Fatal and Nonfatal Cardiovascular Disease and the Use of Therapies for Secondary Prevention in a Rural Region of India

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Background—The rate of cardiovascular disease is widely considered to be increasing throughout India. Precise and reliable data on fatal and nonfatal cardiovascular disease, however, are few, and little is known about the use of preventive therapies. This is particularly true for rural regions.

Methods and Results—Data were collected from 53 villages in the Godavari region of Andhra Pradesh. Mortality data were obtained from a verbal autopsy–based mortality surveillance system during a 12-month period in 2003 to 2004. The prevalence of nonfatal cardiovascular disease and the use of preventive therapies were estimated from a stratified random sample of 4535 adults (≥30 years of age) in 2005. Cardiovascular disease was the leading cause of mortality, accounting for at least 32% of all deaths. The average age at cardiovascular death was 65 years, and 51% of all cardiovascular deaths occurred in patients <70 years of age. Among adults, the prevalence of coronary heart disease was estimated to be 4.8% (95% CI, 4.1 to 5.5), and the prevalence of cerebrovascular disease was estimated at 2.0% (95% CI, 1.5 to 2.4). Among individuals with either diagnosis, 14% (95% CI, 10 to 18) reported taking aspirin, 41% (95% CI, 36 to 47) took a blood pressure–lowering medication, and 5% (95% CI, 3 to 7) reported using a cholesterol-lowering medication.

Conclusion—This region has a large disease burden attributable to cardiovascular disease with significant underuse of proven, low-cost preventive medications. (Circulation. 2009;119:1950-1955.)

Key Words: cardiovascular diseases ■ India ■ morbidity ■ mortality ■ prevention

T he epidemic of cardiovascular disease (CVD) is rapidly gaining pace in low- and middle-income countries, which now contribute more than three quarters of all cardiovascular deaths worldwide.¹ CVD is the leading cause of death in India²–³ and on average occurs at a much younger age compared with developed countries.⁴ It is estimated that half of all cardiovascular deaths in India occur in the working-age population compared with about one quarter in high-income countries.⁵ The younger age at which cardiovascular events occur has major socioeconomic consequences,⁶ and the development and implementation of effective low-cost preventive strategies is a public health priority.

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Much of the information about CVD in India derives from projects done in urban regions, and there are relatively few data defining the burden and management of CVD in rural settings. Reliable information about the pattern of CVD in rural areas is important because >70% of the Indian population lives outside cities.⁷ Furthermore, resources to address the evolving epidemic of CVD in rural areas are even fewer than in urban settings,⁸ and optimal use of scarce healthcare resources is vital.

The objective of this report is to define the fatal and nonfatal burden of CVD in a population from a rural area of India and to describe the current use of proven drug-based preventive strategies in persons living with CVD.

Methods

This report uses data from 2 main sources. First, mortality data were collected with a verbal autopsy–based mortality surveillance for the 12-month period of October 1, 2003, to September 30, 2004. The surveillance system included 45 villages selected to be broadly representative of all villages in the East and West Godavari districts that were participating in a rural development program run by the Byrraju Foundation, a local nongovernment organization and collaborator in the study. Second, disease prevalence and treatment use data were collected as part of a large-scale random sample survey conducted in February through March 2005 in 20 villages represent-
tative of the Godavari districts. The villages were sampled from a list of 88 villages from the East and West Godavari regions for which the community leaders of the villages had consented to participate. Six villages were from East Godavari; 14 villages were from West Godavari; and the mean distance from a large town was ~20 km. Both studies were approved by the ethics committees of the CARE Foundation, Hyderabad, India, and the University of Sydney (Sydney, Australia). All participants provided informed consent. For participants who could not read or write, the participant information sheet and consent form were read by the interviewer, and a thumb impression was taken in place of a signature. The study was conducted in accordance with the Declaration of Helsinki and subsequent amendments.

The Mortality Surveillance System
Mortality data were collected using a verbal autopsy method that is well established in India and is used to define causes of death in many developing countries. The method is based on the assumption that most causes of death can be distinguished by symptoms and signs that can be recognized, recollected, and reported by a respondent present during the period leading up to the death. The verbal autopsy instruments used in the present study have previously been validated in India and other developing countries. The methods for this particular surveillance system have been described in detail previously. In brief, a female multipurpose healthcare worker resident in each village was trained to identify all deaths that occurred in that village using a network of key informants. The village populations were defined on the basis of a census done in 2002 to 2003. For each identified death, the multipurpose healthcare worker conducted a standardized interview with a close relative or caregiver of the deceased using an established verbal autopsy tool. The data collected during the verbal autopsy process were then coded independently by 2 trained physicians, and an underlying cause of death was assigned according to the International Classification of Diseases (ICD; version 10). Immediate and/or contributory causes also were assigned wherever possible. A third physician was involved if there were disagreements between the underlying cause of death assigned by the 2 physicians.

Survey of Disease Prevalence and Treatment Patterns
Disease prevalence and treatment patterns were estimated from a large-scale age- and sex-stratified random sample of adults ≥30 years of age in 20 villages. Details of the design and methodology have been published previously. In brief, the 20 villages were selected on the basis of population size, district, and distance from a large town to achieve a group of villages representative of the Godavari region. Adult individuals from these villages were then randomly selected from population lists stratified by age group (30 to 39, 40 to 49, 50 to 59, ≥60 years) and sex to ensure that approximately equal numbers of individuals were drawn from each of the 8 age and sex groups. Data collection was done by trained interviewers who administered a structured questionnaire based on validated tools and expert advice from a range of sources. The questionnaire was translated into the local language of Telugu with check-back-translation and resolution of discrepancies. A pilot study was conducted to validate the questionnaire and to address logistical issues. Coronary heart disease was defined as present if a participant answered yes to one of the following questions: “Have you been told by a doctor that you have had heart attack?” and “Have you been told by a doctor that you have angina?” Cerebrovascular disease was considered present if a positive response was given to the question, “Have you been told by a doctor that you have had a stroke?” Self-reported diagnoses were checked against written medical records held by the patient or a diagnosis by a local physician in a subsequent validation survey. Patterns of treatment for secondary prevention were based on direct questioning about use of aspirin and blood pressure–lowering and cholesterol-lowering medications with cross-checking against patient-held medication lists, written prescriptions, or packs of medication.

Results
Fatal CVD
Mortality surveillance was done in 45 villages in East and West Godavari. Of the 1354 deaths identified, 1170 occurred in adults ≥30 years of age. Verbal autopsies were completed for 1146 of the adult deaths (98%). The cardiovascular mortality rate was 5.1 per 1000 population (Figure), and the all-cause mortality rate was 7.5 per 1000 population. CVD (coronary heart disease and stroke) was the leading causes of mortality, responsible for more than one third of all deaths in adults ≥30 years of age (Table 1). Coronary heart disease was responsible for 15.8% of all-cause mortality, cerebrovascular disease for 14.7%, heart failure for 2.4%, and other heart diseases (rheumatic heart disease, hypertensive heart disease, and other unspecified cardiovascular conditions) for 3.9%. Sudden unexplained death was responsible for an additional 4.7% of adult mortality. Of the 18% of all deaths classified as ill defined (ICD-10 R00-R99), more than one half were in the elderly (≥70 years of age), and a significant proportion were likely cardiovascular in origin. One half and one third of all cardiovascular deaths (coronary heart disease and stroke) occurred before 70 and 60 years of age, respectively, with rates at all ages greatly surpassing those in the United States (Figure). CVD was responsible for a greater proportion of deaths in men (P=0.022), and there was the anticipated rise in rates of cardiovascular death with increasing age (Figure).
Table 1. Prevalence of CVD Among Adults ≥30 Years of Age in Rural Andhra Pradesh

<table>
<thead>
<tr>
<th>Cardiovascular risk factors</th>
<th>Male, n (%)</th>
<th>Female, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of MI or angina</td>
<td>119 (4.7)</td>
<td>114 (5.0)</td>
</tr>
<tr>
<td>History of stroke</td>
<td>66 (2.5)</td>
<td>39 (1.4)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>361 (14.6)</td>
<td>294 (12.2)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>667 (26.6)</td>
<td>686 (27.5)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1034 (45.2)</td>
<td>120 (4.8)</td>
</tr>
<tr>
<td>Overweight/obesity (BMI ≥25 kg/m²)</td>
<td>405 (18.4)</td>
<td>609 (26.3)</td>
</tr>
<tr>
<td>Total cholesterol &gt;5.2 mmol/L</td>
<td>141 (26.5)</td>
<td>204 (33.9)</td>
</tr>
<tr>
<td>Family history of premature CVD</td>
<td>340 (16.1)</td>
<td>326 (14.2)</td>
</tr>
</tbody>
</table>

Top 5 causes of death*

<table>
<thead>
<tr>
<th>Diseases of the circulatory system</th>
<th>Male, n (%)</th>
<th>Female, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>117 (17.6)</td>
<td>60 (12.4)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>86 (13.0)</td>
<td>82 (17.0)</td>
</tr>
<tr>
<td>Injury</td>
<td>50 (7.5)</td>
<td>28 (5.8)</td>
</tr>
<tr>
<td>Others</td>
<td>78 (11.8)</td>
<td>41 (8.5)</td>
</tr>
<tr>
<td>Infectious and parasitic diseases</td>
<td>69 (10.4)</td>
<td>60 (12.4)</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>38 (5.7)</td>
<td>52 (10.8)</td>
</tr>
</tbody>
</table>

MI indicates myocardial infarction; BMI, body mass index.

*Based in part on data presented in Table 1 of Reference 14. Used with permission from the Oxford University Press.

Nonfatal CVD

The survey was done in 20 villages, 12 of which were also encompassed by the mortality surveillance system. In total, 4535 participants agreed to take part and provided informed consent, giving an overall response rate of 80.6% with questionnaire data for these individuals >99% complete. Nonresponders were similar in age and sex distribution to responders. The population was entirely rural, with 54% (95% CI, 52 to 56) of the population being unskilled manual laborers working mainly in agriculture and aquaculture. Forty-seven percent (95% CI, 45 to 49) were literate, and the mean monthly income per household was Rs 2238 (95% CI, 2107 to 2326) (US $51; 95% CI, 48 to 53).

The overall prevalence of CVD (coronary heart disease or stroke) among adults ≥30 years of age was 6.6% (95% CI, 5.8 to 7.4); 4.8% (95% CI, 4.1 to 5.5) reported coronary heart disease (heart attack or angina), and 2.0% (95% CI, 1.5 to 2.4) reported stroke (Table 1). There were no detectable differences in the rates of coronary heart disease or stroke between men and women, but the prevalence of both tended to increase with age. The mean age of individuals reporting CVD was 54 years (95% CI, 52 to 55). In the subsequent validation of self-reported diagnoses of coronary heart disease and stroke, the diagnosis was confirmed in 74% of cases, and there was insufficient evidence to confirm or refute the other one quarter.

Use of Proven Drug Treatments for Secondary Prevention

Among individuals with a history of CVD, 14% (95% CI, 10 to 18) reported using aspirin, 41% (95% CI, 36 to 47) used blood pressure-lowering therapy, and 4.6% (95% CI, 2.5 to 6.8) were on cholesterol-lowering therapy. Nineteen percent (95% CI, 14.6 to 23.6) reported using ≥2 of these treatments (Table 2).

Knowledge About the Determinants of Cardiovascular Risk

Only 56% (95% CI, 49 to 62) of individuals with CVD answered yes when asked whether cessation of smoking would prevent heart disease. Of these high-risk individuals, 50% (95% CI, 43 to 56%) had knowledge about the benefits of physical activity, only 62% (95% CI, 56 to 68) knew that they should avoid fatty foods, and 62% (56% to 68%) knew the beneficial effects of reducing salt in their diet.

Discussion

The present study is the first to combine morbidity and mortality data with treatment patterns for CVD for a rural region of India. The study shows that CVD is an important health problem in this rural region of South India, with a third of adult mortality attributable to CVD and a high prevalence of CVD among adults. Furthermore, proven low-cost treatments for secondary prevention are infrequently administered, and there is only limited knowledge about key behavioral determinants of cardiovascular conditions among those with established disease. Although these findings paint a bleak picture, they also draw attention to a significant opportunity for evidence-based, low-cost, simple interventions to make a major impact on a leading cause of disease burden.

The study also highlights the problem of premature mortality in this population in which one half and one third of all cardiovascular deaths occurred before 70 and 60 years of age, respectively, with very substantial economic and social implications. Although 41% of all cardiovascular deaths occurred <65 years of age in this Indian population, only 17% of all cardiovascular deaths occurred in the same age group in the United States (Figure). The prematurity of CVD identified here coincides with data from another major study that showed that South Asians suffered first myocardial infarction an average of ~6 years earlier than in other countries.22 In

Table 2. Use of Medications in Patients With CVD

<table>
<thead>
<tr>
<th>Coronary Heart Disease (n=1740)</th>
<th>Stroke (n=713)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n % (95% CI)</td>
<td>n % (95% CI)</td>
</tr>
<tr>
<td>Antplatelet therapy</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>272 15.6 (10.9–20.4)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>66 3.8 (1.0–6.7)</td>
</tr>
<tr>
<td>BP-lowering therapy</td>
<td></td>
</tr>
<tr>
<td>β-Blocker</td>
<td>408 23.5 (17.7–29.2)</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>179 10.3 (5.9–14.6)</td>
</tr>
<tr>
<td>Diuretic</td>
<td>119 6.8 (3.0–10.7)</td>
</tr>
<tr>
<td>Other</td>
<td>9 0.5 (–0.5–1.5)</td>
</tr>
<tr>
<td>Lipid-lowering therapy</td>
<td></td>
</tr>
<tr>
<td>Statin</td>
<td>104 6.0 (3.1–8.9)</td>
</tr>
</tbody>
</table>

BP indicates blood pressure; ACE, angiotensin-converting enzyme.
2000, India was estimated to have lost more potentially productive years of life to CVD than any other country in the world (9.2 million years of life lost among people 35 to 64 years of age).3,23 Without effective intervention, this figure is projected to double in the next 2 decades.23

The cardiovascular mortality fraction identified here is broadly comparable to that reported for a recent study done in urban (38%) and rural (23%) Tamil Nadu23 but slightly greater than reported for a prior study done in Andhra Pradesh in the late 1990s in which 16% of mortality was attributed to ischemic heart disease and 11% to cerebrovascular disease.25 There have been few reports of the prevalence of CVD in India in the last decade,26–30 but recent surveys of urban populations in Delhi30 and Chennai29 have reported a CVD prevalence of 7.3% and 11.0%, respectively. No recent data are available for rural India, but the prevalence rates in Punjab (3.1%)31 and Rajasthan (4.3%)27 reported in the early 1990s are lower than recorded here. Although the prevalence of cerebrovascular disease observed in this population is higher than in the United States (2.0% versus 0.8%), the prevalence of coronary heart disease is similar (4.8% versus 4.7%).32 The proportionate mortality definitely ascribed to CVD in this study is probably an underestimate of the true proportion because a substantial number of sudden or ill-defined deaths are likely also cardiovascular in cause.24,33,34 In regard to nonfatal CVD, the reported prevalence may be an overestimate because only three quarters could be confirmed by the validation process. Conversely, it is also possible that the self-report method used here may have missed cases because it is unlikely to have been fully sensitive. Diagnostic services are limited in the study region, and a large number of those surveyed would not have had the means to access the facilities that are available.35 The key point is that even the lowest plausible estimate of prevalence (assuming no true cases were missed and only three quarters of reported cases were true cases) suggests a substantial burden of CVD (≈4.95% prevalence). Having a truly unbiased estimate of prevalence would clearly be preferable, but the information we provide here about the lower plausible bound of prevalent CVD in this part of rural India is a significant advancement in its own right.

Survivors of CVD are at very high risk of recurrent events36–38 and represent an easily identified group among whom preventive therapies are highly cost-effective. Although clinical trials have clearly demonstrated the benefits of low-dose aspirin, β-blockers, angiotensin-converting enzyme inhibitors, and lipid-lowering therapy among such individuals,39,40 data from developing41 and developed42,43 countries show considerable treatment gaps. The use of these secondary preventive therapies was much lower in rural Andhra Pradesh compared with the other studies. For example, the use of aspirin in our study was 14% compared with 81% in the World Health Organization Prevention of Recurrences of Myocardial Infarction and Stroke (WHO-PREMISe) study41 and 84% in the European Action on Secondary Prevention by Intervention to Reduce Events (EUROASPIRE) trial.42 Similarly, the use of statins was much lower compared with WHO-PREMISe and EUROASPIRE (5% versus 20.8% and 57.7%, respectively). There is strong evidence that secondary prevention would be highly cost-effective even in very resource-poor settings,43,44 and India, with one of the best-developed generic drug industries in the world, is well placed to deliver preventive therapies to large numbers at low cost. Combination drug therapy can reduce the risk of recurrent events by three quarters,45–47 and a polypill comprising low-dose aspirin, β-blocker, angiotensin-converting enzyme inhibitor, and statin may have much to offer in this situation.43,47 Behavioral interventions such as smoking cessation, increased physical activity, weight management, and healthy eating may also have significant potential.36

Although treatments for the prevention of CVD are many, uptake has been limited in low- and middle-income countries.41 This reflects multiple issues related to the unavailability and unaffordability of medicines,46 as well as the shortage and inaccessibility of healthcare providers. Physician-based models of care have been effective in reducing morbidity and mortality from CVD in high-income countries but are not plausible for most low- and middle-income settings where trained physicians are few and the capacity of the populace to pay for their services is limited.48 The problem is further exacerbated for rural regions because the healthcare workforce, particularly physicians, tends to concentrate in urban areas.8 Systems based on nonphysician healthcare providers may be of great value. Not only are nonphysician healthcare providers more numerous and widely distributed than physicians, but their services are affordable to a much larger proportion of the population. There is some evidence to support the notion that nonphysician health workers can be trained to make safe and appropriate treatment decisions for the management of patients with CVD.49 India has a well-established primary healthcare system based on nonphysician healthcare providers that currently focuses on maternal and child health and infectious diseases. Developing this system to provide basic care for chronic conditions such as CVD may be one approach that could be delivered at relatively low cost and in a relatively short timeframe.55

Conclusions

CVD is the leading cause of death and a major cause of disease burden in the Godavari region of Andhra Pradesh. Although this region is more developed than much of rural India, it likely provides a good indicator of future mortality and morbidity patterns for many rural parts of the country. The data identify clear opportunities for CVD prevention, but an evidence base that defines new models of chronic disease care tailored to the unique circumstances of rural India needs to be developed.

Acknowledgment

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Disclosures

None.

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India, the second most populous country in the world, is undergoing rapid epidemiological transition, and vascular disease is known to be a major health issue in urban areas. However, 70% of India’s population resides in rural regions where data about cardiovascular disease are scant. A comprehensive survey of mortality and morbidity in 53 villages in rural Andhra Pradesh showed that cardiovascular disease was the leading cause of mortality, responsible for at least 32% of all deaths. The average age at cardiovascular death was 65 years, and 51% of all cardiovascular deaths occurred in patients <70 years of age. The prevalence of coronary heart disease among adults >30 years of age was also high, estimated to be 4.8%. Prevalent cerebrovascular disease was present in a further 2.0%. Few individuals with a history of vascular disease were using proven preventive treatments; only 14% (95% CI, 10 to 18) were taking aspirin, 41% (95% CI, 36 to 47) were on a blood pressure–lowering medication, and 5% (95% CI, 3 to 7) were taking a cholesterol–lowering medication. Secondary prevention has been identified as a cost-effective vascular disease management strategy for low- and middle-income countries. The challenge now is to identify service delivery mechanisms that can provide these proven low-cost therapies to the very large number at risk. With access to healthcare facilities limited by both availability and capacity to pay, novel nonphysician-based approaches to vascular prevention that use existing facilities may have an important role to play.
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