



## Short Communication

## Kerala acute heart failure registry—Rationale, design and methods

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## ABSTRACT

Heart failure (HF) is recognized as a major public health problem in both the low and high-income countries. However, data are scarce on the burden, prevailing practice patterns and long-term health outcomes of HF patients in India. The Kerala heart failure registry (KHFR) is a multi-centric, prospective, and hospital based registry in Kerala, India. Consecutive patients admitted with the diagnosis of acute heart failure satisfying the European Society of Cardiology (ESC) criteria will be enrolled in the registry. Data on demographic, clinical, laboratory, imaging, other diagnostics and therapeutic approaches employed and the usage of guideline based medical therapy will be collected as part of the registry. Additionally, all registered patients will be followed-up regularly at 1-month, and thereafter at every 3-months. Both mortality and hospital admission data will be collected during the follow-up visits. We will be recruiting 7500 HF patients in the KHFR. Once completed, KHFR is going to be the largest HF registry in India. We will validate a HF mortality risk score developed based on a previously conducted Trivandrum Heart Failure Registry in the KHFR patients.

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Heart failure (HF) is a major public health issue with a current prevalence of over 23 million cases worldwide.<sup>1</sup> Globally, the lifetime risk for HF is one in five.<sup>1</sup> Heart Failure being a problem primarily of elderly population, the prevalence increases with age. For example, the overall prevalence of HF in the United States (US) population is about 1.9%,<sup>2</sup> whereas it is 10% in those above 65 years of age.<sup>3</sup> The incidence of HF is also high in the US population with a rate of 5.64 and 3.27 per 1000 person-years in men and women, respectively.<sup>4</sup>

Data are scarce on the burden of HF in terms of both prevalence and incidence from India and other Low Middle-Income Group Countries (LMIC). Community based prevalence of HF has been estimated as 1.2/1000 population in a study conducted in six North Indian villages (INDia Ukieri Study).<sup>5</sup> Additionally, a handful of hospital-based registries provide data on HF management practices and outcomes in India. The major hospital based HF registries in India are “The Trivandrum Heart Failure Registry” of 1205 patients (THFR),<sup>6,7</sup> the INTER-CHF registry,<sup>8</sup> and the

PINNACLE registry. However, the higher community based prevalence of risk factors indicates the likelihood of relatively higher prevalence of HF in India.<sup>9–11</sup>

Heart failure is a chronic debilitating condition that is often associated with productivity loss. Hospitalization cost is found to be the main cost driver to the total health care spending related to HF.<sup>12</sup> However, data on the economic burden of HF on the health care system, families and individuals are not well documented in the Indian settings.

Adherence to optimal guideline directed therapy is important in achieving better health outcomes in HF patients. The THFR clearly demonstrate very poor adherence to guideline directed therapy and its adverse impact on future hospital admissions and mortality outcomes.<sup>12</sup> However, THFR was conducted in the capital district of Kerala with relatively better health care access and may not be representative of the whole state. Therefore, we propose to establish a multi-centric hospital based registry of acute HF patients across Kerala.

### 1. Aim of the study

To assess the patient profile, practice patterns, economic burden and health outcomes (hospitalization and mortality) of HF patients from multiple hospitals across Kerala, India.

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### 1.1. The specific objectives of the study are

- 1 To describe the clinical features and demographic data and etiology of patients admitted with acute HF in Kerala.
- 2 To describe the diagnostic and therapeutic approaches employed in HF patients in Kerala.
- 3 To analyze the usage of guideline directed medical therapy (Combination of ACEI/ARB, BB and Aldosterone blocker for HFrEF) and its adherence in HF patients in Kerala.
- 4 To assess the in-hospital, 30-day, 90-day and long term hospitalization and mortality rates in HF patients.
- 5 To validate the heart failure mortality risk score developed based on the Trivandrum heart failure registry in the KHFR patients.
- 6 To estimate the economic burden (both direct and indirect cost) of HF in Kerala.

### 1.2. Materials and methods

The Kerala Heart Failure Registry (KHFR) is planned as a prospective hospital based acute heart failure registry in multiple hospitals across Kerala. All the cardiology centres in Kerala who are admitting patients with HF will be contacted and those willing to participate in the registry will be included. We will be enrolling 60 centres from different parts of Kerala in the registry. The listing of consented hospitals and the respective principal investigators (PIs) are given in Appendix A.

All participating hospitals will register consecutive patients with acute HF. Written informed consent will be obtained from each patient before enrolling in the registry. We will follow the ESC 2012 criteria for the diagnosis of HF.<sup>13</sup> The diagnostic criteria for HF is defined as symptoms and signs of acute HF supported by echocardiographic evidence of systolic or diastolic dysfunction and/or elevated B-type natriuretic peptide (BNP)/N-terminal pro B-type natriuretic peptide (NT pro BNP).

Heart failure patients will be classified as those with reduced ejection fraction (HFrEF: when EF < 40%), preserved ejection fraction (HFpEF: when EF > 50%), and those with mid-range ejection fraction (HFmrEF; when EF = 40–50%) based on the 2016 ESC guidelines.<sup>14</sup>

#### 1.2.1. Exclusion criteria

Only the patients who are unwilling to provide an informed consent will be excluded. Those patients getting re-admitted in a separate centre for the same event after enrollment will be excluded to avoid duplication of data.

The eligible patients will be categorized into:

- a) Acute denovo heart failure – defined as patients without pre-existing HF who are admitted for the first time with acute HF.
- b) Acute on chronic heart failure – defined as patients with pre-existing HF admitted with worsening of symptoms.

### 1.3. Data collection

A dedicated website will be used for data collection and entry. The website with a data entry software specifically developed by M/S Netbios, on the PHP platform and MySQL database will be used for the KHFR (the study questionnaire in word format is given in Appendix B). Validation limits will be set for each items in the data application to limit potential errors. All limits set in the data application will be pre-tested using dummy data. The KHFR registry will be coordinated by the Little Flower (LF) Hospital, Angamaly, Kerala and Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Thiruvananthapuram, Kerala. A dedicated

study coordinator will be employed at each coordinating centers for the smooth conduct of the study. Both coordinators will be trained by the software team and also by the principal investigators.

A paramedical staff, a staff nurse or a physician assistant recruited by the site investigator in each center will be trained in data collection and entry. Training sessions will be conducted in different regions based on the requirement.

The data collection includes demographics, clinical presentation, etiology of heart failure, relevant investigations, guideline based medical therapy and in hospital mortality. The follow-up data will include re-hospitalizations, adherence to guideline based medical therapy and mortality. Patients who undergo percutaneous or surgical intervention for heart ailments (eg PCI/CABG/Valve replacement) will also be captured. The follow-up visits will be conducted at 1-month, and thereafter every three months.

The data entry will be periodically monitored by the principal investigators. Randomly selected 10% of data will be forwarded to the respective site principal investigator for source data verification. Additionally, the study coordinators will be conducting periodic monitoring visits to each centres and complete source data verification independently in at least 10% of the registered patients. Any discrepancy in data will be noted, discussed with the site principal investigator and rectified based on source data.

### Investigators

The principal investigators are well experienced in community based research and also well versed in collecting data from hospital based registries.<sup>15,16</sup>

### Sample size

We will be recruiting 7500 patients from around 60 hospitals in Kerala. The THFR ad a cumulative 90-day all-cause mortality rate of 18%.<sup>6</sup> At this rate, the KHFR will have >90% power to detect a hazard ratio of more than 1.2 at 5% type 1 error rate for any of the predictor variable of mortality outcomes.

### Funding

Funding is obtained from the Kerala Chapter of the Cardiological Society of India (CSI-K). CSI-K has funded the Kerala ACS registry,<sup>16</sup> the largest ACS registry in the country, the CSI-KERALA CRP (CSIK – Cardiac Risk factor Profile study)<sup>17</sup> and the PROKERALA<sup>15</sup> study, the largest pulmonary hypertension registry in LMIC.

### Ethical clearance

Prior approval from the respective Institutional Ethics Committees' (IEC) of each of the participating centers will be sought before the initiation of the study. For those hospitals that do not have their own IEC, the Independent IEC of the CSI-K, will take the ethics oversight responsibility and clear the study proposals based on mutual agreement.

### Long-term plans

The long-term plan is to follow-up the KHFR patients up to five years to study predictors of long-term mortality outcomes.

### Data management and analysis

Data analyses will be started after checking the data set for quality issues and missing variables. We will generate 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 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, 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. If the continuous variables are not normally distributed, they will be presented as median with interquartile range (IQR). In-hospital, 30 day and 90 day mortality rate will be reported as a proportion (number of deaths/total registered patients) and per 1000 person-days of follow-up. Survival analyses will be employed to identify factors associated with mortality outcomes. Univariate survival models will be performed initially using Kaplan–Meier survival plots and 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, Cox proportional hazards models (Cox-PH) will be employed to evaluate potential multivariate adjusted risks of all-cause mortality. The multivariate model will include all relevant covariates/confounders based on existing literature and with a uni-variate  $p < 0.20$ . All analyses will be carried out using Stata 12 (StataCorp, College Station, TX, USA).

#### What this study is going to add to the literature

There is very little data from LMIC on HF, an emerging public health problem in this region. Even though there are few hospital based studies from India, they are small in number and limited to either big teaching hospitals or small geographic areas. The KHFR aims to collect data of 7500 patients from 60 hospitals in Kerala and it will be the largest study on HF from India. The KHFR will help to fill the gap in knowledge in terms of presentation, management and outcomes of HF patients in India. It will also help to validate an Indian heart failure mortality risk score.

#### Conflict of interest

None.

#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.ihj.2018.02.001>.

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