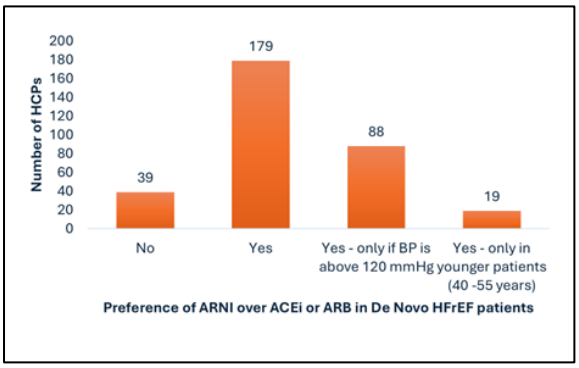

Figure 3: A preference for ARNi over other RAAS inhibitors like ACEi or ARB.

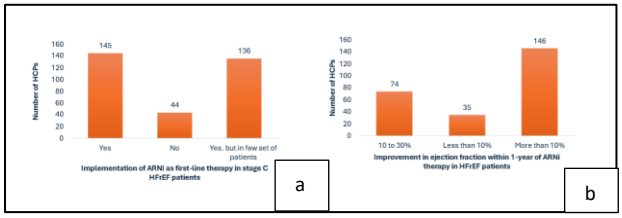

Figure 4 (a and b): Selectively advising ARNi.

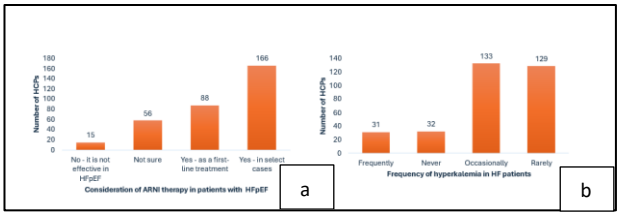

Figure 5 (a and b): ARNi therapy of patients.

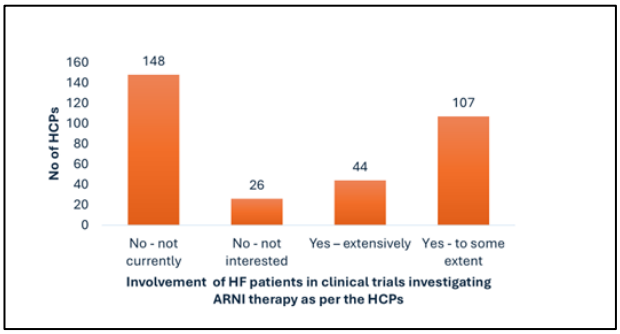

Figure 6: Involvement of HF patients.

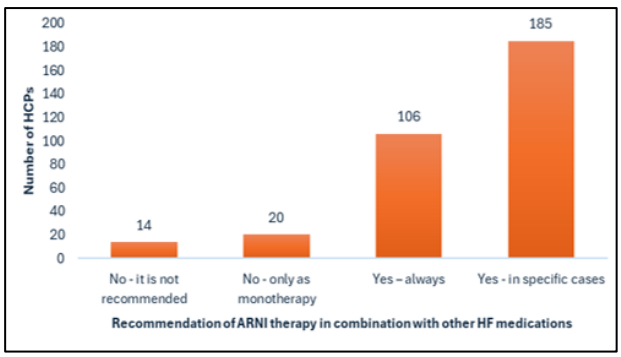

Figure 7: Recommendation of ARNi therapy in combination with other heart failure medications for optimal outcomes in clinical practice.

Regarding implementing four pillar therapies in heart failure patients before discharge from the hospital, 84 (26%) HCPs reported implementing them in 50-80% of the cases. Notably, 52 (16%) HCPs initiated all four pillar therapies in nearly all cases, indicating diverse approaches among practitioners (Figure 2).

Among surveyed HCPs, 179 (55%) of them treating de novo HFrEF patients and a significant majority expressed a preference for ARNi over other RAAS inhibitors like ACEi or ARB, whereas 88 (27%) HCPs recommended it only if the BP is>120 mm Hg and 19 (6%) specifically recommended it for younger patients aged 40 to 55 (Figure 3).

HCP practices vary widely regarding adherence to ACC/AHA guidelines for stage C HFrEF, with 145 (45%) fully compliant, 44 (14%) not recommending ARNi for any patients and 136 (42%) selectively advising ARNi for specific subsets (Figure 4a). There are diverse

observations among HCPs regarding improvement in ejection fraction (EF) with ARNi therapy, with 146 (45%) observing an EF improvement of more than 10%, while 35 (11%) HCPs observed an improvement of >10%. Overall, professionals are optimistic about ARNi therapy's effectiveness in raising EF, with many anticipated increases beyond 10% (Figure 4b).

HCPs hold varied opinions on the use of ARNi therapy for HFpEF. While 88 (27%) HCPs regard it as a first-line treatment, 166 (51%) consider it suitable for specific cases. In contrast, 15 (5%) HCPs believe it is ineffective and 56 (17%) are uncertain about its efficacy (Figure 5a). According to data collected from 133 (41%) HCPs, hyperkalemia appears to occur occasionally in heart failure patients receiving ARNi therapy. Meanwhile, 31(~ 10%) others noted frequent occurrences, suggesting a need for caution and regular monitoring of potassium levels in such cases. Another (10%) 32 HCPs reported no occurrences, indicating that hyperkalemia is not consistently prevalent in these patients (Figure 5b).

Regarding active participation in ARNi therapy research, 107 (33%) HCPs were involved to some extent, while 44 (14%) were actively engaged. This suggests a relatively good level of interest among HCPs in research related to ARNi therapy (Figure 6) and as this is a new therapy so near future, the engagement will gradually increase.

In relation to recommending ARNi therapy in conjunction with other heart failure medications for optimal results, the majority of HCPs opt for a case-specific approach. Specifically, 185 (57%) respondents recommend the combination in specific scenarios. In contrast, a smaller group of 20 (6%) HCPs utilise ARNi solely as monotherapy. This emphasizes the preference for a tailored approach when considering ARNi therapy alongside other medicines (Figure 7).

DISCUSSION

Dyslipidemia, a key modifiable risk factor for cardiovascular disease, significantly impacts heart health. ARNi are essential in heart failure management, as they enhance natriuretic peptides and inhibit RAAS, thereby improving cardiac function and lowering blood pressure.[14] Additionally, ARNis may aid in managing dyslipidemia by potentially enhancing lipid profiles through their broad cardiovascular benefits. Their pleiotropic effects, such as anti-inflammatory and anti-fibrotic actions, further enhance their therapeutic effectiveness, addressing both heart failure and dyslipidemia and promoting overall cardiovascular health.[9,15]

Our survey study represents the frequent coexistence of heart failure and dyslipidemia among patients, often diagnosed during routine clinical assessments. Moreover, HCPs commonly encounter individuals presenting with both conditions. The analysis emphasizes the importance of comprehensively addressing various lipid parameters, with a primary focus on reducing LDL cholesterol due to its pivotal role in the management of dyslipidemia. This assessment of lipid parameters can be conducted periodically, typically every three months. The results demonstrate that clinicians prioritize lowering LDL cholesterol levels in the management of dyslipidemia, with statins being the preferred class of prescribed lipid-lowering medications.

In terms of current adoption rates, HCPs report that approximately 20-40% of eligible heart failure patients are undergoing ARNi therapy. Most practitioners recommend ARNi as the first-line therapy for patients with stage C HFrEF, aligning with recommendations set by ACC and AHA guidelines. Overall, there is a sense of optimism among professionals regarding the efficacy of ARNi therapy in improving ejection fraction. A substantial majority express a preference for ARNi over other inhibitors of RAAS. Concerning the recommendation of ARNi therapy in conjunction with other heart failure medications for optimal outcomes, many HCPs adopt a case-specific approach, with 185 respondents specifically recommending this combination in certain scenarios.

The survey findings indicate that while a considerable portion of HCPs have not encountered angioedema with ARNi therapy, whereas a notable fraction have encountered it in varying degrees. Likewise, data collected from HCPs suggests that hyperkalemia occasionally arises in heart failure patients undergoing ARNi therapy, emphasizing the importance of vigilance and regular monitoring of potassium levels in such cases. In terms of active participation in ARNi therapy research, HCPs have shown some level of involvement, with a significant proportion actively engaged in research endeavors. This indicates a commendable level of interest among HCPs regarding research related to ARNi therapy.

In one of the clinical studies conducted by Selvaraj S et al, in 2021, analysed the treatment effect on lipid levels.[9] When sacubitril/valsartan compared with valsartan, reduced triglycerides most among those with elevated baseline levels (triglycerides≥200 mg/dl) ($p<0.001$) and at 16 weeks by −13.0% (95% CI, −18.1% to −7.6%) or −29.9 (95% CI, −44.3 to −15.5) mg/dAl, in the group. Sacubitril/valsartan significantly reduces triglycerides compared with valsartan, an effect that was nearly threefold stronger in those with elevated baseline triglycerides. Also, modest increases in high-density lipoprotein cholesterol and low-density lipoprotein cholesterol were observed with therapy. Our survey study results showed that 158 (49%) HCPs advocate for addressing all listed lipid parameters mentioned in the above study—HDL, triglycerides, LDL and non-HDL—in the treatment of HF patients with dyslipidemia. This research study supports our findings on the utility of ARNi and lipid level assessments in managing both heart failure and dyslipidemia.

In summary, our survey findings offer a comprehensive view of the current status of ARNi therapy within the realm of heart failure management. Additionally, they shed light on dyslipidemia management and available treatment choices. This data presents a snapshot of clinical practices, identifies areas of ambiguity and highlights opportunities for future research and educational initiatives.

Despite a notable sample size of 325 HCPs, the survey study may not fully reflect the diversity of clinical practices across different regions and healthcare environments. Moreover, its findings might have limited relevance to areas with unique patient populations or healthcare structures, emphasizing the importance of conducting further research to enhance the generalizability and applicability of the results.

CONCLUSION

The survey offers significant insights into India's current landscape of dyslipidemia management and treatment options. Its findings underscore the prevalent utilization of ARNi therapy for heart failure patients with dyslipidemia and indicate a notable preference among surveyed professionals. The data highlights diverse adoption rates of ARNi across various practices, emphasizing its role as a favored choice for a personalized approach alongside other medication options.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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