EDITORIAL COMMENT

Tackling the Growing Epidemic of Cardiovascular Disease in South Asia*

Salim Yusuf, MD, FRCP, DPHIL,
Stephanie Ôunpuu, PHD
Hamilton, Ontario, Canada

Cardiovascular disease will likely become a major public health and clinical problem in South Asia (India, Pakistan, Bangladesh, Nepal). Estimates from the Global Burden of Disease Study suggest that by the year 2020 India will have more individuals with atherothrombotic cardiovascular disease than any other region (1). Over the last 50 years, life expectancy in India has increased from 41 years between 1951 and 1961 to 61.4 years in the period 1991 to 1996. It is projected to reach 72 years by 2030. This change in life expectancy is due to a substantial decline in both infectious disease mortality and childhood deaths from perinatal causes. Furthermore, with increasing rates of urbanization in India, major changes in lifestyle patterns have occurred for a large proportion of individuals. This has led to a trend toward decreasing physical activity, increasing weight and, consequently, increasing rates of diabetes, hypertension and dyslipidemia in urban populations. The shift from a predominance of infectious diseases to a predominance of chronic diseases, such as cardiovascular disease or cancer, is called the "epidemiological transition."

See page 682

Various projections indicate that over the next 20 years the rates of atherothrombotic cardiovascular disease will rise substantially in developing countries, including India. These projections have at least three limitations. First, there are few good national or regional data available from many developing nations (including those in the Indian subcontinent) that document the rates of various cardiovascular diseases. Second, no large prospective cohort studies have been done in these regions that relate various risk factors to cardiovascular disease. Third, data suggest that migrant Indians have higher rates of cardiovascular disease compared to indigenous populations (2). Therefore, South Asians may have certain genetic or other risk factors that predispose them to higher risks of atherothrombotic complications for the same level of risk factors.

In this context, the Chennai Urban Population Study (CUPS), discussed in this issue of the *Journal* (3), is welcomed. This is a moderate-sized study done in a large South Indian city. The

sampling is primarily from a middle-class residential area and should not be assumed to represent the prevalence of disease either in the city of Chennai as a whole, in the state (Tamil Nadu) nor in the country. Nevertheless, the study is a major step in providing useful prevalence data and could potentially be the foundation for future larger and longer-term studies. The key findings of CUPS are the following. First, the rate of clearly documented ischemic heart disease (Q-wave myocardial infarctions [MI] or clear history of MI) is about 2.1%. An additional 8.5% had nonspecific changes on the electrocardiogram (ECG), but these findings are difficult to interpret given their nonspecificity, as well as the fact that T-wave changes and ST-segment changes were unrelated to the usual risk factors or age in this study. On univariate analyses, many of the classical risk factors, such as a history of diabetes, hypertension, dyslipidemia and others, were associated with the presence of coronary artery disease (CAD) (using documented MI or Q-waves on the ECG). However, marked differences in ages existed between those with and without documented CAD, so that on multivariate analyses only two risk factors (age and elevated cholesterol) were statistically significant. These data should not be interpreted as indicating that the classical risk factors (such as tobacco use, diabetes or hypertension) are of no importance in this South Asian population. Instead, this is likely a function of the very few events (under 50), such that the study had low power to detect real associations (beta-error).

How do the CUPS data compare with other data among South Asians? In India a few recent prevalence studies using variable methodologies have been done over the last few years (summarized by Gupta et al. [4]). The prevalence rates of coronary heart disease varied from 7.6% to 12.6%, but the criteria varied by study and many included ST-T changes, which are nonspecific. However, compared to the prevalence rates of clearly documented MI or Q-waves among migrant Indians in the UK (4.2%) (5) or Canada (5.2%) (6), the rates in Chennai, India, appear to be lower. Whether these differences are due to small sample sizes, to differing age groups covered by the studies, to the fact that the epidemiological transition has not yet had its full impact among urban Indians compared to those who have emigrated to the UK or North America, to differences in risk factor levels or to other differences in study design simply cannot be addressed at the moment.

Despite the useful information that the CUPS report provides, one should recognize its limitations so that future studies can be more informative. As stated earlier, the study is relatively small, with only 1,000 individuals and <50 cases of documented events of MI or Q-waves on the ECG. Therefore, any analyses correlating risk factors to disease prevalence is substantially underpowered, and the failure to show a clear relationship with the classical risk factors should not be interpreted as a lack of importance of these factors among South Asians. Second, the study at present is a prevalence study. The investigators intend to conduct a longitudinal follow-up of these individuals, and useful data regarding association of risk factors and disease should emerge in the future. It is hoped that the investigators will also expand their study so as to be substantially larger. Data from a case-control study in Bangalore (from the adjacent state of Karnataka) suggest that

some of the classical risk factors do indeed matter. For instance, Pais et al. (7) discovered that tobacco use (both cigarettes and "beedies," an indigenous form of smoking) is significantly associated with the risk of MI. In addition, this study showed a clear relationship among hypertension, diabetes and elevation of glucose levels, even within normal range, with MI. In particular, abdominal obesity (but not overall body mass index) was clearly related to disease. These data reflect similar experiences by other investigators such as McKeigue et al. (8).

Given that cardiovascular disease is already a major problem in India and is likely to be substantially more common in the future, much larger prevalence and cohort studies involving 50,000 to 100,000 individuals should be considered. Ideally, these studies should be geographically representative, as Indians in different parts of the country have both diverse lifestyles (diet, physical activity, among others) and social structures. Therefore, one would expect marked variations in risk-factor levels. Furthermore, there also appear to be marked urban and rural differences in both lifestyle and risk factors (9,10). An initial prevalence study involving a number of regions across the country, with long-term follow-up of these individuals for at least 10 years, will provide much needed data on the relationship between traditional and novel risk factors with the development of clinical disease. Several investigators in India are either conducting or are currently planning prevalence studies with the intention of following the individuals long term. Collaboration among these investigators would enable standardization of data collection across the studies. This would enable the results to be compared or even combined; this would make a substantial impact that would be of great value for several countries in the region.

Other important sources of data are registries for the management of common conditions. Clinical investigators should join together to develop simple registries to assess compliance with evidence-based guidelines, associated outcomes and complications of current patterns of practice. Registries have already been established in a limited number of centers for unstable angina (the OASIS Registry involves about 1,000 patients; unpublished data) and MI (11). A large national registry in acute coronary syndromes (the CREATE Registry) is currently underway. This registry aims to involve over 100 centers representing various regions of the country. Establishment of national registries would also be useful for stroke, heart failure, atrial fibrillation or valvular heart disease.

Finally, with the leadership of key scientists, national societies such as the Association of Physicians of India, the Cardiological Society of India, the Indian Council of Medical Research and the state and national governments, a broad and sustainable strategy for cardiovascular research and prevention should be developed. Such a strategy should recognize the unique societal influences, regional cultural diversity and the changing lifestyles as rates of urbanization continue to increase dramatically. Emphasis on prevention in the education of medical graduates will facilitate the involvement of the medical community in prevention efforts. Strong methods to control the use of and exposure to tobacco, coupled with promotion of healthy lifestyles, such as increased physical activity and decreased fat and carbohydrate consumption, should be an integral part of any national program. A comprehensive strategy should be designed so that all stages of the life cycle are targeted, including young children in schools and the prenatal period.

Globally, there is a realization that cardiovascular disease will soon overtake infectious diseases as the major cause of mortality and morbidity in low-income and middle-income countries. Consequently, the Global Forum of Health Research has established the Cardiovascular Disease in Developing Countries Initiative, with its secretariat based in Delhi, India. It is essential that this well-intentioned and very important effort is strongly supported by leading international agencies such as the World Health Organization, the World Heart Federation and the World Bank to ensure success. Collaborative efforts among active researchers located in several parts of India and other developing and developed countries could form the infrastructure for an international network dedicated to the prevention of cardiovascular disease (12).

REFERENCES

1. Murray JL, Lopez AD. The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability From Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020. Boston, MA: The Harvard School of Public Health, 1996.
2. McKeigue PM, Miller GJ, Marmot MG. Coronary heart disease in South Asians overseas: a review. J Clin Epidemiol 1989;42:597–609.
3. Mohan V, Deepa R, Rani SS, Premalatha G. Prevalence of coronary artery disease and its relationship to lipids in a selected population in south India–the Chennai Urban Population Study (CUPS No. 5). J Am Coll Cardiol 2001;38:682–7.
4. Gupta R, Gupta VP. Meta-analysis of coronary heart disease prevalence in India. Indian Heart J 1996;48:241–5.
5. McKeigue PM, Ferrie JE, Pierpoint T, Marmot MG. Association of early-onset coronary heart disease in South Asian men with glucose intolerance and hyperinsulinemia. Circulation 1993;87:152–61.
6. Anand SS, Yusuf S, Vuksan V, et al., for the SHARE investigators. Differences in risk factors, atherosclerosis, and cardiovascular disease between ethnic groups in Canada: the Study of Health Assessment and Risk in Ethnic Groups (SHARE). Lancet 2000;356:279–84.
7. Pais P, Pogue J, Gerstein H, et al. Risk factors for acute myocardial infarction in Indians: a case-control study. Lancet 1996;348:358–63.
8. McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. Lancet 1991;337:382–6.
9. sz;7;1Reddy KS. Cardiovascular diseases in India. World Health Stat Q 1993;46:101–7.
10. Gupta R. Lifestyle risk factors and coronary heart disease prevalence in Indian men. J Assoc Physicians India 1996;44:689–93.
11. George E, Hunsberger S, Savitha D, Pais P. Treatment of acute myocardial infarction: does the type of hospital make a difference? PPAMI Study Group. Indian Heart J 1999;51:161–6.
12. Ôunpuu S, Yusuf S, Negassa A, for the INTER-HEART investigators. INTER-HEART: a global study of risk factors for acute myocardial infarction. Am Heart J 2001;141:711–21.