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Research Article

A Study on Patients of Heart Failure with Focus on Management, Extent of Adherence to Treatment Guidelines and Health Related Quality of Life

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Abstract

Introduction: Heart failure is a chronic, progressive condition characterised by low cardiac output and decreased exercise ability. The data on heart failure in India is limited. The pattern of adherence to the ACC/AHA guidelines on treatment of heart failure using medication, as well as the quality of life in these patients has not been recorded in India previously.

Materials and Methods: A cross sectional study with 208 patients attending the cardiology department of a tertiary care hospital was conducted. The use of the 5 primary drug groups for heart failure- Beta blockers, ACEI/ARBs, Diuretics, Mineralocorticoid Receptor Antagonists and Inotropes was recorded and Guideline Adherence Index was calculated (GAI5). The Left Ventricular Dysfunction 36 (LVD36) questionnaire and the Minnesota Living with Heart Failure questionnaire (MLHFQ) were used to record the quality of life in 201 patients.

Results: The GAI5 was found to be 77.435%. There was 95% adherence to prescriptions of Beta blockers and ACEI/ARBs, 77% for Diuretics, 62% for MRAs and 58% for Inotropes. Complete adherence was seen in 78 patients out of 208 (37.5%). The mean score of patients on LVD 36 was 62.84%. The highest frequency of scores was in the range of 65.1% - 70.0%. The mean score on MLHFQ was 64.17 out of 105. The physical and emotional quotients were also calculated. The highest physical score was 37 out of 40 and the highest emotional score 24 out of 25. Most patients scored between 26 - 30 out of 40 on the physical score and between 16 - 20 out of 25 on the emotional score. The highest frequency of scores was in the range of 66-70. A strong correlation was found between the scores of the two questionnaires.

Conclusion: The prescribing pattern of doctors for heart failure in a tertiary care teaching hospital is fairly compliant to the guidelines that have been laid down by the ACC/AHA. A decrease in prescribing of Inotropes such as Digoxin may be due to changes in the guidelines over the years. The scores for the LVD36 questionnaire were high (> 60%) for 121 patients, indicating that the QoL of these patients has significantly suffered due to heart failure. Similarly, the mean score on the MLHFQ for patients was 64.17 out of 105, demonstrating an adversely affected quality of life due to heart failure.

Keywords: *Heart Failure; Treatment Guidelines; Guideline Adherence; Quality of Life*

Abbreviations

LVD36: Left Ventricular Dysfunction 36 Questionnaire; MLHFQ: Minesota Living with Heart Failure questionnaire; NYHA: New York Heart Association; ACC: American College of Cardiology; AHA: American Heart Association; ACEI: Angiotensin Converting Enzyme Inhibitor; ARB: Angiotensin Receptor Blocker; MRA: Mineralocorticoid Receptor Antagonist; BB: Beta blocker; GAI: Guideline Adherence Index; QoL: Quality of Life; HF: Heart Failure

Introduction

Heart failure is a chronic, progressive condition wherein the heart cannot pump enough blood to meet the needs of the body. Heart failure has been divided into 2 main types based on the pathologic changes taking place in the heart, echocardiographic changes and clinical features-Systolic dysfunction and Diastolic dysfunction.

In Asia and specifically the Indian subcontinent the data for heart failure is few and far between. However, the burden of chronic cardiovascular disorders in India is on the rise with rapid urbanization and the epidemiologic transition taking place [1]. Indian patients who have acute coronary syndrome are younger than their western counterparts and arrive at the hospital too late to receive thrombolytic and cardiac reperfusion therapy [2]. As the life expectancy in India continues to increase, we can assume that these factors will eventually lead to increase in burden in chronic heart failure in the Indian subcontinent [1]. Hence there is an urgent need in India to undertake pharmaco-epidemiological studies in heart failure.

Unlike the Western world, the epidemiology of HF is still an unfinished agenda in the developing countries like India where no large studies have been done to explore the burden of HF. This burden is likely to be large, as is already realized by practicing internist and cardiologists, given the fact that India is home to 16% of global population, 25% of the world's coronary heart disease (CHD) burden, 120 million hypertensives, and a large number of individuals with RHD [3].

The challenge is to make quality healthcare services accessible and affordable to a socioeconomically and linguistically diverse population of more than 1.3 billion spread over 3.287 million km^2, with inadequate infrastructure to deliver services and lack of strict quality control measures. Only basic health care facilities are available at most of the primary health centres, which are often understaffed, and their services overstretched. Most of the tertiary healthcare resources are concentrated in the large cities and that too mostly in the big Metropolis. This inequality in healthcare distribution is a major impediment for implementation of universal health care in India [4].

The American College of Cardiology/American Heart Association (ACC/AHA) has in its latest guidelines placed emphasis on the concept of primary prevention of heart failure by appropriate control of risk factors like hypertension, diabetes, and coronary artery disease through evidence based pharmacotherapy, before overt heart failure sets in.

The ACC/AHA/HFSA guideline update gives a Class I recommendation for the clinical strategy of inhibition of the renin-angiotensin system with angiotensin-converting enzyme (ACE) inhibitors, OR angiotensin-receptor blockers (ARBs), OR angiotensin receptor-neprilysin inhibitors (ARNI) in conjunction with evidence-based beta blockers and aldosterone antagonists in selected patients with chronic heart failure with reduced ejection fraction to reduce morbidity and mortality [5].

Even in the developed world, medications are under-used [6]. In the CREATE study published in 2008, it was found that use of key treatments differed by socioeconomic status in the treatment of heart disease: more rich patients than poor patients were given thrombolytics (60.6% vs 52.3%), beta blockers (58.8% vs 49.6%), lipid-lowering drugs (61.2% vs 36.0%), ACE inhibitors or ARBs (63.2% vs 54.1%), percutaneous coronary intervention (15.3% vs 2.0%), and coronary artery bypass graft surgery (7.5% vs 0.7%, $p < 0.0001$ for all comparisons). Mortality was higher for poor patients than for rich patients (8.2% vs 5.5%, $p < 0.0001$). Adjustment for treatments (but not risk factors and baseline characteristics) eliminated this difference in mortality [1]. For the last 2 - 3 decades angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonists (MRAs), ß-adrenergic blockers, and the combination of isosorbide dinitrate and hydralazine, have been the standard of care to improve outcomes in patients with HF and reduced ejection fraction. Sacubitril/valsartan treatment in addition to guideline-directed medical treatment demonstrated a substantial benefit in reducing the primary composite of CV-related death or heart failure hospitalization compared to enalapril in the PARADIGM-HF trial [7].

Hence, it becomes important for the physician to adhere to these standard treatment guidelines to ensure success in therapy. One area this study would like to throw a light upon is to evaluate the extent of adherence of physicians to these ACC/AHA guidelines.

Health related quality of life is defined as the functional effect of an illness and its consequent therapy upon a patient as perceived by the patient. Congestive heart failure is a major health problem with an increasing incidence and a gloomy prognosis that is often accompanied by restricted physical activity and severe complaints in several areas of health-related quality of life [8]. Despite its high prevalence there have been few studies on impact of CHF on health related QOL and these studies are even scarcer in a developing country like ours. One goal of the measurement of HRQOL is to have objective evaluations of how and how much the disease influences patients' life and how patients cope with it.

Advances in the therapy of heart failure (HF) have delayed disease progression and prolonged survival. Maintaining adequate quality of life (QoL) is an important therapeutic objective for patients with advanced heart failure and, for some patients, may take precedence over prolonging life. Achieving good QoL in this context may involve aspects of patient care that lie outside the familiar limits of heart failure treatment [9].

One recent investigation of this issue found correlations between New York Heart Association (NYHA) class and all HRQoL domains. Strikingly, an improvement in disease severity was not always accompanied by an improvement in HRQoL, suggesting that while decompensation of HF may be the factor that precipitates a decline in HRQoL, haemodynamic or arrhythmia-based influences may contribute to its persistence once established [10]. An additional consideration is that HRQoL is not the entirety of QoL. Particularly for patients who sense that the end of life is imminent, 'quality' relates as much to needs fulfilment, which can embrace a very wide range of priorities, such as satisfaction with either the process of care or its effects on symptoms [9].

Clinical practice guidelines have been slowly and inconsistently applied in clinical practice, and certain evidence-based, guideline-driven therapies for heart failure (HF) have been significantly underused. The Asia-Pacific region is very diverse in terms of living standards, ethnicity, and population. However, little is known about the adherence to HF-recommended medication in the follow-up period and its effects on clinical outcomes in patients with HF, especially in Asian countries [11].

Keeping the above in mind, this study was undertaken to assess the socio demographic characteristics, etiology, risk factors, drug use pattern, extent of adherence of prescriptions and evaluate health related quality of life (QOL) in patients of heart failure, evaluate of patients and to determine to ACC/AHA guidelines, 2017.

Materials and Methodology

The present study was done in the cardiology department of a tertiary care teaching hospital of Ahmedabad.

Study design

This cross-sectional study began after obtaining permission form the Institutional Review Board. Study was carried out over a period of 2 months (June and July 2019). The approval of the Head of Department and Hospital Superintendent was taken. Written informed consent of the patient was obtained in their vernacular language.

Consenting patients were given a questionnaire translated into their vernacular language and informed that their participation was entirely voluntary, and they could leave the study at any time with no consequences. All patients confirmed with diagnosis of Heart failure present in the Inpatient and attending the Outpatient department were part of this study. Demographic data such as age, sex, address, socio economic class were recorded in the case record form. Thereafter clinical diagnoses as per NYHA was recorded. History of present illness, history and co morbid illness related to heart failure were noted.

The prescription of the patient including the drug prescribed, dose, frequency and duration of treatment were also noted. Drug utilization pattern was recorded in Case Record form. The patients were categorized as per NYHA and ACC/AHA classification. Adherence to ACC/AHA guidelines for heart failure was also analysed, quantitatively as well as qualitatively.

Statistical analysis

The data analysis was done using the latest SPSS version. P value less than 0.05 was considered statistically significant. Pharmacotherapy of patients was compared to ACC/AHA guidelines 2017.

Guideline Adherence Index 5- GAI 5 was also evaluated for 5 major drug groups of heart failure- ACE Inhibitors/Angiotensin receptor blockers, Beta blockers, Aldosterone antagonists, Diuretics and Inotropes. Each drug group was allotted 20% GAI so given score was calculated out of 20. GAI was calculated as follows [12,13]:

$$\frac{\text{Number of patients using the medication}}{\text{Number of eligible patients}} \times 100$$

Pearson correlation coefficient was used to find out correlation between different variables like NYHA class, number of drugs prescribed per patient etc. Current recommendations of drugs to be prescribed as well as the Level of evidence have been recorded. The guidelines laid down by ACC/AHA give indications for which certain drug groups may be prescribed. These recommendations and the level to which adherence has occurred have been recorded in the results.

Questionnaires

The Left Ventricular Dysfunction 36 (LVD 36) questionnaire is composed of 36 questions. The patient is expected to answer each question with 'true' or 'false'. The total score is derived by converting the number of 'true' answers to a percentage of the total. The worst score is 100% and the best score is 0% [14].

The Minnesota Living with Heart Failure Questionnaire is composed of 21 questions, with two subscales- physical (8 items) and emotional (5 items). The patient is expected to grade each question from 0 to 5. Their judgement must be based on how much their heart condition influenced the specific activity over the last month. The best score is 0 and the worst score is 105 [14].

The inclusion criteria consisted of patients above 18 years of age, diagnosed with heart failure who were willing to give consent and able to comprehend the QoL questionnaires provided.

Results

The study was a cross sectional study, carried out at the cardiology department of a tertiary care hospital. The total number of patients who participated in the study were 208.

Demographic and clinical characteristics

Age

The mean age of the patients was found to be 61 + 11.057 years. The highest frequency of patients was found to be in the age group of 61 - 70 years (70 patients- 33.65%), while the lowest frequency of patients was found to be in the age group of 21 - 30 years (1 patient- 0.480%).

Gender

120 patients were male (57%) and 88 were female (43%).

Co-morbidities

The most common co morbidity was found to be hypertension with 86 patients (41.346%) suffering from the disease. Diabetes was found to be the next most common co morbidity. Other co morbidities were asthma, chronic kidney disease, LV hypertrophy and prior MI.

Family history

The most common familial history was found to be of a myocardial infarction with a 5.97% occurrence, other diseases were hypertension (2%) and diabetes (4.97%).

The patients were classified according to the severity of their symptoms based on the New York Heart Association classification, with NHYA 1 patients having few symptoms and NYHA 4 patients having severe limitations due to symptoms [22].

Most patients (141 patients, 67.78%) belonged to NYHA 2 (stable heart failure) severity followed by NYHA III (49 patients, 23.557%). NYHA 1 had 6 patients (2.88%) and NYHA 4 had 12 patients (5.769%).

Drug prescription pattern

A total of 770 drugs were prescribed to 208 patients. The mean number of cardiovascular drugs prescribed per patient was 3.701(in a range of 1 to 7 drugs per person). Beta blockers were the most frequently prescribed drug group in patients followed by diuretics.

Drug Group	Number of patients	Percentage
Beta blockers	198	95.192%
Diuretics	157	75.480%
Aldosterone antagonists	131	62.980%
ACE Inhibitors	104	50.00%
ARBs	94	45.192%
Ivabradine	42	20.192%
Sacubitril-Valsartan	37	17.788%
Inotropes	7	3.365%

Table 1: *Frequency of major drug classes prescribed (n = 208).*

Beta blockers were prescribed to 198 patients (95%), with Metoprolol being the most prescribed beta blocker (96 patients- 48.48%). Diuretics were the second most prescribed drug group with 157 patients receiving diuretics (75%). The most prescribed diuretic was Furosemide (77 patients- 49.04%). Mineralocorticoid receptor antagonists were prescribed to 131 patients (62.98%), with Spironolactone being the most frequently prescribed MRA (102 patients- 77.86%). ACE inhibitors were prescribed to 104 patients (50.00%), with the most common drug being Ramipril (59 patients- 56.73%). ARBs were prescribed to 94 patients (45.19%), with Losartan being the most prescribed (56 patients- 59.57%).

Other drugs that were also prescribed to these patients include Sacubitril Valsartan with 37 patients (17.78%), Ivabradine with 42 patients (20.19%) and Inotropes with 7 patients (3.36%).

Quality of life questionnaires

Left ventricular dysfunction 36

The average percentage of the scores was found to be 62.84% with the highest frequency in the range of 65.1 - 70.0% (33 patients- 16.417%). The lowest score was 29.6%, while the highest score was 89.3%. The higher the score, the more the quality of life is negatively affected due to Heart failure.

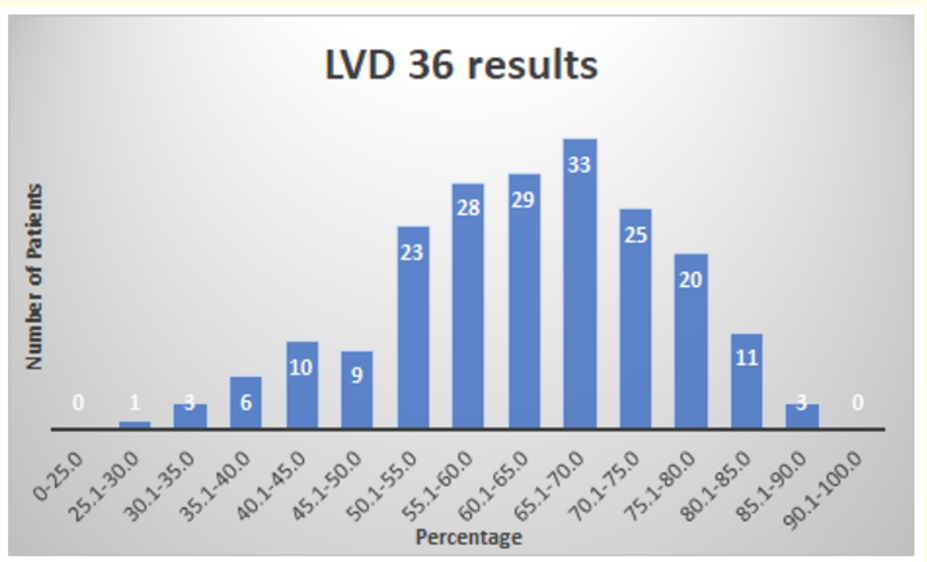

Figure 1: *LVD 36 questionnaire results (n = 201).*

Minnesota living with heart failure

The score was calculated out of 105.

The average score was found to be 64+14 with the highest frequency in the range of 66 - 70 (32 patients- 15.920%). The lowest score was 27, while the highest score was 97. Increasing scores show higher dysfunction and lower quality of life due to heart failure.

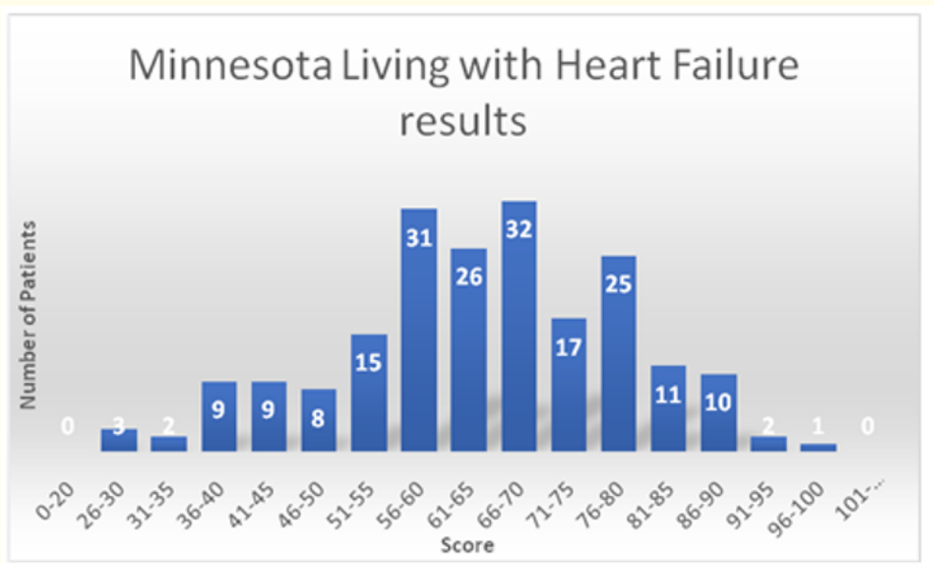

Figure 2: *Minnesota living with heart failure questionnaire results (n = 201).*

The physical score of the Minnesota living with heart failure questionnaire was out of 40 (8 questions). The highest number of patients scored between 26 and 30 (70 patients- 34.825%). The highest score was found to be 37 out of 40 with 9 patients (4.447%). The lowest score was found to be 8 out of 40 with 1 patient (0.497%).

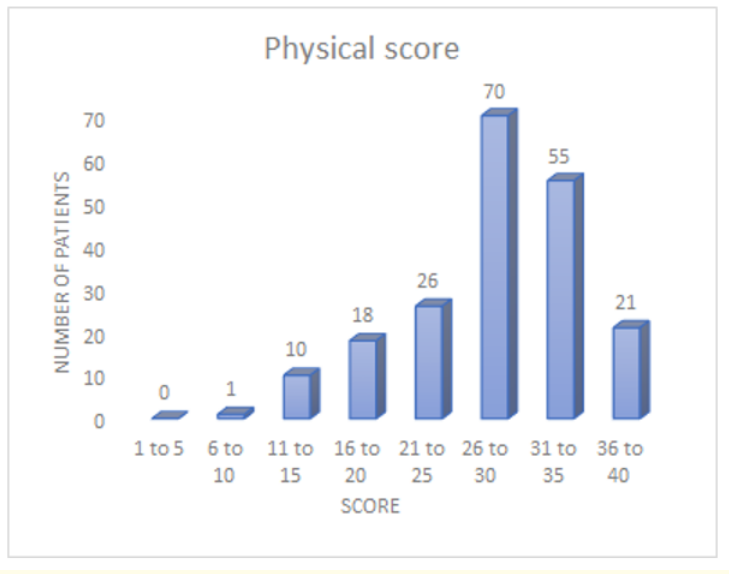

Figure 3: *Physical score on Minnesota living with heart failure questionnaire (n = 201).*

The emotional score of the Minnesota living with heart failure questionnaire is scored out of 25 (5 questions). The highest number of patients scored between 16 and 20 out of 25 (98 patients- 48.756%). The lowest score was found to be 8 out of 25 with 1 patient (0.497%). The highest score was found to be 24 with 8 patients (3.98%).

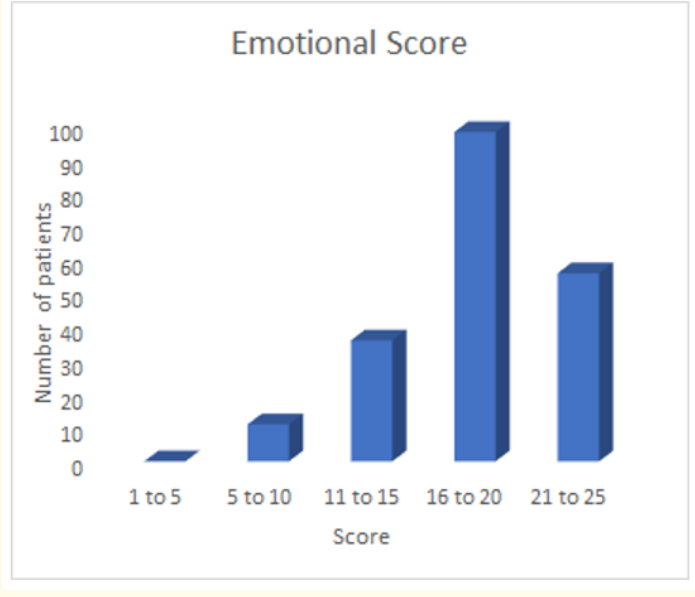

Figure 4: *Emotional score on Minnesota living with heart failure questionnaire (n = 201).*

Drug group	Recommendations	COR	LOE	No. of patients	% of patients
Diuretics	In patients with HFrEF with fluid retention	I	C	157	75.48%
ACE Inhibitors	All patients of HFrEF	IIa	A	104	50%
ARBs	Patients intolerant to ACE inhibitors	I	A	0	0
	Alternatives to ACE inhibitors as first line therapy	IIa	A	94	45.192%
	In persistently symptomatic patients with HFrEF on GDMT	IIb	A	0	0
	Routine combined use of ACEI, ARB and aldosterone antagonist is potentially harmful	III-harm	C	0	0
Beta blockers	Use of 1 of 4 beta blockers proven to reduce mortality is recommended for all stable patients	I	A	198	95.192%
Aldosterone antagonists	Patients of NYHA class II-IV who have LVEF< 35%	I	A	131	62.98%
	Patients following acute MI with LVEF < 40% with symptoms of HF or DM	I	B	0	0
	Inappropriate use of aldosterone antagonists may be harmful	III-harm	B	0	0
Inotropes	Beneficial in patients with Heart Failure with reduced ejection fraction	IIa	B	7	3.365%
Sacubitril-Valsartan	Patients of NYHA II, III with adequate control of BP	I	A	37	17.788%
Ivabradine	Beneficial in NYHA II-III on maximal dose of beta blocker	IIa	B	42	20.192%

Table 2: *Guideline adherence for drug prescriptions.*

COR: Current Recommendation; LOE: Level of Evidence.

Drugs	ACEI/ARB	Diuretics	Aldosterone antagonists	Beta blockers	Inotropes
Adherence	198	157	131	198	7
Nonadherence	10	45	44	10	5
Total	208	202	175	208	12
% Adherence	95.192%	77.72%	62.98%	95.192%	58.333%
Score out of 20	19.03	15.544	14.971	19.03	11.666

Table 3: *Frequency of drug prescriptions in heart failure.*

GAI 5- 77.435% The guideline adherence index was calculated to be 77.435. This signifies that 77% of the drugs that were prescribed to the patients were adherent to the guidelines as laid down by the ACC/AHA in their 2017 update.

Some patients have overlapping omitted drug groups.

A study of age, scores of LVD 36 and Minnesota Living with Heart Failure with the GAI showed many significant correlations.

Complete adherence	78 Patients- 37.5%
Beta blocker omitted	10 Patients- 4.807%
Diuretic omitted	45 Patients- 21.634%
ACEI/ARB omitted	10 Patients- 4.807%
Aldosterone antagonist omitted	44 Patients- 21.153%
Inotropes omitted	5 Patients- 2.403%
Sacubitril-Valsartan omitted	23 Patients- 11.057%
Ivabradine omitted	28 Patients- 13.461%

Table 4: *Adherence of drugs is calculated according to the number of patients who need the drug group. Adherence to the 2017 guidelines by the ACC/AHA.*

Gender			Age	LVD36	MLHFQ	GAI	Emotional score	Physical score
Female	Age	Pearson Correlation	1	.516**	.529**	.267*	.476**	.380**
		Sig. (2-tailed)		.000	.000	.012	.000	.000
		N	87	85	85	87	85	85
	LVD36	Pearson Correlation	.516**	1	.922**	.434**	.794**	.819**
		Sig. (2-tailed)	.000		.000	.000	.000	.000
		N	85	85	85	85	85	85
	MLHFQ	Pearson Correlation	.529**	.922**	1	.362**	.885**	.873**
		Sig. (2-tailed)	.000	.000		.001	.000	.000
		N	85	85	85	85	85	85
	GAI	Pearson Correlation	.267*	.434**	.362**	1	.337**	.266*
		Sig. (2-tailed)	.012	.000	.001		.002	.014
		N	87	85	85	87	85	85
	Emotional score	Pearson Correlation	.476**	.794**	.885**	.337**	1	.792**
		Sig. (2-tailed)	.000	.000	.000	.002		.000
		N	85	85	85	85	85	85
	Physical score	Pearson Correlation	.380**	.819**	.873**	.266*	.792**	1
		Sig. (2-tailed)	.000	.000	.000	.014	.000	
		N	85	85	85	85	85	85

Table 5: *The correlations between the guideline adherence index, and the scores of the LVD36 and MLHFQ in females.*

The table above shows that females have a correlation between the GAI and the scores of both questionnaires (0.434 with LVD36 and 0.362 with MLHFQ). There is also a correlation found between the scores of the two questionnaires (0.922) which means that the increase in score of LVD36 is followed by an increase in the score in MLHFQ- that is, an increase in the severity of decreasing quality of life. A correlation was also found in the scores of the emotional and physical components of the MLHFQ questionnaire (0.792), which means that a decrease in the physical quality of life is accompanied by a decrease in the emotional quality of life as well.

Gender			Age	LVD36	MLHFQ	GAI	Emotional score	Physical score
Male	Age	Pearson Correlation	1	.492**	.496**	-.054	.401**	.427**
		Sig. (2-tailed)		.000	.000	.556	.000	.000
		N	120	115	115	120	115	115
	LVD36	Pearson Correlation	.492**	1	.934**	.106	.852**	.855**
		Sig. (2-tailed)	.000		.000	.261	.000	.000
		N	115	115	115	115	115	115
	MLHFQ	Pearson Correlation	.496**	.934**	1	.095	.910**	.903**
		Sig. (2-tailed)	.000	.000		.313	.000	.000
		N	115	115	115	115	115	115
	GAI	Pearson Correlation	-.054	.106	.095	1	.142	.069
		Sig. (2-tailed)	.556	.261	.313		.129	.463
		N	120	115	115	120	115	115
	Emotionalscore	Pearson Correlation	.401**	.852**	.910**	.142	1	.854**
		Sig. (2-tailed)	.000	.000	.000	.129		.000
		N	115	115	115	115	115	115
	Physicalscore	Pearson Correlation	.427**	.855**	.903**	.069	.854**	1
		Sig. (2-tailed)	.000	.000	.000	.463	.000	
		N	115	115	115	115	115	115

Table 6: *The correlations between the guideline adherence index, and the scores of the LVD36 and MLHFQ in males.*

The table above shows that males have a correlation between the GAI and the scores of both questionnaires (0.106 with LVD36 and 0.95 with MLHFQ). There is also a correlation found between the scores of the two questionnaires (0.934) which means that the increase in score of LVD36 is followed by an increase in the score in MLHFQ- that is, an increase in the severity of decreasing quality of life. A correlation was also found in the scores of the emotional and physical components of the MLHFQ questionnaire (0.854s), which means that a decrease in the physical quality of life is accompanied by a decrease in the emotional quality of life as well.

Discussion

Heart failure is considered an epidemic disease in the modern world affecting approximately 1% to 2% of adult population. It presents a multifactorial, systemic disease, in which after cardiac injury- structural, neurohumoral, cellular, and molecular mechanisms are activated and act as a network to maintain physiological functioning. The most important, outcome determining factor in heart failure is its constant progression. Constant optimizing of therapeutic regimes, novel targets, and fine regulation of these processes try to keep these compensatory mechanisms in a physiological range [15]. Heart failure is a major public health problem associated with significant hospital admission rates, mortality, and costly health care expenditures, despite advances in the treatment and management of heart failure and heart failure-related risk factors [16]. In Asia-Pacific regions, HF is associated with a significant socioeconomic burden and high rates of hospital admission.

Epidemiological data that could help to improve management approaches to address this burden in Asia-Pacific regions are limited but suggest patients with HF in the Asia-Pacific are younger and have more severe signs and symptoms of HF than those of Western coun-

tries. However, local guidelines are based largely on the European Society of Cardiology and American College of Cardiology Foundation/ American Heart Association guidelines, which draw their evidence from studies where Western patients form the major demographic and patients from the Asia-Pacific region are under-represented [17].

The average age of patients in our study was found to be 61 + 11.057 years which is lower than the mean age found in other studies conducted over the years. In the ADHERE International-Asia Pacific, the patients registered from the eight Asian-Pacific countries between 2006 and 2008 were relatively younger than those in Western countries, with a median age of 67 years, ranging from 53 years in the Philippines to 77 years in Hong Kong, Taiwan, and Australia [19]. Although available information is limited in South Asia, Khan., *et al.* reported that the mean age of HF patients was 54.4 years in Punjab Institute of Cardiology Lahore in Pakistan in 2008 [20], lower than what has been recorded in our study. However, in small study conducted in North India, the mean age of patients suffering from heart failure was found to be 61.2 years [21]. This difference in age of presentation could be because in a developing world like ours, people seek medical management later, when symptoms become predominant. In the West, due to a higher literacy rate, a better health care providing system and better economy drugs modifying progression of HF are started as soon as the risk factors are identified.

Treatment and management of heart failure in South Asia is varied due to wide differences in availability of drugs as well as the cost of treatment. In Asia, the most commonly used medication during hospitalization and/or at discharge were diuretics, followed by renin-angiotensin system (RAS) inhibitors, including ACE inhibitors and ARBs, and beta-blockers, although the prevalence of treatment with beta-blockers varied widely between 25.4% and 49% [22]. In the ASIAN-HF study, it was found that China had the lowest uptake for ACE inhibitors or ARBs (286 [60%] of 477) but had the highest uptake for MRAs (372 [78%] of 477).

Indonesia had the highest uptake for ACE inhibitors or ARBs (236 [87%] of 272) and the lowest uptake of β blockers (167 [61%] of 272). The guideline-recommended combination of ACE inhibitors or ARB and β blockers was prescribed in only 2914 (55%) of the overall ASIAN-HF cohort (5276). The high-income countries-for example, Singapore (757 [71%] of 1066), Hong Kong (35 [70%] of 50), Korea (207 [65%] of 317), and Japan (340 [63%] of 540), but not Taiwan (127 [46%] of 274)-were more likely to prescribe the dual first-line medications than were lower income countries ($p < 0.001$). In China, however, 317 (66%) of 477 patients received the combination therapy of β blockers with MRA [23].

The prevalence of beta blocker prescribing is low in Asian countries which is not positive with respect to the treatment of heart failure. Guidelines direct that Beta blockers should be used in all grades of HF except acute decompensated stage unless contraindicated.

In contrast to other studies, our study found that 95% (198 out of 208) of patients were prescribed beta blockers. Metoprolol, a relatively selective beta1 blocker is devoid of intrinsic sympathomimetic activity and possesses weak membrane stabilising activity(46) and thus may have been prescribed more as compared to the other cardio selective beta blockers due to its comparatively milder adverse effects, as well as its use as a sustained release formulation. The beta blockers used primarily were Metoprolol (96 patients), Bisoprolol (51 patients), Carvedilol (33 patients) and Nebivolol (18 patients). These beta blockers have been found to have cardioprotective action. Due to their anti-ischemic and anti-arrhythmic effects, β-blockers (BBs) reduce mortality in patients with acute myocardial infarction (AMI) and heart failure [24]. Physicians might be sceptical regarding the use of beta blockers, since it itself is a cardio-depressant drug. This could be one of the reasons for underutilisation of beta blockers. The benefits of use of beta blockers in HF outweigh their risks. In a recent review to determine the effects of beta blockers, multiple studies investigating beta blockers were examined. A pooled analysis indicated a reduction in cardiovascular mortality [25]. The ACC/AHA guidelines state that a beta blocker must be added to the drug regime for patients of NYHA classes I-IV, unless contraindications are present [26].

ACE inhibitors or ARBs are indicated in all patients of NYHA class I-IV. ARBs may be substituted for ACEI in the case of intolerable adverse effects. As has been indicated by the ACC/AHA guidelines these two classes of drugs must not be prescribed together, as no benefit

has been found of this drug combination. Over and above, this combination can cause more chances of angioedema and renal side effects. Our study did not find any prescription with both an ACEI and ARB prescribed together.

Our study found that 50% (104 patients) were prescribed ACE inhibitors. The drugs used were Ramipril (59 patients), Perindopril (27 patients) and Enalapril (18 patients). ACEI have been shown in many studies to attenuate ventricular remodelling and improve ventricular function in patients with HF [27]. ACEI can also inhibit ventricular remodelling by actions at a cellular level, specifically by limiting cardiac hypertrophy and myocardial fibrosis, while also attenuating cardiomyocyte apoptosis [28]. In addition to the ACE dependent pathway of production of angiotensin II, other ACE independent pathways also function, especially in the heart and kidney to slowly produce angiotensin II from angiotensin I. A heptapeptide may also be produced from angiotensin I or II by action of ACE 2, which produces vasodilation and anti-ischemic effects. ACE inhibitors do not block ACE 2. A comparison of the different ACE inhibitors showed that a larger average decrease in plasma ACE activity was achieved with ramipril over all dosages (71%) compared with that for enalapril (48%), suggesting that ramipril has greater ACE inhibition in the circulation [29].

45.192% (94 patients) were prescribed ARBs in our study. The drugs used were Losartan (56 patients), Valsartan (25 patients) and Telmisartan (13 patients). Blockade of the AT1-receptor, with agents such as candesartan, produces more specific and, more complete blockade of the major negative cardiovascular effects of angiotensin II than is possible using ACE inhibitors, whilst maintaining placebo-like tolerability. Furthermore, AT1-receptor blockade leads to increased stimulation of the angiotensin II type 2 (AT2) receptor, which has favourable cardiovascular effects [30].

Mineralocorticoid receptor antagonists (MRA) are prescribed in heart failure as they provide mortality benefit. 62.98% (131 patients) in our study received MRAs. The drugs used in this study were Spironolactone (102 patients) and Eplerenone (29 patients). The RALES study found that treatment with spironolactone reduced the risk of death from all causes, death from cardiac causes, hospitalization for cardiac causes, and the combined end point of death from cardiac causes or hospitalization for cardiac causes among patients who had severe heart failure as a result of left ventricular systolic dysfunction and who were receiving standard therapy including an ACE inhibitor. Spironolactone also improved the symptoms of heart failure, as measured by changes in the NYHA functional class [31]. HF is a state of secondary hyperaldosteronism. Aldosterone itself is an independent mediator of fibrotic changes in the myocardium and sodium and water retention. Its use in HF as a weak diuretic along with loop diuretics is undermines its importance in HF.

Neprilysin inhibitors is another drug group that has been recently added to control heart failure. The drug used is a combination of Sacubitril-Valsartan. 14.92% (30 patients) were prescribed Sacubitril-Valsartan in our study. These patients were diagnosed as NYHA III and IV. All patients of NYHA IV received this prescription. A few NYHA III patients were not given this combination. Upon oral administration, sacubitril/valsartan dissociates and sacubitril is converted to its active metabolite sacubitrilat. Sacubitrilat and valsartan have half-lives of approximately 12 and 9.9 hours respectively and given twice daily ensure sustained neprilysin and RAAS inhibition over the 24-hour period [32]. A recent study on the effects of the combination of Sacubitril-Valsartan on exercise tolerance showed an improvement of LVEF and a decrease of left ventricular end-systolic volume at follow-up [33].

Diuretics have been used in heart failure to ameliorate the symptoms of fluid overload. 75.48% (157 patients) were prescribed diuretics in our study. The drugs used were Furosemide (77 patients), Torsemide (55 patients), Hydrochlorothiazide (16 patients) and Chlorthalidone (9 patients). They effectively reduce blood pressure, while at the same time decreasing the morbidity and mortality associated with hypertension [34]. Diuretics are the only drugs able to reduce fluid retention in CHF, although they are unable to maintain clinical stability for long periods of time when used in isolation [35].

The most common use of inotropes is among hospitalized patients with acute decompensated heart failure, with reduced left ventricular ejection fraction and with signs of end-organ dysfunction in the setting of a low cardiac output. Inotropes can be used in patients with

severe systolic heart failure awaiting heart transplant to maintain hemodynamic stability, or as a bridge to decision [36]. Our study found that 7 patients in severe heart failure (NYHA IV) were prescribed inotropes. Digoxin was prescribed to 2 of these patients, and Milrinone to 5 patients.

Digoxin is one of the positive inotropic agents that improve hemodynamics and do not have a deteriorating effect on blood pressure or heart rate. Digoxin plays a role in suppressing the neurohormonal activation which is helpful in chronic systolic heart failure patients and can be used for long-term therapy [37].

Although Digoxin in the only available oral inotropic agent and improves the symptoms of HF, it is also a drug with a narrow therapeutic index and a tendency to cause different types of rhythm disturbances in the heart. No study has shown evidence of decreasing progression of HF with the use of digoxin.

Milrinone is a widely used positive inotropic agent in patients with end-stage heart failure and cardiogenic shock [38]. Milrinone also reduces left ventricular filling pressure in chronic heart failure patients. It is a bipyridine and inhibits the phosphodiesterase-3 intracellular enzyme, thus preventing the degradation of cyclic adenosine monophosphate (cAMP) within the cell. Increased cAMP levels increase activation of protein kinase A, which in turn leads to more influx of calcium into the cell. Increase in intracellular calcium stimulates myocardial contractility. This mechanism of action makes use of milrinone preferable in advanced heart failure patients who are on β blockers as part of optimal medical therapy [36].

Ivabradine is a heart-rate-lowering agent that acts by selectively and specifically inhibiting the cardiac pacemaker current (If), a mixed sodium-potassium inward current that controls the spontaneous diastolic depolarization in the sinoatrial (SA) node and hence regulates the heart rate [39]. The cardiac effects of ivabradine are specific to the SA node [40].

Diabetes and heart failure are closely related: patients with diabetes have an increased risk of developing heart failure and those with heart failure are at higher risk of developing diabetes [41]. In patients with diabetes mellitus, advanced age, duration of the disease, insulin use, presence of coronary artery disease and elevated serum creatinine are all independent risk factors for the development of heart failure [22]. Our study recorded 76 patients who were suffering from type 2 diabetes and HF.

In the Framingham Heart Study cohort in a total population of 5,143 subjects, hypertension antedated the development of HF in 91% of all newly diagnosed HF patients during up to 20 years of follow-up (mean 14.1 years) [42]. In most hypertensive patients, LV diastolic dysfunction is the first discernible manifestation of heart disease. Cardiac remodeling to a predominant pressure overload consists of concentric LV hypertrophy (increase in cardiac mass at the expense of chamber volume) [46]. Our study recorded 86 patients with hypertension who suffered from HF.

Heart failure (HF) is a common complication of myocardial infarction (MI), which may develop early or late and persist, resolve or recur [43]. An MI dramatically increases the chance to contract HF in later life. Our study recorded 13 patients with prior MI's who suffered from HF.

The quality of life in patients of HF has historically been low. There have been no large-scale studies to determine the quality of life of Indian patients of heart failure. A small study conducted on 50 patients was done in Tamil Nadu, which found a slight correlation between increasing age and worsening quality of life [44]. Improvement in treatment strategies has led to an increase in the life expectancy of these patients.

Previous studies have shown that HRQOL in CHF patients is predominantly influenced by New York Heart Association (NYHA) class, indicating that those with higher NYHA class have poorer HRQOL [46]. MLHFQ measures the physical (eight items; range 0-40) and emo-

tional (five items; range 0-25) dimensions of HRQOL, in addition to the whole score out of 105 [45]. Our study found that patients with a higher emotional and physical scores corresponded to higher NYHA classes, as well as to increasing LVD 36 scores. The average emotional score was found to be 18 out of 25, while the average physical score was found to be 28 out of 40.

7 patients out of 208 patients in our study were unable to fill in the questionnaires that were provided due to advanced HF. Their prescriptions were recorded and have been incorporated in the results. These patients were classified in NYHA IV.

A correlation was found in female patients between the GAI and scores of the LVD36 (0.434) and MLHFQ (0.362). The correlation in males between the GAI and the questionnaires was- LVD36 (0.106) MLFHQ (0.95).

Strengths of the Study

The major strengths of the study include the fact that it was a prospective study done on patients diagnosed and living with heart failure in a developing country like India. The major focus of this study was the evaluation of adherence of our prescribers to the existing standardised guidelines; no other Indian study has accomplished this goal. Data on quality of life of patients is lacking for Indian patients suffering from chronic diseases. Heart failure fits into the class of diseases which are chronic and can affect the quality of life of patients adversely. This study was an attempt to record the quality of life as well as the adherence to treatment guidelines in Indian patients. Through evaluation of the prescription pattern we could analyse the extent of usage and conventional drugs for heart failure (such as digoxin and vasodilators) in comparison to the use of combinations such as Sacubitril-Valsartan and Ivabradine.

Limitations of the Study

This study was completed under time constraints, and so only 208 patients could be evaluated under this study. This study was a cross sectional study, and hence we were unable to evaluate the changes in the quality of life of patients with respect to drug therapy. A future study can be planned to evaluate the quality of life on follow up or subsequent visits.

Conclusion

Heart failure is a disease that affects millions over the world. In India, this disease has an earlier presentation and more dire results, with higher mortality seen in younger patients. The health care in our country is inadequate for the masses of our population. Presentation of symptoms heralding heart failure are often ignored by patients, leading to full blown heart failure presenting earlier in these patients, increasing the load on the overburdened health care facilities in India.

The relatively lower socio-economic status of patients also has many effects on the care of patients. As patients are unable to afford medication that is more effective, they are stabilised on generic medicines, or on sub-standard therapy. As seen in this study, some patients received fewer medicines than what were needed for their disease, and as such, their quality of life suffered.

Nevertheless, a very sincere effort to adhere to guidelines laid down by ACC/AHA has been noted in our study. No patients were prescribed an ACE inhibitor and ARB together, as indicated in the new guidelines. Judicious use of beta blockers was also noted, with most patients receiving some beta blocker. This exceeded the norm, as other studies show less use of beta blockers.

However, it was also noted that a few patients received a thiazide diuretic alone. It has been shown that a thiazide diuretic alone in HF has no role, and must be combined with loop diuretics if they are to be used for HF.

The use of inotropes in outpatients recorded in this study is low. This may be because no mortality benefit has been noticed in use of inotropes. Hence, therapeutic practice has shifted form drugs that provide just symptomatic relief to drugs which reverse or halt the progression of HF.

The use of drugs such as Ivabradine and Sacubitril-Valsartan is gratifying, as these drugs have been shown to have fewer mortalities, as well as better disease modifying effects.

A gradual decrease in the quality of life of patients has been noticed with increasing age. This may be due to the worsening of heart failure with age, as well as with the increased load on patients as well as their families. The emotional quotient in the Minnesota Living with Heart Failure questionnaire shows that patients have higher scores (worsening quality of life) with increasing age as well as worsening stages of HF.

The quality of life of patients of heart failure in India has never been recorded in such a manner, with the LVD36 and MLHFQ questionnaires. Likewise, the prescription pattern of patients of heart failure patients has not been recorded for Indian patients. This is the first Indian study to calculate GAI5 for patients of heart failure in India.

Summary

The purpose of this study was to record the adherence of prescribers to guidelines laid down by ACC/AHA as well as to record the demographics of patients suffering from heart failure. This study also recorded the quality of life of patients of Heart failure. The mean age of patients in our study was found to be 61 years. The severity of heart failure according to NYHA classification was found to increase with increase in age. Comorbidities such as hypertension and diabetes were common, with many patients suffering from both. Prior MI was also a significant finding in patients.

The drug prescription pattern showed judicious use of beta blockers as well as ACEI/ARBs. The use of inotropes such as digoxin was found to be low, which exhibits a pattern of shift to use of drugs that have mortality benefit, as compared to drugs that only provide symptom relief. The use of Ivabradine as well as the combination of Sacubitril-Valsartan in worsening stages of heart failure is heartening, as these drugs have proven to be beneficial to patients suffering from heart failure.

The Guideline Adherence Index was found to be 77.435%. This value reflects the judicious use of drugs in patients warranting the use of certain drugs according to the severity of their heart failure. 5 drug groups were recorded for the GAI- Beta blockers, ACEI/ARBs, Diuretics, Mineralocorticoid receptor antagonists and Inotropes.

The quality of life of patients was recorded using 2 questionnaires to be thorough. The LVD 36 questionnaire and the Minnesota living with Heart failure questionnaires were used. The emotional and physical subdivisions of the Minnesota living with heart failure questionnaire were also recorded. Significant correlations were found in the scores of both questionnaires, with an increase in the score of one questionnaire being followed be an increase in the score of the other questionnaire as well.

Significant correlations were found between values of GAI and the scores of the questionnaires, with an increase in the GAI followed by an increase in the scores of both questionnaires.

Our study is the first of its kind to be conducted in India, where quality of life of patients as well as the drug prescription adherence pattern has been recorded for more than 200 patients.

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