



Review Article

A Kerala model for cardiovascular research?

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ABSTRACT

India's contribution to cardiovascular research has been dismal with a share of only 1% of total number of papers published in the world during the period 1999–2008. Based on two recent studies published from Kerala, the Kerala ACS Registry and the CSI Kerala CRP Study and four other studies being undertaken in Kerala, we think that a Kerala model for cardiovascular research can be conceptualized. This model which consists of funding by professional organization of cardiologists with wide participation of cardiologists, physicians, health workers, nurses, and in some situations general public, logistics looked after by a central coordinator and study design by panel of experts or institutions of repute in the region and carried out at low cost can be considered for implementation in rest of India. Studies based on such a model may change practice pattern of cardiovascular diseases in India.

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The Kerala model of economic development has been discussed and debated by developmental economists for years. Briefly, Kerala model implies a set of high material quality of life indicators coinciding with low per capita incomes both distributed across Kerala.¹ The idea can be simplified as a model of achievement of high quality output in a resource poor environment. A similar model can be conceptualized in improving cardiovascular research output in India.

India's contribution to medical research has been poor. In an analysis of world medical research output during the period 1999–2008, India's contribution was only 1.59% when compared to 26.19% by US, 8.56% by UK and 3.38% by China. When China improved its medical research output from 0.98% in 1999 to 5.28% in 2008, India improved only marginally from 1.17% in 1999 to 1.88% in 2008. In the same period, 6801 papers published in India on cardiovascular diseases formed only 1.17% of the world's contribution.² Clearly, we have to go a long way forward. There are many reasons for this dismal show in medical research in India, foremost among these being inadequate infrastructure, poor accessibility to research funds, weak administrative support, lack of formal training in research methodology, deficient expression

capabilities, unenthusiastic attitude of doctors, and low self-esteem.³

Recently, two important studies on Cardiovascular Sciences were published from Kerala, the Kerala Acute Coronary Syndrome (ACS) Registry and the Cardiological Society of India (CSI), Kerala Chapter Coronary Artery Disease and its Risk Factors Prevalence Study (CSI Kerala CRP Study). These studies had many aspects which may be adopted for future research.

1. The Kerala ACS Registry

It is the largest acute coronary syndrome (ACS) registry ever conducted in India. It enrolled prospectively 25,748 patients with ACS from 125 hospitals spread across Kerala during the period 2007–2009.⁴ Mean age of the patients was 60.4 years (men 77.4%). ST-segment myocardial infarction (STEMI) accounted for 37%, non-STEMI 31%, and unstable angina 32% of ACS patients. Thrombolytics were used in 41% of STEMI, 19% of non-STEMI, and 11% of unstable angina admissions. Symptom onset to presentation of more than 6 h was noted in 41% of STEMI patients. In-hospital medical therapy was relatively high overall for all groups, with anti-platelet therapy being the most common (97%). Discharge medication rates were variable and generally suboptimal (80%). Angiography and Percutaneous Coronary Intervention (PCI) use was substantially lower when compared to other registries from the developed world.⁴ Rate of thrombolysis in STEMI was lower than in another large Indian ACS registry, the CREATE Registry.⁵

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Less than 50% of STEMI patients received reperfusion in the form of thrombolysis/PCI or CABG. The registry opened a window of opportunities for ACS care in Kerala like improving symptom onset to door time in STEMI, improving reperfusion in STEMI using thrombolysis or angioplasty, improving discharge medication prescription in ACS, avoiding inappropriate thrombolysis, and improving in-hospital mortality.

2. CSI Kerala CRP Study

This was a community-based cross-sectional study in Kerala, where 5167 adults (mean age 51 years, men 40.1%) were selected using a multistage cluster sampling method.⁶ Information on socio-demographics, smoking, alcohol use, physical activity, dietary habits and personal history of hypertension, diabetes, and coronary artery disease (CAD) was collected using a structured interview schedule. Anthropometry, blood pressure, electrocardiogram, and biochemical investigations were done using standard protocols. Results showed that age-adjusted prevalence of definite CAD was 3.5%, while prevalence of any CAD was 12.5%. There was no difference in definite CAD between urban and rural populations. Most risk factors for CAD were highly prevalent in the state. Hypertension was detected in 28%, diabetes in 15%, high total cholesterol in 52%, and current smoking among men in 28%. Authors of the study concluded that prevalence of definite CAD in Kerala increased nearly three times since 1993 without any difference in urban and rural areas. They suggested both population and individual level approaches to address the high levels of CAD risk factors to reduce the increasing prevalence of CAD in this population.

3. What was common in the two studies?

Both studies were funded by the Kerala chapter of Cardiological Society of India, a professional organization of cardiologists of Kerala. Apart from saving the hurdle of getting financial support, this ensured backing of the whole cardiology community of the state for the study. The design and methodology of the studies were discussed in detail at the meetings of Kerala chapter and progress was presented periodically. In the case of Kerala ACS Registry, the cardiologists and physicians who participated in the study had great sense of involvement. They cooperated voluntarily and encouraged their paramedical team to provide the necessary support for recruiting patients, getting informed consent, helping to record the case report forms (CRF), and ensuring entry of follow-up data. In the CSI Kerala CRP Study, credibility of CSI- Kerala Chapter helped in getting the active participation of local people, which was crucial for the success of the study. At each recruitment center, several meetings were held under the supervision of local administrative bodies, with participation of elected ward/division representatives, doctors from the local government hospitals, health centers and private clinics, health workers, and the public. In these meetings, doubts raised were clarified, and the purpose of study was explained. Being a study carried out by Cardiological Society of India- Kerala Chapter helped immensely to get the trust of the people.

Central role played by the coordinators for these studies needs to be emphasized.

Two of the authors were the coordinators for Kerala ACS Registry and CSI Kerala CRP Study (MP and GZ respectively). Having a central coordinator solved to a large extent the problem of inadequate research infrastructure in our country. They were responsible for submitting the initial proposal. Once the projects were approved, they finalized the design and methodology, selected the co-investigators, developed communication channels, set up the steering committee, and obtained approval of ethics

committee. They also looked after purchase of equipments and maintenance of proper book of accounts.

Lack of prior research experience is often mentioned as a stumbling block in our country. In Kerala ACS Registry, a panel of experts constituted by heads of academic institutions in Kerala prepared the protocols and CRFs. The design and methodology of CSI Kerala CRP Study was developed by public health department of Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), Trivandrum.⁷ This considerably reduced the burden on the investigators.

However, more important was the participation of large number of people in these studies, often without any monetary gain. In the case of Kerala ACS Registry, cardiologists and physicians in 125 hospitals voluntarily participated in the project and attended the meetings. In addition, the contribution of the nurses in ICUs was invaluable. They attended the sessions held periodically for imparting knowledge on ACS management and training the proper method of filling the CRFs, without receiving any remuneration. Their enthusiasm for learning and being part of the project was a revelation for the investigators. In the case of CSI Kerala CRP Study, the tireless work of the 'Kudumbashree' (a female-oriented, community-based, poverty reduction project of the government of Kerala) workers and ASHAs (accredited social health activists), mostly women, need to be appreciated. Each of them was asked to visit all households in their allotted area three times, firstly to list the members of each household, secondly to invite the selected participants from each household to the designated center for data collection, and thirdly to hand over the results of investigations and brief recommendations. They were paid only very small amount, yet were very active and primarily responsible for the good response rate of the study. In both studies, special care was taken to impart knowledge on research methodology to the investigators. In the Kerala ACS Registry, investigators were invited periodically to learn about registries in general and registries on ACS. In CSI Kerala CRP Study, two workshops were done at SCTIMST public health department, one on methodologies of epidemiologic studies and another on biostatistics.

These were low budget studies. The budget for Kerala ACS Registry was Rupees two million (Rupees 500,000 from national CSI) and that of the CSI Kerala CRP Study was Rupees 2.5 million. It is worthwhile to note that the concept of low budget collaborative research studies on cardiovascular disease is not new and has been utilized in at least three previous studies from India, namely early phase of INTERHEART study,⁸ CREATE registry,⁵ and India Heart Watch study.⁹ Kerala studies differed in that they were supported by the Kerala chapter of CSI, which helped in getting the cooperation of not only cardiologists and physicians of the state but also the public.

4. What constitutes the Kerala model of cardiovascular research?

We, therefore, propose that even in a resource-poor setting, high quality cardiovascular research can be undertaken successfully. Such a model envisages funding of the study by a professional organization like Kerala Chapter of Cardiological Society of India to ensure the whole-hearted support and involvement of all cardiologists. There is a need to identify a central coordinator who can remedy deficiencies of research infrastructure. Such a model may involve not only the cardiologists and physicians, but also health care workers and nurses if it is a hospital-based study and the health care workers, members of local self Government, and general public in studies where screening of asymptomatic people is involved. The Kerala model implies low budgetary allocation and studies may be carried out by people's participation.

In such a model, the task of designing the study can be entrusted with a panel of experts or reputed institutions in the region. Deficiencies in prior research experience can be tackled by focused workshops and training sessions.

5. Impact of the Kerala studies

These studies made considerable impact on practice of cardiovascular diseases in the state. The Kerala ACS Registry brought forward many inadequacies in the management of ACS prevailing in Kerala. Prolonged symptom to door time in STEMI, low reperfusion rates in STEMI, drop in discharge prescription of standard drugs, inappropriate thrombolysis in non-STEMI, and low utilization of PCI were some of these issues. In an editorial in *European Heart Journal*, Hitinder S. Gurm and Kim A. Eagle, while applauding the initiative of Kerala chapter of CSI for developing the ACS Registry, noted that registries not only serve to identify the lacunae in care, but can be used to develop and deliver simple tools that can overcome these.¹⁰ The registry prompted interest in how to improve quality of care in ACS in the state and lot of discussions ensued which culminated in the Acute Coronary Syndrome Quality Improvement in Kerala (ACS QUIK) study with collaboration of North Western University, Chicago and Centre for Chronic Disease Control (CCDC), New Delhi and funded by National Heart, Lung and Blood Institute (NHLBI), USA. This study, which is the first quality improvement study in ACS in India is ongoing and expected to be completed by the end of this year. Knowledge of high prevalence of CAD and its risk factors in Kerala has stimulated thought processes among cardiologists and physicians as well as government agencies. More important was the catalytic influence of these studies in kindling research initiatives among the cardiologists of Kerala. There is huge clamor for such studies. Already Primary Angioplasty Registry of Kerala (PARK registry) and Pulmonary Hypertension Registry of Kerala (PROKERALA), both funded by CSI Kerala Chapter, are progressing and have completed 75% of recruitment of patients, and the study results are expected early next year.

Two more studies, Kerala Heart Failure Registry and Kerala Atrial Fibrillation Registry, again funded by CSI – Kerala Chapter are approved and have begun recruitment from March 2016. Obviously, the Kerala model of cardiovascular research is taking deep roots and stimulating interest in carrying out cardiovascular research in the state.

6. Is the Kerala model of cardiovascular research applicable to the rest of India?

One can argue that this model is alright for Kerala with its high literacy rate and well-developed system of local self-government where people's participation is a proven concept and widely practiced. However, it may be possible to implement the model in other parts of India, if the professional organizations are willing to prioritize cardiovascular research. Already many cardiologists from other states have expressed readiness to cooperate with such studies. Involving the health workers and the public will not be a big problem if cardiologists are prepared to spend time in motivating them. If the professional organizations in the states are unable to fund projects, they can get support from the central organization and industry partners. We realize that all type of studies may not be suitable for such a model. Cross-sectional studies and registries are likely to fit into this model. These studies can be hypothesis generating and may pave the way for more studies of an interventional nature. It is possible to encounter many stumbling blocks for implementation of this model. The model works on the assumption that all members of professional organization of cardiologists of each state will be committed to the task of generating data pertaining to their region. State coordinator

has to play a crucial role and should be dedicated to the project. Inadequate funds at the disposal of the chapters could be another issue. In the case of population-based studies, inability to identify motivated groups especially at rural levels and lack of support from local administration could pose major problems.

7. An action plan

Easiest of studies that can be carried out as per this model are registries of disease entities like ACS, heart failure, pulmonary hypertension, atrial fibrillation or primary angioplasty. Since data on ACS are not available from many parts of India, we can first consider developing regional ACS registries. Professional societies of cardiologists, like CSI, can act as the nodal agency for conducting such studies.

CSI may constitute ACS Registry Committee consisting of members of the Research Council and principal investigators of published ACS registries from India. The Chairman, CSI Registry Affairs Advisory Committee can be the convener of this body. If necessary, other experts in the field of cardiovascular research in India can be inducted. ACS Registry Committee will be responsible for formulating the design and methodology of the ACS Registry. This body will also be entrusted with the task of creating the CRFs, protocol manual, and other required documents.

CSI headquarters should then write to presidents and secretaries of each chapter about the need for carrying out an ACS registry in their region and invite them to participate. Details of the study, including the design and methodology and protocol manual will be made available to them. Since participation of all cardiologists in a chapter is essential, the idea should be discussed at the meetings of the CSI chapters. It is preferable to organize the study state wise. Smaller states can be combined to form group of states. In states having multiple chapters, all chapters in that state may be joined.

Each state or group of states select a State Coordinator (SC). The SC has a key role and should be selected on the basis of prior research expertise, ability to command respect, and communication skills. Each SC will select 4–8 Zonal Coordinators (ZC) from among the cardiologists of that chapter or chapters. ZCs together with the SC will function as State Steering Committee (SSC). The SSC should have a team of dedicated support staff consisting of Non-Medical Coordinators (NMC), two for each zone who will interact with each participating hospital. The National Steering Committee (NSC) may consist of all SCs and should be headed by the Chairman, CSI Registry Affairs Advisory Committee who will be the National Coordinator.

It is desirable to conduct at first a pilot study in a district of the region, under direct supervision of the SSC. All the hospitals in that district managing ACS may be invited to take part in the pilot registry. Each hospital is requested to select a site investigator, either a cardiologist or a physician and two or more paramedical staff members, either ICU nurses or catheterization laboratory technicians. They will identify the ACS patients, get informed consent and fill up the CRFs. A meeting of the site investigators may be held to explain why it is important to know about ACS care in their locality. Two or more training sessions should be held to teach the paramedical staff members about ACS management and how to fill the CRFs. Each completed CRF has to be verified by the site investigator. The NMCs may visit each participating hospital periodically and guide the paramedical staff members regarding the proper way to identify ACS patients, get the informed consents, and fill CRFs. They may also collect the completed CRFs as well as the follow-up information and enter data using centrally designed software. The pilot study can be for 6 months and should also aim to collect 30-day follow-up data.

Results of the pilot registry may be presented and discussed at the CSI chapter meetings. The experience of conducting the pilot study may help to anticipate possible roadblocks and find ways to tackle them for the main study. The SSC may then identify all the hospitals in the state with ICU facilities and willing to participate in the main registry. Each ZC will have a certain number of hospitals under his supervision. He conducts meetings of all site investigators under him, explaining the study design and methodology and protocols. He should also convene periodic meetings of paramedical staff members responsible for data collection. Like in the pilot study, NMCs may collect and enter the data according to protocol. They may also disburse the remunerations to the paramedical staff. SSC should constantly interact with the site investigators. Special attention should be given to sites where recruitment is erratic or slow. Follow-up information is vital for the registry. Site investigators should be encouraged to ensure that all patients are followed up and information collected regularly.

The study will be supervised by the NSC which may hold periodic meetings to assess progress of the study and correct mistakes in each state. Each SC may be asked to present a report on the progress of the study in their region. Corrective steps can be discussed in these meetings. NSC may set up a panel of experts for data analysis. Results pertaining to each state should be presented at the meetings of the members of the chapter. SSC will be responsible for publishing the paper related to data from their region. The NSC may analyze and interpret national data emerging from the studies from the states.

The cost of conducting the study can be borne by the national CSI and the chapters. The national CSI can provide seed money to each participating state. Rest of the required amount has to be raised by the chapters, either from their own sources or from the Industry as unrestricted grants. In this model, participation of all members of the chapter is important. SSC should be responsible for motivating the members. Most cardiologists in India are busy with huge patient load and have very little time for research. However, there is increasing awareness of need for research to improve delivery of care. They may be prepared to cooperate with research studies without financial gains, provided not much time is spent on the effort. The model demands very little time from them and provides a framework for research with which it is easy to cooperate.

8. Conclusions

We propose the Kerala model of cardiovascular research on the basis of lessons learned by two studies done in Kerala, the Kerala ACS Registry, and CSI Kerala CRP Study. This model where funding is by professional organization of cardiologists with wide participation of cardiologists, physicians, health workers, nurses, and in some situations general public, logistics looked after by a central coordinator and study design by a panel of experts or institutions of repute in the region is a low budget model and can be implemented in rest of India with minor modifications. Studies based on such a model can change practice pattern of cardiovascular diseases in India and will herald a new dawn in Indian medical research.

Conflicts of interest

The authors have none to declare.

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