Clinical Medicine and Medical Research
Clinical Medicine and Medical Research. CMMR05(02),263−272 (2024)
Received 9 Dec. 2024 | Revised 18 Dec. 2024 | Accepted 24 Dec 2024 | Published Online 03 Jan 2025
https://doi.org/10.52845/CMMR/2025-6-1-1 | Page no. 273-281

Clinical Pharmacist as Facilitator for Prescribing Sacubitril/Valsartan Combination in Patients with Heart Failure and Reduced Ejection Fraction: A Single Centre Study in Iraq

Pharmacist Zainab Abbas Hasan Manshad [1], Assistant Professor Nagham Yahya Ghafil [2]

1. Al-Hussein Teaching Hospital / Thi-Qar Health Directorate

2. Kufa University / Faculty of Pharmacy

Abstract:
Background: Although Sacubitril/Valsartan approved in 2015 to use in heart failure patients with reduced ejection fraction and dramatic results gained, the prescription of it still lower than expected by most cardiologists in Iraq. Aim of study: In essence confirm the impact role of clinical pharmacist as facilitator to increase the prescription of Sacubitril/Valsartan combination as ARNi in HF patients in AL Nasiriyaha Cardiac Centre by clinical pharmacist revealing to the real obstacles that prevent cardiologists from prescribing. Patients and Methods: this is interventional study that included 73 patients with HFrEF who visited the cardiac outpatient clinic in AL Nasiriyaha Cardiac Centre –Thiqar-Iraq who received Sacubitril/Valsartan as ARNi, study period was two months. Results: This study explained the role of clinical pharmacist in increase the attitudes and the clinical views of cardiologist about Sacubitril/Valsartan combination. Also explained the causes behind non-adherence to the guidelines by them. Conclusions: The clinical pharmacist plays important role as facilitator to increase the prescription of (S.V.) combination and make large proportion of cardiologists to be more adherent to the published guidelines.

Key Words: Sacubitril/Valsartan, ARNi, Heart failure with reduced ejection fraction, Clinical pharmacist.

Introduction

The combination of sacubitril and valsartan, is a angiotensin receptor-neprilysin inhibitor (ARNI, formerly known as LCZ696), has gotten a lot of attention as a way to treat heart failure because it works on both the renin-angiotensin system (RAS) and the natriuretic peptide system (NEP) (Zhang et al., 2022).

Mechanism of action of (S./V.) combination

(S./V.) combination is a drug with dual-acting, this is due to its combination of two components; -first ingredient, Sacubitril is a prodrug that, after activation converts to sacubitrilat by esterase. Sacubitril prevents breakdown of endogenous (NP). The NP system can be improved by blocking neprilysin or neutral endopeptidase (NEP), the major enzyme responsible for NP degradation. Sacubitril inhibits the metabolism of endogenous enkephalins, which causes a rise in their levels. Isolated NEP inhibition (NEPi) activates the reflex RAS (renin-angiotensin system) and inhibits AgII breakdown, preventing endogenous (NP) deterioration while counteracting any potentially positive effects. Sacubitril alone does not have an evident superiority; thus, it must be paired with a RAAS blocker, represented by the second portion of the medicine, valsartan. The RAS is activated in HF, boosting sympathetic nerve activity and causing cardiac remodeling, which exacerbates the course of HF. Renin and angiotensin-converting enzyme generate angiotensin II from angiotensinogen. Valsartan suppresses (Ang II) effects by specifically inhibiting the type-1 angiotensin receptor (AT1

receptor). As a result, this unique mechanism prolongs the beneficial benefits of NPs while also preventing the detrimental consequences of RAAS. Collectively, the net results following systemic vasodilation, a decrease in peripheral vascular resistance, an increase in both diuresis and natriuresis with the resultant decrease in plasma volume, and inhibition of the release of Ang II-dependent aldosterone, inhibiting deleterious effects mediated by Ang II, such as vasoconstriction, hypertrophy, and fibrosis, as well as improvement of cardiac remodeling and dysfunction in HF patients. The synergistic actions of neprilysin inhibition and angiotensin receptor blocking boost effectiveness and provide a novel mechanism of action (McMurray et al., 2014) (Han et al., 2023) (Judge et al., 2017).

The Clinical Trials on (S./V.) combination as a (ARNi)

The guideline recommends use of (S./V.) combination in chronic and symptomatic HFrEF patients (class II or III to reduce morbidity and mortality if no contraindications are found (Sauer et al., 2019a). (S./V.) combination is indicated to be used as an alternate therapy to RAAS -inhibitors along with the traditional heart failure medications, including beta-blockers and mineralocorticoid receptor antagonists (MRA). (EL KAFOURY A.M,2021) (S./V.) combination, along with BB, MRA, and SGLT2 inhibitors, is a basic therapy. It should be administered to HFrEF patients whenever possible to minimize hospitalization risk and all-cause death. (S./V.) combination is a great medicine for minimizing hospitalizations and enhancing the overall quality of life(QOL) in people with HFrEF by improving heart shape and functionality. When administered early in the course at the correct dosage, it decreases the risk of adverse cardiovascular events and consequently readmission rates (Sakhamuri et al., 2023).

The hospital-based initiation method provides a potentially new path for improving (S./V.) combination clinical acceptance. Over the last five years, (S./V.) combination has been recognized as a cornerstone component of comprehensive disease-modifying medicinal treatment in the management of chronic HFrEF(Zhang et al., 2022). The combination approved by FDA in 2015, recommended in the 2016, and also in the 2017 updated from the (ACC/AHA/HFSA-Heart Failure Society of America) and with other a therapy to minimize mortality and morbidity in HFrEF. (Proudfoot et al., 2021).

Primary barriers to implementation of S/V

Although (S./V.) combination was accepted in clinical practice as Class I recommendation in HF guidelines, use of this combination has been lower than prognosticated (Tan et al., 2020). The highest barrier to clinical application is hypothesized that the price of this novel agent despite there are several cost-effective analyses that can predict the collective advantages when an ARNI (S/V) is used suitably (Veltri, 2019). Despite data proving the advantages of ARNI treatment above standard of care, only a percentage of eligible patients receive the (S/V) combination, and barriers preventing practitioners from prescribing it in those eligible patients may address practitioners' unfamiliarity with (S/V) combination; some cardiologists may lack confidence in identifying the appropriate patient population in clinical practice for compelling indication of (S./V.) combination , safety concerns, and fear of causing worsening symptoms in the optimal utilization of the (S./V.) combination in clinical practice has the potential to minimize the the total burden of HF.

According to HF recommendations of US, European Union, and Canadian, as well as developing evidence, implementing (S./V.) combination in recommended patients can lead to additional mortality reductions. The proper and timely application of this powerful drug has the possibility to greatly enhance global and public health. Medication intolerance and adherence difficulties remain a barrier to

medication optimization. (Patil et al., 2022) and (Sauer et al., 2019).

Role of clinical pharmacist in implementation of S/V for HF Patients

Even experienced professionals find it difficult to integrate a new medicine into clinical practice (Sauer et al., 2019a), Given the complexity of the disease state and the drug load, a multidisciplinary strategy to managing HFrEF patients that involves a pharmacist, as recommended by the ACC, AHA, and Heart Failure Society of America (HFSA) recommendations, is invaluable. Previous research suggests that pharmacist-led HF care improves patient outcomes by increasing the number of patients using GDMT. Pharmacist-led initiatives have been found to improve patient outcomes, such as reducing hospitalizations and readmissions (Patil et al., 2022). Clinical pharmacists play an important role in heart failure therapy by improving the transfer of care from the hospital to the community/home. This is crucial for improving outcomes and lowering high hospital readmission rates, which are associated with higher morbidity, death, and expenditures. Pharmacists who work on both inpatient and outpatient teams can provide a number of services that have been proved to minimize hospital readmission rates and improve patient management and care.

Clinical pharmacists play an important role in heart failure therapy by improving the transfer of care from the hospital to the community/home. This is crucial for improving outcomes and lowering high hospital readmission rates, which are associated with higher morbidity, death, and expenditures. Pharmacists who work on both inpatient and outpatient teams can provide a number of services that have been proved to minimize hospital readmission rates and improve patient management and care (Prakasam et al., 2021).

The pharmacist's involvement in the medication titration of outpatient clinic includes delivering personalized patient education about heart failure, pharmaceutical management, and lifestyle adjustments. The pharmacist's decision to start, stop, or change medication dosages was based on a standardized HF symptom questionnaire as well as laboratory and physical tests. During the appointment, the pharmacist does a thorough physical exam to check for lung and heart sounds, lower extremities edema, jugular vein distention, and hepatojugular reflux.The inclusion of pharmacists in patients' HF treatment has demonstrated great impacts on hospitalization rates, improvements in the usage of GDMT, symptoms, and drug adherence(Ingram, Valente and Dzurec, 2021).

Aims of the study

Reinforcing the real role of clinical pharmacists in patients' HF treatment has demonstrated favorable impacts on hospitalization rates, improvements in the usage of GDMT, symptoms, and drug adherence. Clinical pharmacist as part of the multidisciplinary (MD) team in adherence to the guideline for management of patients with HF by cardiologists in AL Nasiriyah Cardiac Centre-ThiQar by making interventions and assessing the impact of these interventions to optimize the benefit (S./V.) combination as one of the fundamental therapeutics in heart failure

Methodology

Study design

This current study had quasi-experimental design was conducted at the Al–Nasiriyah Cardiac Center–DhiQar governorate- Iraq, during seven months (from November 2023 to May 2024) during2 months. The study included 73patients who previously diagnosed with HF. The collection of patient’s data during their visiting’s to the cardiac outpatient clinic in the center. Statistics The data was analyzed with version 25 of the Statistical Package for the Social Sciences (SPSS). Descriptive statistics were used for all research items. Categorical data were reported as frequencies and

percentages, whereas continuous variables were represented as means ± standard deviation (SD).

Results

The distribution of socio-demographic characteristics in (HFrEF) patients whom on (S./V.) combination Data as age, BMI,gender distribution and smoking number explained in table (1.1)

Table (1.1): The distribution of socio-demographic characteristics for (S./V.) combination received group

Characteristics	Number	Mean ± SD	Range	P-value
Age	73	63.89±10.65	36-80	0.469
BMI(Kg/m^2)	73	29.57±4.48	20.7-42	0.056
		Male	Female	
Gender Number (%)	73	48 (65.8 %)	25 (34.2 %)	0.307
		No	Yes	
Smoking Number (%)	73	37 (50.7 %)	36 (49.3 %)	0.74

The impact role of clinical pharmacist intervention to increase prescription of (S. /V.) combination by cardiologists to indicated HF patients the pharmacist-led education to the hospital physicians (cardiologists) resulted to increase the number of prescribers of the (S./V.) combination from two to six out of ten cardiologists as showed in (figure 1.1).

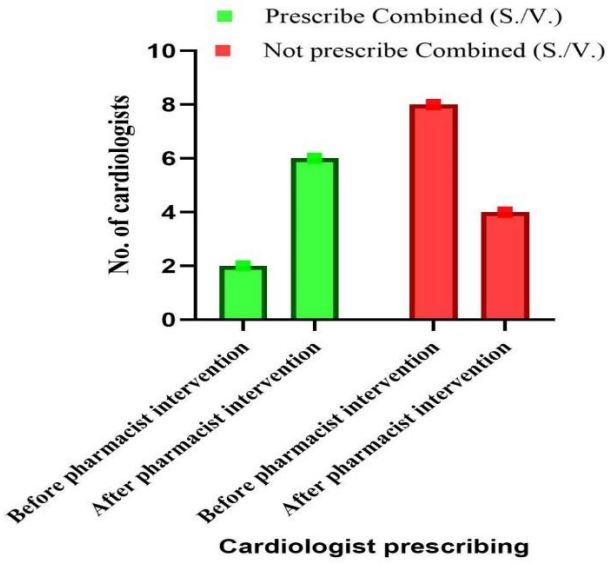

Figure (1.1): The number of cardiologists prescribed (S. / V.) combination before and after the pharmacist intervention

Discussion

Socio-demographic Characteristics of Patients

The current study stated that the age ranges of patients were (36-80). Of note that this result inconsistent with another study performed on Chinese HF patients included age range (51-72) (Hu, Liu and Lou, 2023). This difference might be explained by longer survival and better treatment results for HF patients in China compared to Iraq. The younger ages of Iraqi patients with HF may be reflected by the delay in treatment of HF etiologies and no or little adherence to CVD medications. There is a lack of understanding of the variables that contribute to medication nonadherence in CVD patients, with insufficient research on knowledge, attitudes, beliefs, and associated behaviours. Most Iraqi hospitals were trying to recover after years of violence, health facility and personnel shortages, insufficiently qualified healthcare workers, and limited healthcare financing. Iraq's healthcare system, particularly heart disease management, is still in the early stages of development, which might explain the poor rates of adherence to cardiac drugs. Iraqi individuals with CVD may have had difficulty receiving effective health

treatments because to a lack of or restricted resources, such as shortage of drugs in public hospitals. (Al-Ganmi, A. H. A., et al., 2019).

The number of male patients in the current study was 48 patients (65.8 %) and it included 25 female patients (34.2%), the male-to-female ratios were 1.92:1. This means that HF has greater incidence in male Iraqi patients than in female patients. This result came in line with that obtained by (Damman et al., 2018), the post-hoc study to evaluate the renal effects of S/V in patients with HFrEF, which showed that most patients were males (79.4 %) and the ratio of male to female was 3.6:1. This congruent with the facts related to the pathophysiology of HF in both male and female. A prospective study of HF patients who had been admitted to the Coronary Care Unit (CCU) of Teaching Hospital- Qurdistan, Iraq; females accounted for the majority of HFmrEF followed by HFpEF and HFrEF. (HFrEF) has a greater prevalence in men. (Regitz- Zagrosek, 2020), (Rahman and Al-Othman, 2022). Regarding BMI, there was similarity to some extent between this study finding in where 29.57±4.48 was the Mean ± SD of BMI and that presented by study performed by (El-Battrawy et al., 2023) The present study showed that 49.3 % of the patints were active smokers during the study period. The role of smoking in developing of CVD is clear. Smoking has been associated with nonadherence to medications, this could lead to less well- controlled hypertension over time, and poorer adherence to HF drugs, causing more HF hospitalizations. Smoking is potentially associated with an increase in the left ventricular mass index, left ventricular concentric remodeling and hypertrophy which is a risk factor for the onset of HF. In the community- based cohort study published in the journal of the AHA; on Black adults, current smoking was associated with both incident HFrEF and HFpEF hospitalizations (Egan and Orgain, 2010)

The role of clinical pharmacist intervention to increase prescription of (S. /V.) combination by cardiologists to indicated HF patients

This study showed that the total number of cardiologists in Al–Nasiriyah Cardiac Center was 10 who had specialized degrees in interventional catheterization and cardiac diseases in addition to FICMS degrees (Fellow of Iraqi Commission for Medical Specializations) in the internal medicine. The presence of such a specialized team is crucial for addressing the increasing demand for cardiac care in the province. Furthermore, the expertise of these cardiologists plays a vital role in improving patient outcomes and advancing the overall quality of healthcare in DhiQar . Just 2 of them were prescribing S/V before pharmacist intervention, while the most of them, (8) were still prescribing ACEi or ARBs as RAAS inhibitors.

It's agreed that the drugs represent the cornerstone in the treatment and symptomatic relief in HF patients, so when there are defects related to prescribers or receivers, the prognosis will be poor. Barriers to optimal beginning of (S./V.) combination may include healthcare providers' unfamiliarity with its therapeutic advantages, physician reluctance to initiate, patients' inertia to adopt, poor awareness for HF therapy, loss of follow-up, and fears about its detrimental effects, among others(Pandey et al., 2024).

Medication nonadherence is the most significant patient-related factor.They have low drug adherence rates. According to reports, at least one in every four HF patients is non-adherent, which can lead to a poor prognosis characterized by deteriorating symptoms, repeated hospitalizations, and, finally, death (Jarab et al., 2023). Cost is a significant potential obstacle to the usage of S/V. These high expenses might create many hurdles to beginning and continuance. Most HF patients take many daily drugs and, in the absence of infinite financial means, are sometimes faced with difficult decisions about how much they

can afford to spend on a single prescription, even if it is successful at improving outcomes. Over one-third of patients who started on S/V did not adhere to the regimen over the next 180 days. The refill patterns indicate that almost half of non-adherent patients stopped taking S/V entirely. Future research should look at whether this was caused by cost, hemodynamic, renal, or other intolerances (Sangaralingham et al., 2018). The systematic review of data on the cost-effective models of S/V found that S/V was reported to be a cost-effective therapy in chronic HFrEF patients when introduced in the outpatient environment. This finding underscores the importance of early intervention and optimal management strategies for heart failure patients. By integrating S/V therapy into outpatient care, healthcare systems may not only improve patient outcomes but also reduce overall healthcare costs associated with hospitalizations and complications (Proudfoot et al., 2023). Adherence to medicine is critical in sever illnesses, and necessitates the therapeutic assisstance between physician and patient, including cooperative decision-making and self-care assistance. Non-adherence is widespread, but it is not necessarily clinically inappropriate. For example, medication withdrawal or dose decrease due to pharmaceutical side effects or intolerance may be misunderstood as clinical lethargy. This is especially true in the lack of clinical information, as in the case of administrative claims-based research.

Other factors related to patient involve overall mistrust in and refuse of recommended treatment because state of denial the disease severity, delay in seeking medical care, attitude toward medications, poor health care literacy, resistance to adopting lifestyle changes, and being unconvinced of the efficacy of the medications. (Verhestraeten, Heggermont and Maris, 2021).

Lack of alignment with guidelines in physician related to clinical inertia which defined as “the lack of treatment intensification in a patient not at evidence-based goals for care” or it refers to a physician's failure to deviate from established practice. It plays significant role in decrease new drugs prescribing. Clinical inertia, on the other hand, encompasses more than simply failing to commence or escalate therapy when advised. It considerably increases the probability of negative outcomes and elevates health-care expenses in numerous chronic conditions. O'Connor et al. attributed clinical inertia to three major components of their conceptual model: system-related variables, patient-related factors, and physician-related factors, which account for 20%, 30%, and 50%, respectively. Other patient-related factors include overall mistrust and refusal of recommended treatment due to denial of disease severity, delay in seeking medical care, attitude toward medications, low health care literacy, resistance to lifestyle changes, and doubts about the efficacy of medications.Nearly half of doctors were "hesitant" to give SGLT2i and ARNi because they were unfamiliar with the classes and believed they were "novel" drugs for treating HFrEF.Some cardiologists justified their reluctance to prescribe the (S./V.) combination by citing its unfamiliarity and the fact that it is not widely acknowledged by physicians. Others explained their initial preference for ACEi, claiming that it was simply how they were raised. They utilized ARB as well. The other classes (ARNi and SGLT2i) were not seen sufficiently to start. They usually target ACE first for some reason; it's just how they were raised. However, they utilize ARB as well. Given the complexities of the condition and the medication load, a multidisciplinary approach to managing HFrEF patients that includes a pharmacist, as suggested by the ACC, AHA, and Heart Failure Society of America (HFSA), is crucial. Previous studies demonstrate that pharmacist-led HF treatment improves patient outcomes by increasing the number of patients who take GDMT.

Pharmacist-led initiatives have been shown to enhance patient outcomes by lowering hospitalizations and readmissions. Despite well-established standards for the majority of chronic illnesses, they are still not followed in clinical practice. Aujoulat et al. discovered that the primary reasons physicians do not follow these guidelines are a lack of knowledge of evidence-based objectives of treatment, a lack of familiarity with the guidelines, or a disagreement with the standards. The Heart Failure Adherence and Retention Trial (HART) found that the combined adherence of physicians and patients is low, with just 41% of cases where both physicians and patients were adherent to both prescribing and using evidence-based therapy. Physicians were considered non-adherent if they failed to prescribe any of the guideline-recommended medications in the absence of contraindications or provided a medicine with a known contraindication. Calvin et al. suggested that improved adherence to prescription and taking guideline-recommended medicine should be a joint duty of the clinician and the patient. He advocated improving HF education and raising awareness of the necessity of successful treatment among both clinicians and patients as a viable remedy to clinical inertia. Physician-related reasons for non-prescription of guideline-recommended therapy may include a concern of adverse events that might occur during the introduction or dosage escalation of guideline-recommended drugs.Increased awareness among HF experts should result in ways to reduce or abandon clinical inertia. (Verhestraeten, Heggermont and Maris, 2021) and (Pradhan et al., 2024).

On focusing on pharmacist role in HF treatment, they found that a pharmacist-led clinic increased prescription uptake optimal medical therapy (Turgeon et al., 2023).

An observational cross-sectional study was conducted in Southern India. The study concluded that there was gap found in knowledge about (S./V.) combination regarding when dosage needs to be modified and when the drug is contraindicated among physicians and clinical pharmacists. Despite having a good attitude toward S/V, its acceptability has been poor in patients of low socioeconomic status as it is unaffordable (Prakasam et al., 2021).

As noted in the (figure 1.1), the number of cardiologists who prescribed S/V increased to be (6), while the number of cardiologists who didn't prescribed S/V decreased to be only (4). This mean that the clinical pharmacist intervention had positive impact on cardiologists' clinical decisions about the suitable selection of indicated drug, (S./V.) combination. Clinical pharmacist acted as facilitator to prescribe the S/V drug to HF patients. This was involved make face to face interventions with cardiologists in outpatient clinic during patients' examination, make scientific lectures in the attendance of medical staff as pharmacists, nurses and to large extent from cardiologists.

Follow up patients by mobile callings and ensure their adherence to S/V during study period and told their physicians if any adverse effect occurred also support clinical pharmacist role and create state of contentment to his role beside other members of medical team.

Limitations: there are some limitation in this study, first the small size sample for both patients and cardiologists. Second the absence of facilities in cardiac center. Third, the short duration of the study. Recommendation Conduct more concentrated clinical research by PharmD to establish their role in the improvement of the healthcare system.

References

1. Al-Ganmi, A. H. A., Al-Fayyadh, S., Abd Ali, M. B. H., Alotaibi, A. M., Gholizadeh, L., & Perry, L. (2019) 'Medication adherence and predictive factors in patients with cardiovascular disease: A comparison study between Australia and Iraq', Medication

adherence and predictive factors in patients with cardiovascular disease: A comparison study between Australia and Iraq. Collegian, .3),26 ,), pp. 355–366.
2. Egan, T.D. and Orgain, N. (2010) 'Cigarette Smoking Cessation', Essence of Anesthesia Practice E-Book, p. 86. Available at: https://doi.org/10.1016/B978-1-4377-1720-4.00076-5.
3. EL KAFOURY A., M. (2021) 'Safety and Efficacy of Sacubitril/Valsartan Early Initiation in Hospitalized Patients with Heart Failure and Reduced Ejection Fraction', The Medical Journal of Cairo University, 89(9), pp. 2143–2149. Available at: https://doi.org/10.21608/mjcu.2021.203444
4. El-Battrawy, I. et al. (2023) 'The impact of sacubitril/valsartan on outcome in patients suffering from heart failure with a concomitant diabetes mellitus', ESC Heart Failure, 10(2), pp. 943–954. Available at: https://doi.org/10.1002/ehf2.14239.
5. Han, Y. et al. (2023) 'Efficacy and Safety Comparative of Sacubitril/Valsartan vs. Olmesartan in the Treatment of hypertension: A Meta-analysis of RCTs', American Journal of Hypertension, 36(12), pp. 643–650. Available at: https://doi.org/10.1093/ajh/hpad075.
6. Hu, T., Liu, Y. and Lou, Y. (2023) 'Sacubitril–valsartan versus enalapril for the treatment of acute decompensated heart failure in Chinese settings: A cost-effectiveness analysis', Frontiers in Pharmacology, 14. Available at: https://doi.org/10.3389/fphar.2023.925375
7. Ingram, A., Valente, M. and Dzurec, M.A. (2021) 'Evaluating Pharmacist Impact on Guideline-Directed Medical Therapy in Patients With Reduced Ejection Fraction Heart Failure', Journal of Pharmacy Practice, 34(2), pp. 239–246. Available at: https://doi.org/10.1177/0897190019866930
8. Judge, P.K. et al. (2017) 'Randomized multicentre pilot study of sacubitril/valsartan versus irbesartan in patients with chronic kidney disease: United Kingdom Heart and Renal Protection (HARP)- III - Rationale, trial design and baseline data', Nephrology Dialysis Transplantation, 32(12), pp. 2043–2051. Available at: https://doi.org/10.1093/ndt/gfw321
9. Pandey, B.P. et al. (2024) 'Impact of Sacubitril / Valsartan in Improving Home Time for Patients With Heart Failure', 16(11). Available at: https://doi.org/10.7759/cureus.73175.
10. Patil, T. et al. (2022) 'Impact of Pharmacist-Led Heart Failure Clinic on Optimization of Guideline-Directed Medical Therapy (PHARM-HF)', Journal of Cardiovascular Translational Research, 15(6), pp. 1424–1435. Available at: https://doi.org/10.1007/s12265-022-10262-9.
11. Prakasam et al., 2021 'An Assessment of Knowledge, Attitude, Practices of Sacubitril/Valsartan Among Physicians in The Department of Cardiology and Clinical Pharmacists in Southern India', International journal of pharmacy & pharmaceutical research,3(22),pp. 509-520.
12. Prakasam, A.K. et al. (2021) An Assessment of Knowledge, Attitude, Practices of Sacubitril/Valsartan Among Physicians in The Department of Cardiology and Clinical Pharmacists in Southern India An Assessment of Knowledge, Attitude, Practices of Sacubitril. Available at: www.ijppr.humanjournals.com.

13. Proudfoot, C. et al. (2021) 'Real-world effectiveness and safety of sacubitril/valsartan in heart failure: A systematic review', International Journal of Cardiology, 331, pp. 164–171. Available at: https://doi.org/10.1016/j.ijcard.2021.01.061.
14. Rahman, G.A. and Al-Othman, A.A. (2022) 'Clinical characteristics and outcomes of heart failure with preserved, mildly reduced, and reduced ejection fraction: A 6-month follow-up study', Medical Journal of Babylon, 19(2), pp. 265–270. Available at: https://doi.org/10.4103/MJBL.MJBL_26_22.
15. Regitz-Zagrosek, V. (2020) 'Sex and Gender Differences in Heart Failure', International Journal of Heart Failure, 2(3), pp. 157–181. Available at: https://doi.org/10.36628/ijhf.2020.0004.
16. Sakhamuri, N. et al. (2023a) 'Sacubitril/Valsartan in Heart Failure Hospitalization: Two Pills a Day to Keep Hospitalizations Away?', Cureus, 15(4), pp. 1–11. Available at: https://doi.org/10.7759/cureus.37335.
17. Sangaralingham, L.R. et al. (2018) 'Adoption of sacubitril/valsartan for the management of patients with heart failure', Circulation: Heart Failure, 11(2). Available at: https://doi.org/10.1161/CIRCHEARTFAILURE.117.004302
18. Tan, N.Y. et al. (2020) 'Comparative Effectiveness of Sacubitril-Valsartan Versus ACE/ARB Therapy in Heart Failure With Reduced Ejection Fraction', JACC: Heart Failure, 8(1), pp. 43–54. Available at: https://doi.org/10.1016/j.jchf.2019.08.003.
19. Turgeon, R. et al. (2023) 'Cardiovascular Nursing and Allied Professions – Advanced Clinical Practice Evaluation of PHARM-HF , a pharmacist-led heart failure medication titration clinic', 44, pp. 1–2
20. Veltri, K.T. (2019) 'Novel Agent, Sacubitril-Valsartan: Prescribing Patterns and Perceived Barriers to Hospital Formulary Inclusion', Clinical Studies & Medical Case Reports, 6(1), pp. 1–7. Available at: https://doi.org/10.24966/csmc-8801/100062
21. Verhestraeten, C., Heggermont, W.A. and Maris, M. (2021) 'Clinical inertia in the treatment of heart failure: a major issue to tackle', Heart Failure Reviews. Springer, pp. 1359–1370. Available at: https://doi.org/10.1007/s10741-020-09979-z.
22. Zhang, M. et al. (2023a) 'The history and mystery of sacubitril/valsartan: From clinical trial to the real world', Frontiers in Cardiovascular Medicine, 10(March). Available at: https://doi.org/10.3389/fcvm.2023.1102521.
23. Zhang, R. et al. (2022) 'The Efficacy and Safety of Sacubitril/Valsartan in Heart Failure Patients: A Review', Journal of Cardiovascular Pharmacology and Therapeutics. SAGE Publications Ltd. Available at: https://doi.org/10.1177/10742484211058681.