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REVIEW

Regional variations in cardiovascular risk factors in India: India heart watch

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Abstract

Cardiovascular disease (CVD) is an important cause of mortality and morbidity in India. Mortality statistics and morbidity surveys indicate substantial regional variations in CVD prevalence and mortality rates. Data from the Registrar General of India reported greater age-adjusted cardiovascular mortality in southern and eastern states of the country. Coronary heart disease (CHD) mortality is greater in south India while stroke is more common in the eastern Indian states. CHD prevalence is higher in urban Indian populations while stroke mortality is similar in urban and rural regions. Case-control studies in India have identified that the common major risk factors account for more than 90% of incident myocardial infarctions and stroke. The case-control INTERHEART and INTERSTROKE studies reported that hypertension, lipid abnormalities, smoking, obesity, diabetes, sedentary lifestyle, low fruit and vegetable intake, and psychosocial stress are as important in India as in other populations of the world. Individual studies have reported that there are substantial regional variations in risk factors in India. At a macro-level these regional variations in risk factors explain some of the regional differences in CVD mortality. However, there is need to study the prevalence of multiple cardiovascular risk factors in different regions of India and to correlate them with variations in CVD mortality using a uniform protocol. There is also a need to determine the "causes of the causes" or fundamental determinants of these risk factors. The India Heart Watch study has been designed to study socioeconomic, anthropometric and biochemical risk factors in urban populations in different regions of the country in order to identify regional differences.

Key words: Cardiovascular disease; Risk factors; Socioeconomics; Epidemiology; Hypertension; Obesity; Lipids

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INTRODUCTION

Cardiovascular disease (CVD), including coronary heart disease (CHD) and stroke, is the largest cause of mortal-

ity in the world, and the majority of deaths occur in low- and middle-income countries such as India and China[1]. These diseases are epidemic in urban locations of these countries and are rapidly increasing in rural areas as well[2]. With demographic shifts, epidemiological transition and increasing urbanization associated with increase in CVD risk factors (smoking, sedentary lifestyle, obesity, hypertension and hypercholesterolemia), and a lack of policy directives aimed at chronic disease control, CVDs are poised to accelerate further[3]. This review summarizes the current information on CVD mortality in India with a focus on CHD. It evaluates studies that reported regional variations in CVD prevalence and mortality. The article also focuses on studies of risk factor prevalence, and highlights the urban-rural differences and regional variations in these risk factors. Finally, we identify gaps in existing knowledge regarding epidemiology of CVD in India and suggest the way forward for research to curb the CVD epidemic currently sweeping India. This article also sets the background for the India Heart Watch study, a cross-sectional and prospective epidemiological study, that is designed to study multiple socioeconomic and biological cardiovascular risk factors in different regions of the country.

CARDIOVASCULAR DISEASES IN INDIA

There are no detailed reports on CVD mortality by the Indian government. The World Health Organization (WHO) periodically reports on the proportion of deaths from CVD in India but trends are not reported due to lack of specific data. Prior to 1998, the Indian mortality data were obtained from predominantly rural populations where vital registration varied from 5% to 15%. Accordingly, the Registrar General of India reported that from the 1990s the proportion of mortality attributed to CVD or circulatory system diseases remained almost static at 15%-17%[4]. However, these rates were based on limited data, mainly rural, and the only significant information on CVD mortality in urban subjects was from Maharashtra. We previously discussed the shortcomings of these reports[4]. However, it was reported that there were significant regional variations, with high CVD mortality in Goa, Tamil Nadu, Andhra Pradesh and Punjab, and low mortality in the central Indian states of Uttar Pradesh, Madhya Pradesh and Rajasthan[4].

Since 2001, the Registrar General of India and Million Death Study investigators have systematically collected mortality statistics from all Indian states using the country-wide Sample Registration System[5]. In the first phase of this study from 2001-2003, causes of deaths in more than 113 000 subjects from 1.1 million homes were retrospectively analyzed using a validated verbal autopsy instrument[5]. CVD was the largest cause of deaths in males (20.3%) as well as females (16.9%) and led to about 2 million deaths annually. Mortality data from CVD in India are also reported by the WHO. The Global Status on Non-Communicable Diseases Report (2011)[1] has reported that there were more than 2.5 million deaths from CVD in India in 2008, two-thirds due to CHD and one-third to stroke. These estimates are significantly greater than those reported by the Registrar General of India, and shows that CVD mortality is increasing rapidly in the country.

There are national differences in cardiovascular mortality across the world. The report on CVD in low income countries by the United States Institute of Medicine[2] shows that there are substantial national variations. The highest age-adjusted mortality is observed in countries of central Asia, east and central Europe, some countries in Africa, while the lowest rates are observed in west European and north American countries. There are within-country variations also, and the report presents data on significant differences in regions and locations within countries and in many large nations such as the United States, Russia and China.

In India, CVD is the largest cause of mortality in all regions of the country. Table 1 shows the top 5 causes of deaths in different populations (rural *vs* urban, economically backward *vs* developed states, men *vs* women, and at all-ages *vs* middle aged individuals). CVD is the largest cause of mortality in each of these groups. There are large regional differences in cardiovascular mortality in India among both men and women[6]. The mortality is highest in south Indian states, eastern and north-eastern states and Punjab in both men and women, while mortality is the lowest in the central Indian states of Rajasthan, Uttar Pradesh and Bihar. Sub-analysis of the mortality trends shows that CHD mortality is higher in the south Indian states while stroke mortality is higher in the eastern Indian states[6]. There is no currently available information on trends in CVD mortality in India or different regions and states. The prospective phase of the ongoing Million Deaths Study[7] from 2004-2013 shall provide robust data on regional variations and trends in CVD mortality in India.

Morbidity

WHO has predicted that from years 2000 to 2020 disability-adjusted life years lost (DALYs) from CHD in India shall double in both men and women from 7.7 and 5.5 million, respectively[8]. It has also been reported that cerebrovascular diseases will account for more DALYs than CHD. These data do not report on regional variations within a large country such as India and more region-specific data are needed.

In the last 50 years there have been multiple cardiovascular epidemiological studies in India that have defined prevalence of CHD and stroke and identified the burden of disease[8]. Prevalence studies have diagnosed CHD using history and electrocardiographic changes (Q-wave, ST-T changes). A meta-analysis of these studies reported that prevalence rates have more than trebled in the Indian population[9]. The increase in CHD is largely an urban phenomenon and only recently a rapid rise in rural populations has been reported. Studies in the

Table 1 Top five causes of deaths in India classified according to areas of residence and gender

Rank	India (all age groups)	Economically backward states	Economically advanced states	Rural populations	Urban populations	Men	Women	Middle-age (25-69 yr)
1	Cardiovascular	Cardiovascular	Cardiovascular	Cardiovascular	Cardiovascular	Cardiovascular	Cardiovascular	Cardiovascular
2	COPD, asthma	Diarrhea	COPD, asthma	COPD, asthma	Cancers	COPD, asthma	Diarrhea	COPD, asthma
3	Diarrhea	Respiratory infections	Cancers	Diarrhea	COPD, asthma	Tuberculosis	COPD, asthma	Tuberculosis
4	Perinatal	COPD, asthma	Senility	Perinatal	Tuberculosis	Diarrhea	Respiratory infections	Cancers
5	Respiratory infections	Perinatal	Diarrheas	Respiratory infections	Senility	Perinatal	Senility	Ill-defined

Adapted from Registrar General of India Report[5]. COPD: Chronic obstructive pulmonary disease.

Table 2 Population attributable risks (%) of various cardiovascular risk factors for coronary heart disease and stroke in [11,12]

Risk factor	INTERHEART (acute myocardial infarction)	INTERSTROKE (thrombotic or hemorrhagic strokes)
Apolipoprotein A/B ratio	49.2	24.9
Hypertension	17.9 (history)	34.6
Smoking	35.7	18.9
Diabetes history	9.9	5.0
High waist-hip ratio	20.1	26.5
Psychosocial stress	32.5	9.8
Regular physical activity	12.2	28.5
Diet/diet score	13.7	18.8
Lack of alcohol intake	6.7	3.8
Cardiac causes	-	6.7

middle of the last century reported a low prevalence of 1%-2% in urban locations and 0.5%-1% in rural locations with very little urban-rural difference. In the intervening years the CHD prevalence in urban areas increased to10%-12% while it increased to only 4%-5% in rural adults[8]. Stroke prevalence studies report a substantial burden of stroke in urban and rural subjects[8]. Stroke is also increasing in India and incidence registries using population-based surveillance have reported that the annual incidence of stroke varies from 100-150/100 000 population in urban locations with greater incidence in rural regions[10]. However, these studies provide only limited information and there is a need for properly designed prospective studies to correctly identify trends. Regional variations in the burden of CVD using a uniform protocol have not been studied and there is a need to conduct such studies.

CARDIOVASCULAR RISK FACTORS

There are no prospective cardiovascular epidemiological studies that have identified risk factors of importance in India. Multiple case-control studies exist. The largest of these case-control studies is the INTERHEART study[11]. This study was performed in 27 000 cases of acute myocardial infarction and controls in 52 countries of the world and assessed multiple cardiovascular psychosocial and biological risk factors in both the groups. Of these subjects more than 2000 cases and controls were from South Asian regions[11]. This study reported that standard risk factors such as smoking, abnormal lipids, hypertension, diabetes, high waist-hip ratio, sedentary lifestyle, psychosocial stress, and a lack of consumption of fruit and vegetables explained more than 90% of acute CHD events in South Asians. Similar conclusions were reached in smaller case-control studies[8].

The INTERSTROKE study[12] reported 10 common risk factors explained more than 90% of incident hemorrhagic and thrombotic strokes. The risk factors were similar to the INTERHEART study (hypertension, smoking, dyslipidemia, diabetes, high waist-hip ratio, sedentary lifestyle, psychosocial stress, poor quality diet, and cardiac causes), but the population-attributable risks were different with greater importance of hypertension and lesser importance of diabetes and lipids (Table 2).

Reviews of epidemiological studies suggest that all the major cardiovascular risk factors are increasing in India (Figure 1). Tobacco production and consumption has increased significantly. Smoking is increasing among young subjects (20-35 years), according to second and third National Family Health Surveys (NFHS)[6]. In urban populations, smoking is increasing among the low educational status subjects[13]. The prevalence of hypertension has increased in both urban and rural subjects and presently is 25%-40% in urban adults and 10%-15% among rural adults (Table 3)[14]. Lipids levels are increasing and serial studies from a north Indian city reported increasing mean levels of total, low density lipoprotein and non-high density lipoprotein (HDL) cholesterol and triglycerides, and decreasing HDL cholesterol[15]. Although there are large regional variations in the prevalence of diabetes it has more than quadrupled in the last 20 years from < 1%-3% to 10%-15% in urban areas and 3%-5% in rural areas (Figure 1)[16]. Studies have reported increasing obesity as well as truncal obesity due to sedentary lifestyles, and psychosocial stress in the country[8].

Regional variations

In India there has been no national study that used uniform methodologies to assess regional variations in the prevalence of multiple cardiovascular risk factors. A study in the 1940s by Chopra *et al*[17] assessed the difference in mean blood pressure (BP) levels among army recruits belonging to different states in India, and reported

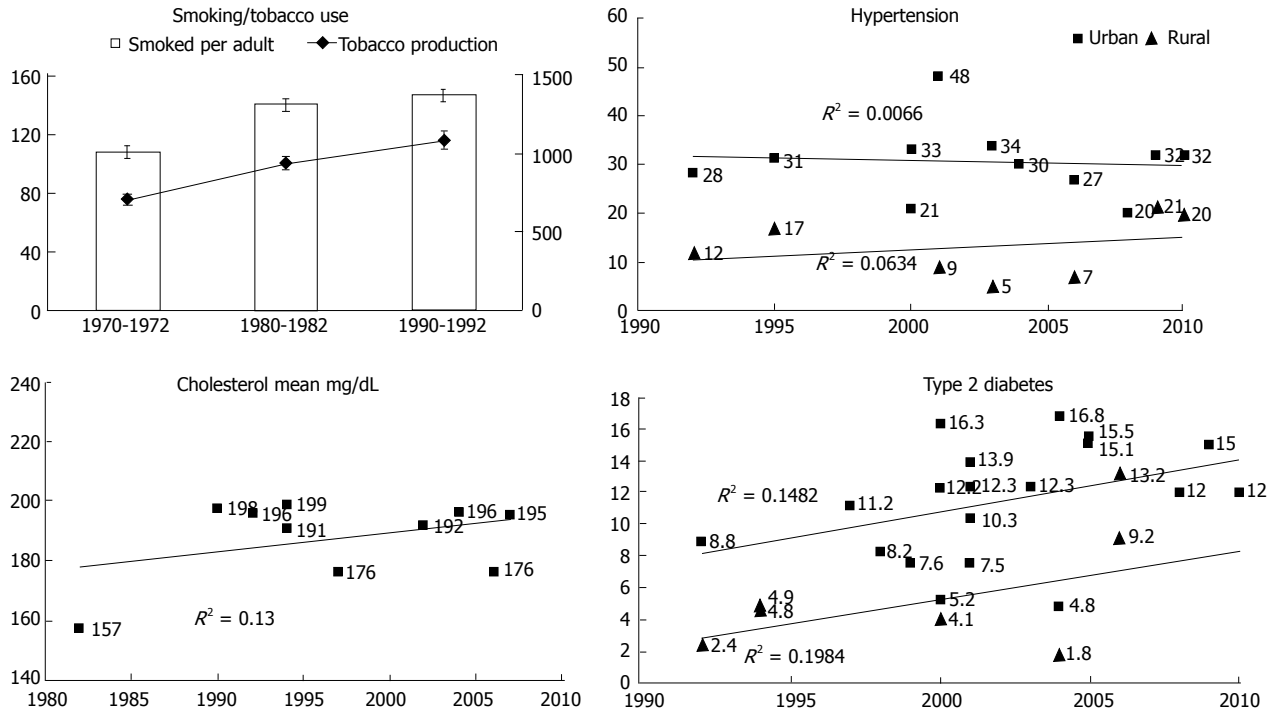

Figure 1 Secular trends in prevalence of major coronary risk factors in India. There is increasing prevalence of smoking, hypercholesterolemia and diabetes while hypertension prevalence has stabilised in urban (squares) and increasing in rural locations (triangles).

Table 3 Recent studies of hypertension prevalence in India

First author	Year	Place	Age (yr)	Sample size	Prevalence (%)
Urban Populations					
Gupta R	1995	Jaipur	≥ 20	2212	30.9
Anand MP	2000	Mumbai	30-60	1662	34.0
Gupta R	2002	Jaipur	≥ 20	1123	33.4
Shanthirani CS	2003	Chennai	≥ 20	1262	21.1
Gupta PC	2004	Mumbai	≥ 35	88 653	47.9
Prabhakaran D	2005	Delhi	20-59	2935	30.0
Reddy KS	2006	National	20-69	19 973	27.2
Mohan V	2007	Chennai	≥ 20	2350	20.0
Kaur P	2007	Chennai	18-69	2262	27.2
Yadav S	2008	Lucknow	≥ 30	1746	32.2
Rural Populations					
Gupta R	1994	Rajasthan	≥ 20	3148	16.9
Kusuma Y	2004	Andhra	≥ 20	1316	21.0
Hazarika NC	2004	Assam	≥ 30	3180	33.3
Krishnan A	2008	Haryana	15-64	2828	9.3
Todkar SS	2009	Maharashtra	≥ 20	1297	7.2
Bhardwaj R	2010	Himachal	≥ 18	1092	35.9
By Y	2010	Karnataka	≥ 18	1900	18.3
Kinra S	2010	National	20-69	1983	20.0

higher mean levels in those from north Indian states as compared to the south. Malhotra[18] performed a study among railway employees in the 1960s to investigate variations in dietary habits and cardiovascular mortality in different regions of India. Greater cardiovascular mortality was observed among north Indian railway men, which was related to greater consumption of calories and fats. The multisite Prevalence of Diabetes in India Study[19] focused on the epidemiology of diabetes prevalence in the country and performed studies in all large Indian states, but did not report on regional variations. The multi-city Diabetes Epidemiology Study in India reported on differences in prevalence of diabetes in 8 urban locations[20]. A higher prevalence of diabetes was reported in south India compared with other regions. NFHS-3[21] investigated the prevalence of self-reported diabetes and reported a low prevalence of this condition, which precluded further analyses for regional differences.

A few studies evaluated the prevalence of multiple cardiovascular risk factors in 2 or more cities in India using uniform methodology. An Indian Council of Medical Research (ICMR) study in the 1990s evaluated risk factors in Delhi in north India and Vellore in south India and reported a significantly greater prevalence of risk factors in north India[22]. A multisite Indian Industrial Population Surveillance Study (8 sites) reported variable prevalence of risk factors among industrial workers[23]. A multisite study involving 5 rural and 4 urban sites in middle-aged women reported the prevalence of cardiovascular risk factors in different regions of India[24]. The results focused on assessment of urban-rural differences and not on regional variations. An ICMR surveillance study evaluated the differences in self-reported prevalence of behavioral and anthropometric cardiovascular risk factors in different Indian states in rural and urban populations (Table 4)[25]. Epidemiological studies were performed in urban and rural populations in states of south India (Kerala, Tamilnadu, Andhra Pradesh), west India (Maharashtra), central India (Madhya Pradesh), east India (Mizoram) and north India (Uttarakhand). The prevalence of smoking was highest in Mizoram

Table 4 Risk factor prevalence (%) among men and women (15-64 years) in 8 Indian states in Indian Council of Medical Research Noncommunicable Disease Risk Factor Surveillance Study[25]

Risk factor	Andhra Pradesh		Madhya Pradesh		Maharashtra		Mizoram		Kerala		Tamilnadu		Uttarakhand	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
Numbers	2719	3499	2857	2996	3084	3007	2297	2198	1710	3128	2077	3028	2147	3286
Current smoking	31.5	4.0	41.2	0.9	15.9	2.5	67	18.8	27.3	0.2	27.4	0.0	35.2	5.0
Smokeless tobacco use	13.6	4.5	53.8	22.6	40.7	23.6	46.5	55.4	7.0	3.4	13.6	8.4	21.0	2.2
Low physical activity	55.9	79.7	33.5	52.0	75.4	87.7	60.9	82.4	64.7	86.2	57.3	74.2	64.6	69.7
Obese, BMI ⩾ 25 kg/m^2	19.4		8.2		13.1		10.3		27.1		22.6		14.5	
Hypertension	16.6		21.1		20.1		19.4		18.0		17.7		18.8	
Diabetes history	2.7	1.7	0.6	0.6	0.9	1.0	0.7	0.5	6.5	5.3	3.4	2.6	1.2	1.1

BMI: Body mass index.

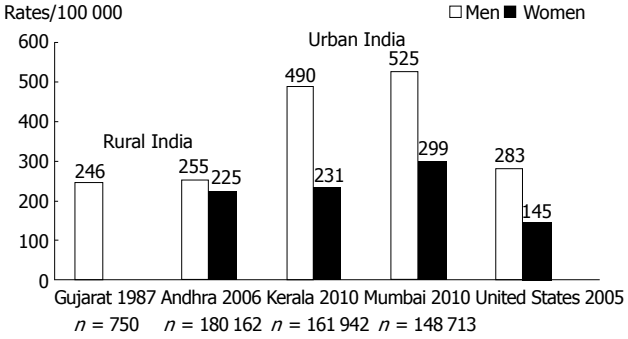

Figure 2 Prospective studies of cardiovascular mortality in urban and rural Indian populations[29-32]: Age-adjusted cardiovascular disease mortality in urban India is almost twice that of the United States[2].

and overweight/obesity, hypertension and self-reported diabetes highest in the south Indian states of Kerala and Tamilnadu. The study focused on limited lifestyle and anthropometric risk factors and no data were obtained for more important risk factors such as lipid abnormalities and hyperglycemia. The INTERHEART study reported that these biochemical risk factors explained more than 50% of cardiovascular events among South Asians[11].

On the other hand, reviews of CVD risk factor epidemiological studies from India showed significant regional variations in the prevalence of the important CVD risk factors of smoking, obesity, hypertension, diabetes and lipid abnormalities. The second and third NFHS reported the prevalence of smoking and tobacco use in populations of all Indian states[6]. There were significant state-level and regional variations in smoking[6,21]. The smoking rates were the highest in eastern Indian states and the lowest in Punjab[26]. The second and third NFHS also reported on differences in prevalence of overweight and obesity among men and women in different Indian states[21]. Prevalence of overweight and obesity was the highest in southern and northern Indian states and the lowest in central Indian states[27].

Regional variations in other cardiovascular risk factors are not well reported within a single study using uniform methodology. A review of epidemiological hypertension studies reported that the prevalence of hypertension was significantly higher in urban populations in India compared with rural populations[14]. However, no consistent trends were observed for regional variations. In rural populations the prevalence of hypertension was higher in Rajasthan while in urban studies prevalence rates were not significantly different in different regions[14]. The prevalence of hypertension was highest in metropolitan cities such as Mumbai and lower in less populated cities (Table 3)[28]. An important finding of the current studies is that the prevalence of hypertension in rural populations is now approaching the rates in urban subjects (Figure 1).

Urban-rural differences

CVD is epidemic in urban regions of low income countries such as India[8]. Cardiovascular mortality data from India has reported large regional variations with annual mortality rates greater than 250/100 000 in southern and eastern regions of the country and less than 100/100 000 in central India[6]. There are large urban-rural differences in cardiovascular mortality also, with rates of less than 200/100 000 in rural areas and 450-500/100 000 in metropolitan urban locations. Only a few prospective studies of cardiovascular mortality are available in India. A small study in rural Gujarat[29], and a larger study in rural Andhra Pradesh[30], reported age-adjusted annual mortality rates of 200-250/100 000 while studies in urbanized Kerala[31] and Mumbai[32] have reported very high cardiovascular mortality with age-adjusted rates approaching 500/100 000 for men and 250/100 000 for women. These rates are almost twice that of United States[1] (Figure 2).

The causes for these urban-rural differences in CVD mortality have not been systematically evaluated, but previous studies from India have reported that there are significant urban-rural differences in cardiovascular risk factors[8]. The prevalence of smoking is greater in rural men, while all other risk factors such as sedentary lifestyle, obesity, central obesity, hypercholesterolemia, diabetes and metabolic syndrome are more prevalent in urban men and women[33]. A recent nationwide study among women has reported a greater prevalence of multiple CVD risk factors in urban women (Table 5)[24]. This is similar to previous studies on urban-rural differences in cardiovascular risk factors using uniform protocols

Table 5 Greater prevalence of cardiovascular risk factors among urban women in India[24]

Variable	Urban (n = 2008)	Rural (n = 2616)	Age-adjusted urban-rural relative risk (95% CI)
Smoking/tobacco use			
Current users	326 (19.6)	871 (41.6)	0.35 (0.18-0.65)[1]
Smoking	14 (0.7)	276 (10.6)	0.09 (0.01-0.70)
Non-smoked tobacco use	325 (16.2)	607 (23.2)	0.64 (0.31-1.30)
Sedentary lifestyle PALs < 1.55 units	1406 (71.0)	1558 (60.1)	1.63 (0.90-2.94)
Overweight/obesity			
BMI 23.0-24.99 kg/m^2	355 (11.6)	324 (12.5)	0.91 (0.40-2.11)
BMI 25.0-29.99 kg/m^2	640 (31.7)	451 (16.8)	2.30 (1.12-3.47)[1]
BMI ≥ 30.0 kg/m^2	288 (13.9)	152 (5.7)	2.55 (1.61-3.49)[1]
Truncal obesity			
WHR > 0.9	880 (44.3)	318 (13.03)	5.26 (2.61-10.63)[1]
Waist circumference > 90 cm	638 (31.4)	226 (8.4)	5.17 (2.24-11.94)[1]
Hypertension	925 (48.2)	746 (31.6)	1.96 (1.10-3.49)[1]
Hypercholesterolemia ≥ 200 mg/dL	552 (27.7)	322 (13.5)	2.39 (1.17-4.88)[1]
Diabetes (history or fasting glucose ≥ 126 mg/dL)	292 (15.1)	98 (4.3)	4.24 (1.35-13.26)[1]

[1]Significant. PAL: Physical activity levels; WHR: Waist-hip ratio; BMI: Body mass index.

and have been reported from Haryana, Delhi, Rajasthan and Tamilnadu[8].

The higher prevalence of cardiovascular risk factors in urban areas in India is in contrast to high income countries where the CVD risk factors are equal in urban and rural areas[34]. This is due to advancing disease and epidemiological transition and it is likely that the prevalence of risk factors will change in India with socioeconomic development of rural areas. There is recent evidence that, in more developed states of India such as Kerala, the rural-urban differences in cardiometabolic risk factors have largely disappeared and the risk factors are equal or slightly greater in rural subjects[35]. Whether a similar situation emerges in other Indian states is a matter for future studies. Recent studies in certain states have reported a high prevalence of diabetes (Figure 1) and hypertension (Table 3) in some rural locations in south and west India.

Trends in risk factors

An important focus of recent studies is the changing trends in cardiovascular risk factors. Reviews show that all major risk factors are increasing in India (Figure 1)[36]. In the last 30 years, the prevalence of hypertension and hypercholesterolemia has doubled while that of diabetes has trebled. However, there are almost no studies that have evaluated risk factors using a prospective cohort design. The Jaipur Heart Watch studies in India evaluated multiple cardiovascular risk factors in urban middle-class subjects using a multiple cross-sectional study design over a 20-year period from 1991 to 2010[37]. Over this period in these urban subjects, the prevalence of smoking declined, hypertension did not change significantly (due to increased awareness and treatment), while all other risk factors such as obesity, truncal obesity, hypercholesterolemia, diabetes and metabolic syndrome increased significantly[37]. No similar studies that have evaluated multiple cardiovascular risk factors are available from India.

The Global Burden of Diseases Chronic Disease Risk Factors Collaborating Group has reported 35-year (1980-2005) trends in mean levels of body mass index (BMI), systolic BP and cholesterol in 199 high-income, middle-income and low-income countries[38]. These studies evaluated trends in these risk factors using data from local and regional population-based epidemiological studies. A trend for increasing BMI was observed in all 3 regions, with greatest increase in high-income countries and a lesser increase in low-income countries[38]. Mean systolic BP declined in high- and middle-income countries but increased in low-income countries and is now more than in high-income countries[38]. Mean cholesterol levels have also declined in high- and middle-income countries but have increased in low-income countries[38]. The India specific data are similar to the overall trends in low-income countries.

GAPS IN KNOWLEDGE

There are significant gaps in the knowledge of the epidemiology of CVD and associated risk factors in countries of the South Asian region, such as India. The mortality data have been inadequately collected and collated and there is little information on regional variations in CVD incidence and mortality. There are no national studies that have evaluated the disease incidence and prevalence. Studies in similar densely populated regions in Europe[39], North America[40] and China[41] have reported significant regional variations in CVD mortality, CVD prevalence and incidence, and major cardiovascular risk factors. CVD mortality is greater in north European countries than in south Europe[39]. This is associated with greater prevalence of hypertension, hypercholesterolemia and diabetes in the northern European countries. CVD mortality is greater in the north of England than in the south, and is related to socioeconomic factors as well as a higher prevalence of smoking, obesity and lipid abnormalities[42]. CVD mortality, especially stroke, is higher in

the south-west of the United States[40] associated with a greater prevalence of abnormal lifestyles, obesity and hypertension. In China, CVD, especially stroke mortality, is greater in the north-east[41], and this is due to a greater prevalence of obesity and hypertension.

In India, regional variations in cardiovascular risk factors such as smoking, obesity, hypertension, diabetes and lipid abnormalities have not been systematically studied. The government of India sponsored the National Sample Survey Organization surveys and the NFHS have been conducted for many years, but these have not focused on non-communicable diseases and risk factors. Only in the recent NFHS-2 and NFHS-3 has there been an attempt to quantify smoking and tobacco use and adult body weight[21,26]. Other risk factors have not been studied. There have been a number of *ad hoc* population-based surveys for estimation of CVD risk factor prevalence in India as reported above[8]. All these studies have been performed by local investigators using different age groups, variable sample sizes, non-uniform methodology, improper statistical techniques, and reported results inconsistently. There are no prospective studies in India that have evaluated either the incidence of CVD or risk factor associations. The Prospective Urban Rural Epidemiological (PURE) study is the only large study which is prospectively identifying the risk factor-CVD association[43]. Finally, due to lack of national data there are no national efforts to initiate policy change for controlling the CVD epidemic[3]. There are no initiatives to change the population-wide distribution of risk factors or to evaluate the efficacy of high-risk approach for risk factor control and disease management.

There is an obvious need to perform multisite and multicity studies for identification of cardiovascular risk factor prevalence and their trends in different regions of India using uniform methodology. Such studies have been reported from Europe and North America. The United States National Health and Nutrition Evaluation Surveys[44] have periodically assessed risk factors in the country and have reported continuing greater prevalence of hypertension and metabolic risk factors in the south-eastern states. The British Regional Heart Study[45] and many studies in Europe have reported variable prevalence of risk factors in different regions of these countries. Studies in Europe have reported greater prevalence of cardiovascular metabolic risk factors in the North and East European countries as compared to the southern countries[39]. The CARMELA study in 7 Latin American cities in Argentina, Chile, Colombia, Ecuador, Mexico, Peru and Venezuela reported a high prevalence of smoking, hypertension, hypercholesterolemia and diabetes in these cities[45]. The study reported a high prevalence of all these risk factors in urban communities in these countries. Regional studies in China[41] have reported greater hypertension and hypercholesterolemia prevalence in the north-east regions as compared to others.

INDIA HEART WATCH

An investigator-initiated study to identify regional differences of CVD risk factors in India has been organized. Funding has been obtained from South Asian Society of Atherosclerosis and Thrombosis, Bangalore and Minneapolis (United States). The protocol was devised and the study was approved by the institutional ethics committee of the national coordinating center. The proforma focused on demographic characteristics, family history of CHD, stroke, hypertension and diabetes and self-reported details of smoking, alcohol intake, hypertension, diabetes, lipid abnormalities, CVD, physical activity and dietary fat and fruit intake. The proforma is similar to previous studies performed by this group[13,15,37]. Measurements focus on height, weight, sitting BP, waist and hip dimensions, using methodologies prescribed by WHO[46]. Biochemical measurements in fasting blood samples are performed, with uniform sample collection and methods at a national laboratory (Thyrocare Technologies Ltd, Mumbai, India, www.thyrocare.com).

The study has been planned according to the regional variations in cardiovascular mortality reported above[4-6]. Medium-sized cities were identified in each of the large states of India and investigators who had a track record of research in CVD or diabetes epidemiology were invited to participate in the study. A total of 20 investigators were invited from large states of India and 15 agreed to participate in the study. The cities were in northern India (Jammu, Chandigarh, Karnal, Bikaner), western India (Ahmedabad, Jaipur), eastern India (Lucknow, Patna, Dibrugarh), southern India (Madurai, Hyderabad, Belgaum) and central India (Jaipur, Indore, Lucknow). The study used simple cluster sampling at each study site. A middle-class location was identified in each city. This depended upon the municipal classification which is based on municipal reserve land prices and is periodically revised by local government and municipal agencies for taxation purpose. This is based on the cost of land, type of housing, public facilities (roads, water supply, electricity supply and gas), and educational and medical facilities. A sample size of about 250 men and 250 women (n = 500) at each site is considered adequate by WHO to identify a 20% difference in the mean level of biophysical and biochemical risk factors[46]. About 800-1000 subjects in each location were invited to participate in the study, to ensure participation of at least 500 subjects at each site. This number was based on our earlier surveys in urban areas where the response rate for participation in such surveys has been about 60%-70%[13,15,37]. The surveys were preceded by meetings with community leaders to ensure good participation. The subjects were invited to a community center within each locality either twice or thrice a week depending upon the investigator's schedule. Measurements focused on demographic history, socioeconomic status, educational status, type of family, any major previous illnesses, history of known hyperten-

sion, diabetes, lipid abnormalities and CVD. Details of lifestyle risk factors such as smoking, intake of alcohol, dietary fat, fruit and vegetables, physical activity, psychosocial factors and depression were inquired using the validated INTERHEART study questionnaire[47]. Physical examination emphasized the measurement of height, weight, waist and hip, and proper BP measurement. A fasting blood sample was obtained from all individuals after at least 8 h fasting. The study is powered to assess prevalence of various CVD risk factors in urban locations in India, identification of regional differences[6], assessment of influence of social development index[48] on risk factors, and lifestyle determinants of various risk factors. This study is not comparable to the Indian arm of the PURE study[49]. PURE is a prospective study localised to five urban and five rural locations, three in south (Bangalore, Chennai, Trivandrum) and two (Jaipur, Chandigarh) in north India while India Heart Watch has centres all over the country. The PURE study has recruited more than 28 000 subjects from these centres and is larger than the India Heart Watch. It also has a prospective design with proposed follow-up of these individuals for 15 years and is unlike the India Heart Watch study which essentially is a study with cross sectional design and limited follow-up.

CONCLUSION

In conclusion, this review shows that there are wide regional variations in cardiovascular disease mortality and burden in India. Apart from the well known gender based differences, there are variations in mortality in different states and in urban and rural regions and among different socioeconomic groups within states. Although no nationwide study of risk factors exists, review suggests that there are significant state-level and rural-urban differences in major cardiovascular risk factors of smoking, obesity, central obesity, hypertension, hypercholesterolemia and diabetes. However, there is need to perform nationwide studies for determining cardiovascular risk factors using uniform protocols to assess regional differences. There is also a need to determine the "causes of the causes" or primordial determinants of these risk factors. The India Heart Watch study shall be able to provide some of these answers.

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