



Original Article

National Heart Failure Registry, India: Design and methods

Sivadasanpillai Harikrishnan ^{a,*}, Ajay Bahl ^b, Ambuj Roy ^c, Animesh Mishra ^d, Jayesh Prajapati ^e, Manjunath Cholenahally Nanjappa ^f, Rishi Sethi ^g, Santanu Guha ^h, Santhosh Satheesh ⁱ, Manas Chacko ^a, Sanjay Ganapathi ^a, Panniyamakal Jeemon ^a

^a Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum, India

^b Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

^c All India Institute of Medical Sciences (AIIMS), New Delhi, India

^d North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong, India

^e UN Mehta Institute of Cardiology and Research Centre (UNMICRC), Ahmedabad, India

^f Sri Jayadeva Institute of Cardiovascular Sciences and Research (SJICR), Bangalore, India

^g King George's Medical University (KGMU), Lucknow, India

^h Medical College Hospital (MCH), Kolkata, India

ⁱ Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry, India



ARTICLE INFO

Article history:

Received 11 September 2019

Accepted 24 December 2019

Available online 3 January 2020

Keywords:

Heart failure

Registry

India

ABSTRACT

Objective: Heart failure (HF) has emerged as a global public health problem that affects both low and high-income countries. The high HF burden and the need for resource-intensive treatments often lead to health system crisis in resource-poor settings. Data on prevailing practice patterns and long-term clinical outcomes of HF are scarce from the low and middle-income countries. Nationally representative HF data from India are not available.

Methods: The National Heart Failure Registry (NHFR) is a multicentric, hospital-based registry of HF patients from 53 centers across India. Consecutive patients admitted with the diagnosis of acute decompensated HF satisfying the European Society of Cardiology (ESC) 2016 criteria will be enrolled into the registry from January 2019 to December 2019. Each participating center is expected to contribute 200 patients into the registry (i.e., more than 10,000 HF patients from India). We are collecting demographics, clinical, laboratory, imaging, and other diagnostic data at baseline from all registered patients in the registry by using a structured document. Additionally, we are collecting the details of treatment practices and the usage of guideline-directed therapy from all participants. We intend to obtain the in-hospital, 3-months, 6-months and one-year outcome data on mortality, cause of death, and repeated hospitalization events.

Conclusions: In summary, NHFR will be the first nationally representative HF registry aimed at providing crucial information on prevailing etiology, distribution and current practices in the management of HF.

© 2020 Cardiological Society of India. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Background

Heart failure (HF) has emerged as a global pandemic¹ with 26 million people affected and an estimated health expenditure of US\$31 billion worldwide.¹ The hospital-based registries of HF provide key information on patient characteristics, prevailing treatment practices, and survival data.¹ Although the prognosis of HF patients with reduced ejection fraction (HFrEF) has improved due to the availability of evidence-based therapies, the readmission rates, and subsequent mortality, remain unchanged in the last two decades.¹ Additionally, the proportion of HF patients with preserved ejection fraction (HFpEF) is rising rapidly, and their prognosis is equally bad.¹

* Corresponding author. Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum, 695011, India.

E-mail addresses: drharikrishnan@outlook.com (S. Harikrishnan), drajaybahl@hotmail.com (A. Bahl), drambujroy@gmail.com (A. Roy), animesh.shillong@gmail.com (A. Mishra), drjsprajapati@yahoo.co.in (J. Prajapati), drcnmanjunath@gmail.com (M.C. Nanjappa), drrishisethi1@gmail.com (R. Sethi), guhas55@gmail.com (S. Guha), drsanthoshatheesh@gmail.com (S. Satheesh), manaschacko@outlook.com (M. Chacko), drsanjayganesh@gmail.com (S. Ganapathi), pjeemon@gmail.com (P. Jeemon).

The HF burden in a low- and middle-income country (LMIC) settings is unique and different from the pattern in high-income countries. The “double burden” of HF is well documented in LMIC. For example, the persistence of the “preceding era” diseases like rheumatic heart disease and untreated congenital heart diseases along with “modern era” conditions, such as ischemic heart diseases, are propelling the burden of HF in LMIC.² However, the description of the HF burden in LMIC is beleaguered by poor availability and quality of data.

Sparse clinical and demographic data on HF is a concern in India. The major HF registries reported in India are the “Trivandrum Heart Failure Registry,” which enrolled 1205 patients (THFR)^{3–5} and the INTER-CHF registry with 858 Indian patients.⁶ The ongoing Kerala HF registry also has completed the recruitment of 7500 patients.⁷ Another registry from a hospital in the National capital region included over 6000 HFrEF patients.⁸ The available data from these registries show that HF patients in India are younger by 10-years, and the majority of the burden lies below 65years of age, as compared to the patients from high-income countries. However, none of them represents data from different geographical regions in India. Significant disparities in health burden are well documented between the different states and regions of India.⁹ To bridge this gap and to collect representative data, we initiated the National Heart Failure Registry (NHFR). The NHFR is financially supported by the Indian Council of Medical Research (ICMR).

2. Methodology

2.1. Objectives of the National Heart Failure Registry (NHFR)

The objectives of the study are (i) to establish a representative national HF registry in India and study the demographic characteristics, etiology, and modes of presentation of patients admitted with acute decompensated heart failure, (ii) to study the current practices in management of HF, including diagnostic and treatment patterns, (iii) to assess the short-term and long-term mortality outcomes of HF in India, and (iv) to develop a risk prediction/stratification algorithm for survival of HF patients in India.

2.2. Design, sampling, and participating centers

NHFR is a registry of acute decompensated HF patients admitted to the participating hospitals in India during the study period from January 2019 to December 2019. Initially, we identified nine leading cardiology centers as nodal centers across different regions of India. The nodal centers were premier, government-funded medical institutes in the public domain, with adequate experience and expertise in conducting epidemiological studies. The Principal Investigator (PI), who is an experienced researcher and cardiologist at the nodal center, further identified five hospitals (called participating centers), which cater to in-patients with HF in their respective regions. We ensured the representation from different geographical and ethnic diversities in the region while selecting the participating centers.

A total of 53 hospitals from 24 states and 2 union territories took part in the NHFR. The Nodal centers and the five participating centers under each of them were asked to register all consecutive acute decompensated HF patients admitted in their respective hospitals during the study period. We used the European Society of Cardiology (ESC) 2016 criteria for HF diagnosis. Each center was asked to register 200 consecutive patients with the intention to collect data from >10,000 HF patients during the study period. Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum (SCTIMST), acted as the national coordinating center for the NHFR. The details of the nine nodal centers are given in Fig. 1

and their distribution is presented in Fig. 2. The detailed listing of all participating centers is given in Appendix A.

2.3. Definition, inclusion, and exclusion criteria

We used the European Society of Cardiology (ESC) 2016 guidelines¹⁰ for the diagnosis of HF. The inclusion criteria of NHFR enrolment are given below. Patients who had septicemia as their primary diagnosis were excluded from the study.

- 1) Age ≥ 18 years
- 2) Indian citizen
- 3) Confirmation of heart failure

Symptoms and signs of heart failure along with LVEF <40% for heart failure with reduced ejection fraction (HFrEF).

Or.

Symptoms and signs of heart failure along with LVEF 40%–49% for heart failure with mid-range ejection fraction (HFmrEF).¹⁰

Or.

Symptoms and signs along with LVEF >50% and structural heart disease by echo (LVH or LAE) or LV diastolic dysfunction¹¹ for Heart failure with preserved ejection fraction (HFpEF).

Or.

Isolated right heart failure with symptoms and signs.

2.4. Study tool

The study questionnaire (Appendix B) was developed based on the inputs of all investigators in the participating hospitals. The questionnaire was finalized at a national meeting held at ICMR headquarters in New Delhi, before the initiation of the study. Data on demographic characteristics, etiology of HF, medical history, medications, clinical presentation, in-hospital diagnostics, and treatments are collected using the study questionnaire. Initially, the data entry was done in printed paper proforma. Later, an online data entry platform was introduced with provisions for a web application and an Android application. The Android version was developed for data entry with an offline feature. The data were entered into a tablet computer via the Android application or via the web application. The NHFR web server collected data from both data entry platforms and stored them in an encrypted format. The necessary backup of the database is being done every day in the evening (5 PM) to protect the data. The data were protected for privacy with all standard precautions. All the investigators were provided with a username and password for data entry. We have given a unique identification number to all enrolled patients so that they were further identified only by that number. As a quality measure, we developed and circulated a document on the standard operating procedure (SOP) to each participating center (Appendix C).

2.5. Longitudinal follow-up

All the patients enrolled in NHFR are actively followed-up for a minimum period of one year from registration. During the follow-up period, we will collect data at 3-months, 6-months, and one-year time points (Fig. 3). The follow-up data will be either collected during the clinic visits or by conducting telephone calls. Data related to repeated hospitalization, mortality, and cause of death will be collected either directly from the patient or their immediate family members. The date of any of the above-mentioned event will also be collected and recorded as part of the study. A structured questionnaire is used for follow-up data collection (Appendix B).

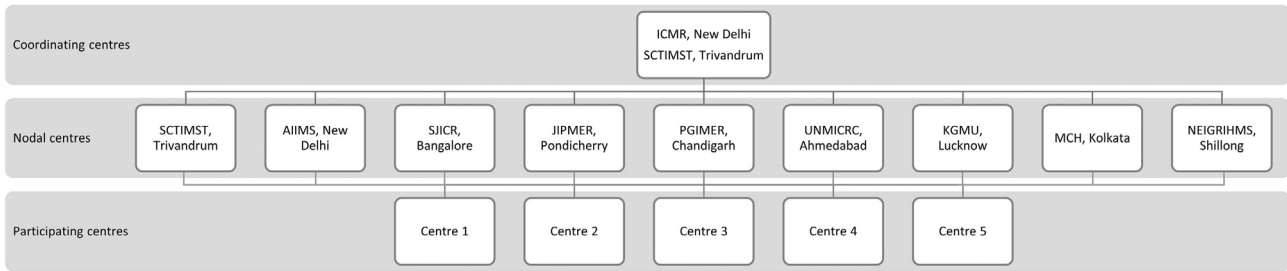


Fig. 1. National Heart Failure Registry study administrative levels. All India Institute of Medical Sciences (AIIMS), New Delhi - (North region), North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong - (North East region), UN Mehta Institute of Cardiology and Research Centre (UNMICRC), Ahmedabad - (West region), Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry - (South East region), Sri Jayadeva Institute of Cardiovascular Sciences and Research (SJICR), Bangalore - (South West), King George’s Medical University (KGMU), Lucknow - (Central region), Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh - (North West region), Medical College Hospital (MCH), Kolkata - (East region), Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum - (South region).

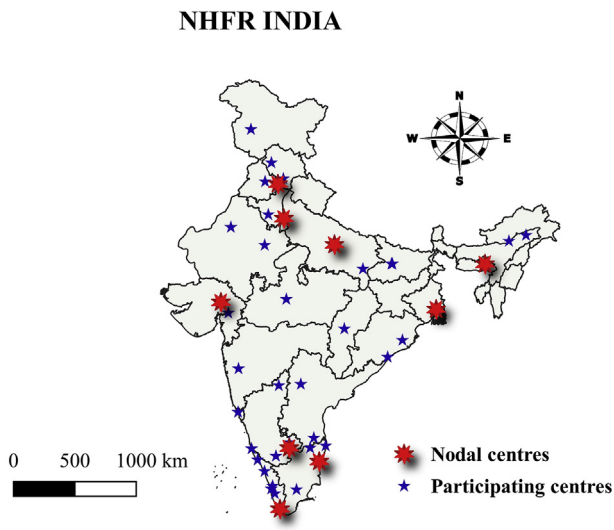


Fig. 2. National Heart Failure Registry nodal and participating centers.

2.6. Administration, functioning, and quality assurance

Before starting the NHFR, training sessions were conducted at each nodal center for the project staff from the participating centers. A trained staff-nurse/project staff recruits patients, collects the data, and then enters the data in the online platform/tablet provided (Fig. 3). The data collected is being synced to the server at the end of the day. Data uploaded on to the NHFR server are being verified for accuracy and completeness by the nodal center coordinator. The nodal center coordinators contact each participating center twice a week and give necessary instructions to improve and

maintain the quality of data collection. All the data entry related queries are answered and being solved by the nodal coordinators with the help of the national coordinating center at SCTIMST. The nodal center staff conducts periodic site visits to all participating centers to verify the data by random cross-check of the source documents (10% of all data fields), as part of quality assurance. The project staff at the national coordinating center monitors the activities of all participating centers and performs random checks.

2.7. Data management and analysis

Data analyses will be started after checking the data set for quality issues and missing variables. We are generating a periodic listing of data queries for the sites to resolve data-related issues. A database lock will be employed to finalize the data set for the final statistical analyses. No statistical analyses will be conducted before the database lock, and no modification of data will be allowed after the database lock. In order to present baseline characteristics, the categorical variables will be presented as proportions with their 95% confidence interval. Distribution of continuous variables will be checked, and normal distribution will be ensured before applying any parametric hypothesis testing. Continuous variables will be presented as means with standard deviation (SD). If the continuous variables are not normally distributed, they will be presented as median with interquartile range (IQR).

In-hospital, 90-days and one-year mortality rate will be reported as a proportion (number of deaths/total registered patients) and per 100 person-days of follow-up. Survival analyses will be employed to identify factors associated with mortality outcomes. Univariate survival models will be initially performed using Kaplan–Meier survival plots, and the groups will be compared using log-rank tests. Any deviation from the proportional hazards assumption will be tested using log-minus-log plots. Later, if they satisfy the proportional hazard assumption, the Cox proportional

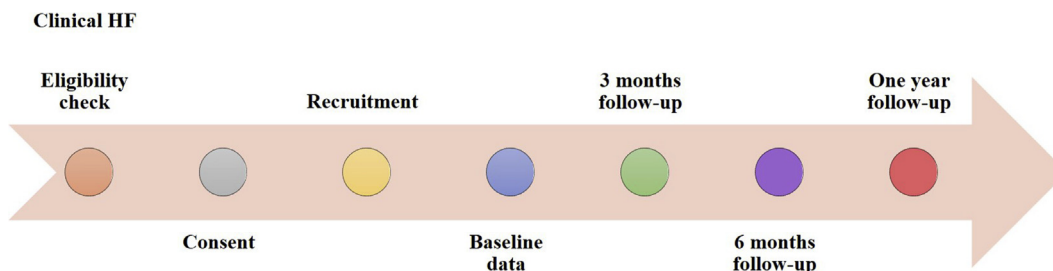


Fig. 3. NHFR study process.

hazards model (Cox-PH) will be employed to evaluate the potential multivariate-adjusted hazard ratio of all-cause mortality. The multivariate model will include all relevant covariates/confounders based on existing literature and with a univariate $p < 0.20$. All analyses will be carried out using Stata 12.¹²

3. Ethical considerations

We have obtained institutional ethics committee approval from each participating center before the commencement of the study. This study was registered in the Clinical Trial Registry of India, and the registration number is CTRI/2019/01/017053. Written informed consent was obtained from all participants before enrolment into the registry.

4. What this study is going to add to the literature

There is limited data from LMIC on HF. Although there are few hospital-based studies from India, they are relatively small and also limited to either big teaching hospitals or small geographic areas. We aim to collect data of 10,000 patients across twenty-four different states and two union territories of India. The baseline demographic and clinical characteristics, etiology, and one-year survival of HF patients may help to influence policies to reduce HF-related burden and mortality in India.

Funding agency

This study is funded by Indian Council of Medical Research (ICMR), Ministry of Health and Family Welfare, Government of India.

Conflicts of interest

The authors have none to declare. Panniyammakal Jeemon was supported by the Wellcome Trust/DBT India Alliance Fellowship [grant number IA/CPHI/14/1/501497]. ICMR – Indian Council for Medical Research is funding the study.

Appendix A, B and C: Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ihj.2019.12.005>.

References

1. Ambrosy AP, Fonarow GC, Butler J, et al. The global health and economic burden of hospitalizations for heart Failure Lessons learned from hospitalized heart failure registries. *J Am Coll Cardiol*. 2014 Apr 1;63(12):1123–1133.
2. Harikrishnan Sivadasan Pillai, Sanjay G. Heart failure in South Asia. *Curr Cardiol Rev*. 2013 May;9(2):102–111.
3. Harikrishnan S, Sanjay G, Anees T, et al. Clinical presentation, management, in-hospital and 90-day outcomes of heart failure patients in Trivandrum, Kerala, India: the Trivandrum Heart Failure Registry. *Eur J Heart Fail*. 2015 Aug;17(8):794–800.
4. Harikrishnan S, Sanjay G, Agarwal A, et al. One-year mortality outcomes and hospital readmissions of patients admitted with acute heart failure: data from the Trivandrum Heart Failure Registry in Kerala, India. *Am Heart J*. 2017 Jul;189:193–199.
5. Sanjay G, Jeemon P, Agarwal A, et al. In-hospital and three-year outcomes of heart failure patients in South India: the Trivandrum heart failure registry. *J Card Fail*. 2018 Dec 1;24(12):842–848.
6. Dokainish H, Teo K, Zhu J, et al. Global mortality variations in patients with heart failure: results from the International Congestive Heart Failure (INTER-CHF) prospective cohort study. *Lancet Glob Health*. 2017 Jul;5(7):e665–e672.
7. Stigi J, Jabir A, Sanjay G, Panniyammakal J, Anwar CV, Harikrishnan S. Kerala acute heart failure registry-Rationale, design and methods. *Indian Heart J*. 2018 Jul;70(Suppl 1):S118–S120.
8. Chopra VK, Mittal S, Bansal M, Singh B, Trehan N. Clinical profile and one-year survival of patients with heart failure with reduced ejection fraction: the largest report from India. *Indian Heart J*. 2019 May;71(3):242–248.
9. India State-Level Disease Burden Initiative CVD Collaborators. The changing patterns of cardiovascular diseases and their risk factors in the states of India: the Global Burden of Disease Study 1990–2016. *Lancet Glob Health*. 2018;6(12):e1339–e1351.
10. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016 Jul 14;37(27):2129–2200.
11. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American society of echocardiography and the European association of cardiovascular imaging. *Eur Heart J Cardiovasc Imaging*. 2016;17(12):1321–1360.
12. StataCorp. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP; 2013.