Indian Heart Journal 70 (2018) 721–730

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Review Article

Epidemiologic studies targeting primary cardiovascular disease prevention in South Asia

Hasan Rehman[a], Zainab Samad[b], Shiva Raj Mishra[c,d], Anwar T. Merchant[e,f], Jagat P. Narula[g], Sundeep Mishra[h], Salim S. Virani[i,j,*]

[a] Houston Methodist Hospital, Houston, TX, USA
[b] Division of Cardiology, Department of Medicine, Duke University Medical Center, Durham, NC, USA
[c] Nepal Development Society, Bharatpur-10, Chitwan, Nepal
[d] Center for Longitudinal and Lifecourse Research, Faculty of Medicine, University of Queensland, Herston, QLD 4006, Australia
[e] Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA
[f] WJB Dorn VA Medical Center, Columbia, SC, USA
[g] Marie-Josée and Henry R. Kravis Center for Cardiovascular Health Mount Sinai School of Medicine, USA
[h] Department of Cardiology, All India Institute of Medical Sciences, New Delhi, India
[i] Section of Cardiology, Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX, USA
[j] Section of Cardiovascular Research, Department of Medicine, Baylor College of Medicine, Houston, TX, USA

ARTICLE INFO

Article history:
Received 2 July 2017
Accepted 16 January 2018
Available online 31 January 2018

Keywords:
Primary prevention
South Asia
Cardiovascular disease
Epidemiology
India
Pakistan
PURE study

ABSTRACT

South Asia has experienced a 73% increase in healthy life years lost due to ischemic heart disease between 1990 and 2010. There is a lack of quality data relating to cardiovascular risk factors and disease from this region.

Several observational and prospective cohorts in South Asia have been established in recent times to evaluate the burden of cardiovascular disease and their risk factors. The Prospective Rural Urban Epidemiology (PURE) study is the largest of these studies that has provided data on social, environmental, behavioral and biologic risk factors that influence heart disease and diabetes. Some studies have also borrowed data from large datasets to provide meaningful insights. These studies have allowed a better understanding of cardiovascular disease risk factors indigenous to the South Asian population along with conventional risk factors. Culturally sensitive interventions geared towards treating risk factors identified in these studies are needed to fully realize the true potential of these epidemiologic studies.

1. Introduction

Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality worldwide.[1] They account for an estimated 17.5 million deaths annually, more than 75% of which occur in lower middle-income countries (LMIC).[2] While the deaths rates due to CVD have declined in several high-income countries (HIC), the trend has not been the same in LMIC.[3,4] South Asia, that represents one of the most densely populated regions in the world, experienced an increase of 73% in healthy life-years lost due to ischemic heart disease between 1990 and 2010, compared to a global increase of 30%.[5] Moreover, South Asians (people from India, Pakistan, Bangladesh, Nepal, Sri Lanka) have been shown to experience their first myocardial infarction (MI) almost 10 years earlier than compared to people from other countries.[6] While growing life expectancy accounts for some of this increase in disease burden, a rise in age-standardized death rates in the region suggest the role of other contributing factors, such as an increase in

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CARRS, Center for cArdiometabolic Risk Reduction in South-Asia; CVD, cardiovascular disease; DHS, Dhulikhel Heart Study; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; hsCRP, high sensitivity C-reactive protein; HIC, high-income countries; HTN, hypertension; LIC, low-income countries; LMIC, Lower middle-income countries; MET, metabolic equivalent of task; MI, myocardial infarction; MIC, Middle-income countries; NCD, Non-communicable diseases; NIRAM, noncommunicable disease Initiatives and Research at AMrita; PROMIS, Pakistan Risk of Myocardial Infarction Study; PURE, Prospective Rural Urban Epidemiology; PURSE-HIS, Population Study of Urban Rural and Semiurban Regions for the Detection of Endovascular Disease and Prevalence of Risk Factors and Holistic Intervention Study; SLDCS, Sri Lanka Diabetes Cardiovascular Study; UMIC, upper middle-income countries; URCDS, Urban Rural Chronic Diseases Study.

* Corresponding author at: Health Services Research and Development (152), Michael E. DeBakey Veterans Affairs Medical Center, 2002 Holcombe Blvd, Houston, TX, USA.
E-mail address: virani@bcm.edu (S.S. Virani).

https://doi.org/10.1016/j.ihj.2018.01.029
0019-4832/

risk exposures linked with dietary, demographic and epidemiologic transitions, as well.

Reduction in risk factors and improved CVD management are credited with the decrease in overall rates of cardiovascular mortality.[4] While large longitudinal cohorts have been a source of quality data relating to CVD in Western countries, this has not been the case in South Asia. Much of the data available is from cross-sectional studies, and only recently has there has been an effort to cover this gap in knowledge. Both, institutional and population based registries, are either absent or remained at primitive stage in these countries, as a result of which the vast array of the medical data that has been collected so far is underused.

2. Objective

In this review, we examine large multi-institutional observational cohorts, epidemiological surveys and population surveys that have targeted study of CVD risk factors in South Asia. This will serve not only to illustrate preexisting data but also help identify gaps in knowledge. The review is not designed to be exhaustive but is rather meant to highlight representative studies. Some of these studies are discussed in Table 1.

3. Large cohorts

3.1. Prospective Rural Urban Epidemiology (PURE) study

The PURE study is a large, prospective, collaborative global study that is designed to investigate social, environmental, genetic, behavioral and biologic factors that influence obesity and chronic health conditions such as heart disease, diabetes and cancer. It consists of two components: (i) a cross-sectional component that examines the relationship between societal determinants, risk factors and prevalence of non-communicable health diseases (NCD) and (ii) a cohort component that studies the relationship between societal determinants and the incidence of NCD events, and changes in rate of selected risk factors.[7] Food and nutritional policy, built environment, psychosocial/socioeconomic factors and tobacco were used as the domains of societal determinants. Initiated in 2003, the study recruited more than 153,996 adults aged between 35 years and 70 years by 2009 from 628 communities in 17 different countries (3 HICs, 7 upper middle-income countries (UMIC), 3 LMICs and 4 lower-income countries (LIC)) with an aim to follow them for 10 years.[8] It is currently in its 9th year of study. A community was defined as a group of people with common characteristics residing in a common geographical area. This was likely to be a group of streets or a contiguous set of postal codes. More than 30,000 participants were from South Asia (Bangladesh, India and Pakistan) that constituted 3 of the 4 LICs in the study with Zimbabwe being the fourth.

In an analysis to determine cardiovascular risk and events in the study population, the PURE investigators utilized the INTERHEART Risk score to quantify risk factor burden.[9] The INTERHEART Risk score is a tool validated to quantify risk burden without the use of laboratory testing.[10] A higher score indicates higher risk burden. The study showed that the mean INTERHEART Risk Score (cardiovascular disease burden) was significantly lower in LICs (8.28; 95% confidence interval [CI], 8.23 to 8.34) compared to both, HICs (12.89, 95% CI 12.79 to 12.98) and middle-income countries (MIC) (10.47; 95% CI, 10.43 to 10.50, $p < 0.001$). In addition, the study observed that within LICs, urban areas had a higher INTERHEART Risk score (9.09) compared to rural areas (7.57, $p < 0.001$). After a mean follow up of 4.1 years, the rate of major cardiovascular events was 6.43 events per 1000 person-years of follow-up in LICs which was significantly higher compared to HICs (3.99 events per 1000 person-years of follow-up) and MICs (5.38 events per 1000 person years of follow-up). Compared to rural areas, urban areas had lower major cardiovascular event rates (6.67 vs 7.70 events per 1000 person-years of follow-up, $p < 0.001$). Case fatality rates among participants with major cardiovascular events were highest in LIC (17.3%) compared to MIC (15.9%) and HIC (6.5%, $p = 0.01$). The authors concluded that, while the INTERHEART Risk score predicts the relative rate of major cardiovascular events in each stratum, the event rates vary within country income groups. The study hence showed that even though LICs had a lower CVD risk factor burden, they had higher rates of major cardiovascular events and a greater risk of death from these events. Similarly, rural areas had more cardiovascular events compared to urban areas despite having a lower CVD risk factor burden. The absence of healthcare systems addressing CVD outcomes in resource depleted settings was proposed as a possible explanation of these findings.

In another study that assessed prevalence, awareness, treatment and control of hypertension (HTN), it was shown that only 40.4% of the 9751 participants from South Asia with HTN ($BP \geq 140/90$ mmHg) were aware of their disease. Furthermore, a mere 31.9% (3113 out of 9751) were being treated, 40.6% (1264 out of 3113) of whom had controlled blood pressures ($BP < 140/90$ mm Hg).[11] Awareness of hypertension was lower in South Asia compared with the overall population (40.4 vs 46.5%), however, among those who were aware of hypertension control was greater in South Asia compared with the overall population (40.6% vs 32.5%). When rural and urban areas were compared in LICs, hypertension prevalence (31.5% vs 44.4%), awareness (31.2% vs 48.4%), treatment (19.9% vs 36.1%) and overall control (6.9% vs 12.8%) were all lower in rural areas compared to urban areas. The use of blood pressure lowering medications was lowest in participants in LICs (31.7%) compared to those in LMICs (36.9%), UMICs (48.3%), and HICs (46.7%). The findings reflect poor knowledge of the disease and its sequelae, likely due to a lack of access to healthcare in LICs, being a significant factor in effective disease management.

PURE study investigators have also evaluated the availability, affordability and consumption of fruits and vegetables.[12] Results showed that the mean daily serving of fruits and vegetables was 2.14 servings daily in LICs compared to 3.76 servings daily in the overall study population. Using available household income data, the absolute cost (adjusted by purchasing price parity, proportion of household income spent on one serving of vegetables and fruits and daily income per household member) of one serving of fruits was highest in LICs. This translated to roughly 57.4% people in LICs being unable to afford the recommended daily intake of fruits and vegetables compared to 0.25% people in HICs. Similarly, when affordability of medications was assessed in another study, it was found that approximately 60% of the households in LICs could not afford four major CVD medications (aspirin, statins, beta-blockers and angiotensin-converting-enzyme inhibitors/angiotensin-receptor blockers).[13] This is in comparison to 0.14% households in HICs. This was despite the absolute cost of medications being lower in all LICs in the study, except India. Furthermore, these medications were only available in 25% of urban and 3% of rural communities in LICs. These findings highlight the significant financial and logistic obstacles faced by the people in LICs (which include South Asian countries) in achieving recommended lifestyle and treatment goals to improve CVD related outcomes.

In another analysis, the PURE investigators examined the effects of cigarette and '*bidi*' smoking on cardiovascular health in South Asia alone.[14] '*Bidis*' are hand-rolled tobacco products commonly smoked in South Asia. The study only included men due to low smoking prevalence among women and showed that of the 14,919 men included in the study, 43.4% smoked tobacco (cigarettes or *bidi*). After a mean follow-up of 5.6 years, the study found that heavy *bidi* smokers (>10 pack-years) had the highest adjusted incidence of cardiovascular events (5.1%, Hazard Ratio [HR]: 1.55,

Table 1
Design of selected studies targeting primary cardiovascular disease prevention in South Asia.

Study Name, Region Studied, Year of Study Name	Region Studied	Study Design; Number of participants; Year Initiated	Objectives of Study	Sampling technique/Study Population
Prospective Rural Urban Epidemiology (PURE) study [7–16]	Bangladesh India Pakistan	Prospective; 30,903; 2003	To examine the relationship of societal influences on lifestyle behaviors, cardiovascular risk factors, and incidence and mortality of chronic diseases.	Broadly representative sampling of adults 35 to 70 years from within each community unit that was identified based on feasibility and geographical location.
Dhulikhel Heart Study (DHS) [17–19]	Nepal: Dhulikhel	Prospective longitudinal study; 1073; 2013	Measure and track trends of CVD by providing comprehensive data using standardized protocols to evaluate CVD prevalence, incidence, and risk factors.	All adults age 18 years and residing in the town of Dhulikhel for a baseline examination and planned 20-year follow-up.
Center for Cardiometabolic Risk Reduction in South Asia (CARRS) Surveillance Study [20–24]	India: Chennai Delhi Pakistan: Karachi	Cross-sectional; 16287; 2010	Capture the prevalence of CVD risk factors and diseases, and their socioeconomic impact through serial surveys.	Multi-stage cluster random sampling. Municipal sub-divisions used sequentially as sampling frames to randomly select households.
Pakistan Risk of Myocardial Infarction Study (PROMIS) [25–28]	Pakistan: Faisalabad Karachi Lahore Multan	Case-control; 16157	Study genetic, lifestyle and other determinants of CHD in South Asia.	Case: Patients admitted with acute MI. Controls: Frequency matched controls from outpatient settings and visitors to hospitals.
Population Study of Urban, Rural, and Semiurban Regions for the Detection of Endovascular Disease and Prevalence of Risk Factors and Holistic Intervention Study (PURSE-HIS) [29–34]	India: Chennai Thiruvallur Kanchipuram	Cross-sectional + Prospective Cohort; 8080	Cross sectional: Estimate the prevalence of risk factors, biomarkers, subclinical endovascular disease and overt endovascular disease. Prospective cohort: Understand the impact of holistic interventions on risk factors and the course of disease.	2 stage cluster sampling. Administrative units identified followed by selection of clusters (streets/wards/panchayats) through random sampling.
Sri Lanka Diabetes, Cardiovascular Study (SLDCS) [35–42]	Sri Lanka	Cross Sectional; 4521; 2005–2006	Determine the prevalence of diabetes and pre-diabetes for the adult population in Sri Lanka.	100 clusters with 50 households in each cluster to be recruited. Clusters selected by a computer-generated random number list from the 'Village Office Units'. Voters' registers used to randomly select the first household in each cluster and a uniform criterion used to select the remaining 49 households.
New Delhi Birth Cohort [41,42]	India: New Delhi	Prospective; 1100; 2006–2009	Evaluate the incidence of CVD risk factors in India.	Participants from earlier phases of the study that recruited newborns from a defined geographical region of New Delhi were recruited.
Health Effects of Arsenic Longitudinal Study (HEALS) [43–46]	Bangladesh: Arihazar	Cross-sectional; Phase I: 11746; 2000–2002 Phase II: 8287; 2006–2008	Originally established to evaluate the effects of full-dose range arsenic (As) exposure on various health outcomes. Cross sectional studies conducted on the study samples to evaluate other health parameters including cardiovascular risk factors.	Systematic sampling based on demographic characteristics and exposure categories after total population in the study area was enumerated and their arsenic exposure and basic sociodemographic characteristics ascertained.
Bangladesh Demographic and Health Survey [47–50]	Bangladesh	Cross-sectional; 8834; 2011	Measurement of biomarkers, including blood pressure and blood glucose in a group of eligible men and women aged 35 and over.	Two-stage stratified sample of households. In the first stage, 600 EAs were selected with probability proportional to the enumeration areas. In the second stage of sampling, a systematic sample of 30 households on average was selected per enumeration area.
North Bengal Non-Communicable Disease Programme of Bangladesh University of Health Sciences [51]	Bangladesh: Pirgonj	Cross-sectional; 63708; 2011–2012	Identify the presence of cardiovascular symptoms in a cohort originally formed for a prospective survey to identify the burden of diabetic retinopathy and associated risk factors from a rural population.	All BADAS eye care project participants aged between 31 and 74 years were asked to participate.

MI: Myocardial Infarction; AIMS: All India Institutes of Medical Sciences; N/A: Not available; IHD: Ischemic Heart Disease; CHD: Coronary Heart Disease; BADAS: Diabetic Association of Bangladesh.

95% CI: 1.17–2.06) followed by heavy cigarette smokers (>10 pack-years) (4.4%, HR: 1.47 95% CI: 1.05–2.06) compared with non-smokers (3.1%, HR 1.0). A study that attempted to evaluate the influence of tobacco policies on these numbers found that knowledge relating to harmful effects of tobacco was lowest in LICs.[15] The study also found greater availability and easier access to cheap cigarettes (<5 cents/cigarette) in LICs (40.4%) compared to HICs (3.2%) and UMICs (0%) indicating poor policy implementation as one reason behind the high smoking prevalence.

Teo et al in another study assessed the prevalence of healthy lifestyle choices among individuals with known CVD.[16] The study found that after a cardiovascular event, only 39.3% participants in

LICs stopped smoking, which was significantly lower than the rate of smoking cessation in the overall study population (53.4%). Similar trends were noted for healthy eating and high level of physical activity. LICs had the lowest prevalence of healthy eating (25.8% in LICs vs 39.0% overall) and physical activity (25.5% in LIC vs 35.1% overall). A trend was observed between smoking cessation and education levels reiterating the need to increase awareness and knowledge in making healthy lifestyle choices.

The strength of the PURE study lies in its inclusion of a large number of countries that allows comparison between different geographical and socioeconomic regions. The samples from each country, however, may be misleading and may not be representative of its population.

3.2. Dhulikhel Heart Study (DHS)

The DHS is a prospective longitudinal cohort study launched in 2013 in Dhulikhel, Nepal that is designed to provide comprehensive data to evaluate CVD prevalence, incidence and risk factors.[17] After a baseline evaluation, the study intends to follow participants for 20 years through repeat visits every 2 years. Baseline evaluation comprised of data collection relating to demographic and socioeconomic characteristics, medical history and health behaviors, physical and cognitive function and anthropometric measurements. In addition, participants underwent blood pressure checks as well as fasting blood glucose, Hemoglobin A1c (HbA1c), and lipid profile measurements and were invited for electrocardiography, echocardiography, carotid Doppler and adipose tissue measurement at the Dhulikhel Hospital. Outcome measures focus on mortality and CVD related morbidities. The first wave of recruitment included 735 households (roughly a third of all households in Dhulikhel) and successfully recruited 1073 participants greater than 18 years of age. Of these, approximately 35.6% of men and 14.2% women were current smokers. Prevalence of obesity (body mass index [BMI] > 30 kg/m^2) was 7.7% (5.4% in men and 9.4% in women) while 39.4% of participants had physical activity levels less than 600 metabolic equivalent of task (MET) minutes/week.[18] There were 298 patients identified as hypertensives, of which 130 (43.6%) were aware of their disease.[19] Awareness increased with age with an estimated 5% greater awareness per year increase in age ($p < 0.001$). Men were also more likely to be aware than women (adjusted OR 0.57, 95% CI 0.31–1.06). Only 99 (33.2%) of the patients were being treated for hypertension and 35 (11.7%) had controlled hypertension (HTN). Being female (86.1% vs 66.1%, $p = 0.007$), unemployed (87.6% vs 61.4%, $p < 0.001$) and being in the lowest quartile of income was positively associated with being treated for HTN. The study also found significant associations between higher BMIs (overweight and obese) and smoking (former or current) with uncontrolled hypertension despite being on treatment. Medication adherence (as assessed by Morisky's Medication Adherence Scale) was high in only 1/3rd of the patients but showed a nonsignificant association with BP control.

In another study, investigators of the DHS study evaluated food patterns among participants.[18] Participants were categorized as consuming 1 of 4 dietary patterns: mixed pattern (lentils, fruits and vegetables, fatty foods, noodled, tea and coffee), fast-food pattern (fast food, sweets, soda), refined-grains-meat-alcohol pattern (refined-grains, meat, fish, alcohol) or solid-fats-and-dairy pattern (solid fats and dairy). This was derived by applying principal component analysis to the frequency of consuming items from each food group in a week. The study found a significant association between being overweight and refined-grains-rice-alcohol pattern (adjusted OR 1.19, 95% CI 1.03–1.39) while the fast food pattern was found to be significantly associated with obesity in individuals greater than 40 years of age (OR 1.69, 95% CI 1.19–2.39).

The prospective design and recruitment of roughly 1/3rd of the households in Dhulikhel limits the effect of potential confounders. It is, however, limited by its inapplicability to the rest of Nepal that is likely to be more heterogeneous. Data has only been cross-sectional thus far. Future findings will better allow casual relationships to be determined.

3.3. Center for cArdiometabolic Risk Reduction in South-Asia (CARRS) surveillance study

The CARRS study is a multistage, multicity cohort that recruited representative samples from 3 major urban centers in South Asia (Chennai and Delhi [India], and Karachi [Pakistan]).[20] The study was designed to be conducted over 4 years to capture the prevalence of CVD risk factors and diseases, and their socioeconomic impact through serial surveys. This would allow development of clinical management systems for tailored care and preventive approaches. Baseline surveys were conducted in 2011 on 13,384 participants (4943 in Chennai, 4425 in Delhi, and 4016 in Karachi) greater than 20 years of age from 8115 households.[20] Initial data gathered included fasting plasma glucose (FPG), glycated hemoglobin, lipid panel, serum urea and creatinine, microalbuminuria, and salivary cotinine levels along with demographic and social characteristics, blood pressures, behavioral risk factors and anthropometric measurements.

The prevalence of diabetes (FPG $\geq$ 126 mg/dl and/or HbA1c $\geq$ 6.5%) was found to be 22.8% (95% CI 21.5%–24.1%), 25.2% (23.6%–26.8%) and 16.3% (15.2%–17.3%) in Chennai, Delhi and Karachi.[21] Similarly, the burden of prediabetes (FPG 100–125 mg/dl and/or HbA1c 5.7–6.4%) was 37.9% (95% CI 36.1%–39.7%), 47.6% (45.6%–49.5%) and 31.1% (29.5%–32.8%) in Chennai, Delhi and Karachi. The study also showed that generalized obesity (BMI $\geq$ 25 kg/m^2) (Odds Ratio (OR) 1.65, 95% CI 1.33–1.98), abdominal obesity (abdominal waist $\geq$ 90 cm in male and $\geq$ 80 cm in female) (OR 1.82, 1.48–2.24), high cholesterol levels (total cholesterol $\geq$ 200 mg/dL) (OR 1.30, 1.12–1.49), hypertension (self-reported and/or BP $\geq$ 140/90 mmHg) (OR 1.38, 1.13–1.68) and low HDL-C (HDL-C < 40 mg/dl for males and <50 mg/dl for females) (OR 1.34, 1.17–1.53) were significantly more likely to be associated with diabetes.

In a study to examine the relationship of socioeconomic status and cardiovascular risk, lower level of education and lower income groups were both associated with higher prevalence of tobacco smoking and smokeless tobacco use.[22] In addition, lower income groups were also associated with low fruit and vegetable use. Diabetes Mellitus, hyperlipidemia and obesity (BMI > 25 kg/m^2) were more common in higher educated and higher income groups. In another study evaluating tobacco use, lifetime tobacco use prevalence was reported as 45.0%, 41.3% and 42.5% among males and 7.6%, 8.5% and 19.7% among females in Chennai, Delhi and Karachi.[23] Prevalence of tobacco use in the past 6 months was 38.6%, 36.1%, and 39.1% among males, and 7.3%, 7.1%, and 18.6% among females in Chennai, Delhi, and Karachi. Cigarette smoking was the most common form of tobacco use in males in Chennai (22.7%) and Karachi (20.8%) while *bidi* was used most commonly by males in Delhi (15.5%). Among females, chewed tobacco was most commonly reported in Chennai (3.1%) and Delhi (2.5%) while *pan with zarda* was most commonly reported in Karachi (11.0%). Multivariate regression analysis showed lower education and lesser income were associated with tobacco use. This, again, highlights the role of improving awareness relating to downstream effects of tobacco use in the community to reduce the prevalence of its use.

In one analysis, Patel et al examined the uniqueness of the cardiometabolic profile of South Asians by comparing the prevalence of combined dyslipidemia and dysglycemia with other populations in the United States (Asians, Black persons, Hispanics, and White persons).[24] While data for South Asians was obtained from CARRS study, the source of data for the United States population was the National Health and Nutritional Examination Survey (NHANES). Asians in the United States included both, East Asians and South Asians, since publicly available NHANES data does not allow distinguishing between these two groups. Dyslipidemia was defined as a triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio >4 while dysglycemia was defined as FPG > 126 mg/dL. A total of 8448 participants were analyzed and compared with 274 Asians, 404 Black persons, 308 Hispanics, and 703 White persons living in the Unites States. The prevalence of combined dysglycemia and dyslipidemia among men and women with normal BMI (18.5–25 kg/m^2) was 33% and 11% in South Asians in CARRS, 15% and 1% in Asians in the United States, 5% and 2% in Black persons, 11% and 2% in Hispanics, and 8% and 2% in White persons. Among males, the prevalence of combined dysglycemia and dyslipidemia was found to be higher in South Asians compared with other groups in all BMI categories. Among females, the prevalence of combined dysglycemia and dyslipidemia was higher in South Asians compared to the other groups in all BMI categories except obesity (BMI > 30) where Asian women in the Unites States had a greater prevalence (30.3% vs 29.3%). Similar figures were seen for metabolic syndrome where the prevalence of metabolic syndrome among men and women with normal BMI was 32% and 24% in South Asians, 16% and 6% in Asians in the Unites States, 10% and 15% in Black persons, 5% and 1% in Hispanics, and 2% and 12% in White persons. South Asians had a greater prevalence of metabolic syndrome compared to the other groups for all categories of BMI. This would suggest that South Asians, even with "healthy-appearing" BMIs (i.e. BMI between 18.5 kg/m^2 and 24.9 kg/m^2), are at greater risk of CVD compared to other population groups.

While the CARRS study has a robust study design with quality control mechanisms, data available so far is only from cross sectional surveys. The study also does not include the rural population. With the study limited to two cities in India and one in Pakistan, data on risk factors such as *pan with zarda* need to be interpreted with caution since this practice may not be prevalent in other urban centers.

3.4. Pakistan Risk of Myocardial Infarction Study (PROMIS)

PROMIS is a case control study of acute myocardial infarction (MI) in participants recruited from 6 different hospitals in 3 cities in Pakistan.[25] Based on our search, it is the only study that is predominantly evaluating genetic information linked to CVD in Pakistani population. Study participants are patients aged between 30 and 80 years, with no history of prior cardiovascular disease who presented to the emergency department at participating hospitals and were subsequently diagnosed with their first MI. Matched controls were identified from outpatients coming for routine checkups. Data collected included demographic information, dietary and lifestyle habits (smoking, tobacco use, physical activity etc.), anthropometric measurements and non-fasting blood samples. DNA was extracted from peripheral leukocytes to obtain genotype information on 95 BMI associated single nucleotide polymorphisms (SNP) variants. By 2009, 5000 cases and 5000 controls had been recruited and the target sample of the study was expanded to 20000 cases and 20000 controls. Among the first 16,157 patients (7925 cases and 8232 controls) available for analysis, 50% cases and 32% controls were active smokers. Prevalence of light, moderate and heavy physical activity was 38%, 51% and 11% in cases and 41%, 50% and 9% in controls. BMI was comparable (25.8 ± 3.9 kg/m^2 in cases and 25.9 ± 4.3 kg/m^2 in controls). When SNP associated with BMI were tested in these participants, 73 of the 95 tested showed directionally consistent effects on BMI as reported in Europeans.[26] They accounted for 1.54% of the phenotypic variance in BMI, which is lower than that observed in a previous study.[27] The most strongly BMI-associated variant in Pakistanis was MC4R locus which was also previously seen in European populations.

In another study, apolipoprotein size and concentration were measured in 9015 patients and 8629 controls.[28] The study identified the minor allele rs2457564 as a variant associated with smaller apolipoprotein(a) isoform size and the minor allele rs3777392 as a variant associated with lipoprotein(a) concentration. After adjusting for several cardiovascular risk factors, the OR in PROMIS for myocardial infarction was 1.10 (95% CI 1.05–1.14; $p < 0.0001$) per 1-SD increment in lipoprotein(a) concentration and 0.93 (95% CI 0.90–0.97; $p < 0.0001$) per 1-SD increment in lipoprotein size. The authors concluded that both, small apolipoprotein(a) isoform size and high lipoprotein(a) concentration, are independent and causal risk factors for coronary heart disease.

The PROMIS study stands out for evaluating genetic information among a large number of South Asians. Recruiting patients and their matched controls from hospitals, however, limits the applicability of the study findings to the general population given the low proportion of population that has access to healthcare in South Asia.

3.5. Population Study of Urban, Rural and Semiurban Regions for the Detection of Endovascular Disease and Prevalence of Risk Factors and Holistic Intervention Study (PURSE-HIS)

The PURSE-HIS was initiated in 2007 to study endovascular disease in urban, semiurban, and rural communities in South India.[29] The cross-sectional component of the study estimated the prevalence of risk factors, biomarkers, subclinical endovascular disease and overt endovascular disease. The prospective cohort component of the study is aimed at understanding the impact of holistic interventions on risk factors and the course of disease. The study used 2-stage cluster sampling where administrative units were identified in the first stage and clusters were randomly selected from these administrative units in the second stage. Baseline demographic data was gathered by an interviewer during a home visit and this was followed by a visit to the University Hospital at Sri Ramachandra University where fasting blood specimens and a urine sample was collected. Glucose tolerance tests were also conducted on all participants. The study recruited 8080 participants by 2012 from Chennai (urban setting, n = 2221), Thiruvallar (semi-urban setting, n = 2821) and Kanchipuram (rural setting, n = 3038).

The study showed that 12.9% of the women and 22.2% of men were hypertensive while 15.4% of women and 21.3% men were diabetic.[30] The prevalence of BMI > 23 kg/m^2 was 56% in males and 70% in females while the prevalence of BMI > 30 kg/m^2 was 6% in males and 16% in females.[31] The prevalence of smoking was 2.1% in women but 30.2% in men. In terms of physical activity (assessed by the WHO Global Physical Activity Questionnaire and analysis guide), 27.2% males and 17.2% female respondents reported low, 65.5% male and 80.5% female reported moderate, and 7.3% male and 2.3% female reported high levels of physical activity.[32]

When looking at sodium intake in the population, the investigators found that the sodium intake in men (4.1 ± 2 g/day) was greater than that in women (3.2 ± 1.7 g/day, $p < 0.01$). Hypertensive men (4.2 g/day) and hypertensive women (3.4 g/day), both, had a higher salt intake than those without hypertension (4.0 g/day in men, 3.2 g/day in women, $p < 0.05$ for both). Multivariate analysis showed that salt intake was independently related to SBP but not DBP in both sexes. Home-made foods were identified as the source of the excess salt intake, which was well above the recommended 2 g/day.

In another study, high sensitivity C-reactive protein (hsCRP) levels were evaluated as markers for metabolic syndrome.[33] They were found to be higher in women (median 2.86 mg/L, CI 2.73–2.97) when compared to men (median 1.80 mg/L, CI 1.71–1.88). After adjusting for gender, age and BMI they were higher in urban communities compared to rural communities ($p = 0.03$). Median hsCRP levels for those with 0, 1, 2, 3, 4, and 5 features of metabolic syndrome (abdominal obesity, atherogenic dyslipidemia, raised blood pressure, insulin resistance ± glucose intolerance, proinflammatory and prothrombotic states) were 1.01, 1.47, 2.3, 3.19, 3.70 and 3.94 mg/L ($p < 0.01$ for trend). This suggests hsCRP to be independently associated with metabolic syndrome among South Indians.

In one study on 5742 participants, plasma triglyceride/high density lipoprotein cholesterol (TG/HDL-C) ratio was evaluated as a marker for increased insulin resistance and cardio-metabolic risk factors.[34] The upper quartile for TGL/HDL-C ratio was identified as 4.26 and 3.27 in men and women. The study found that those falling in the upper quartile had higher values for fasting plasma insulin, blood pressure, body mass index, waist circumference, glucose, ApoB/ApoA1 and TG concentrations and lower HDL-C concentrations compared to those who fell in lower quartiles ($p < 0.001$). This suggests using the plasma TG/HDL-C ratio to identify patients with high risk cardiometabolic risk factor profile.

The strength of the PURSE-HIS study lies in its large sample size and recruitment of participants from rural as well as urban settings. As with other studies mentioned earlier, its cross-sectional design limits the inferences that can be made. Randomized controlled trials are needed to test the TGL/HDL ratio as a marker of cardiovascular risk.

3.6. Sri Lanka Diabetes, Cardiovascular Study (SLDCS)

Sri Lanka Diabetes and Cardiovascular Study (SLDCS) was a cross-sectional study conducted by the Diabetes Research Unit of the University of Colombo and the Oxford Centre for Diabetes Endocrinology and Metabolism, UK.[35] The aim of the study was to determine the prevalence of diabetes and pre-diabetes for the adult population in Sri Lanka. Other cardiovascular risk factors examined in the study include blood pressure, lipids, physical activity and other lifestyle factors.

All adult age groups and different socio-demographic sectors were sampled from seven out of nine provinces in the country through cluster sampling. Data collection took place between August 2005 and September 2006. Of the 5000 adults selected to be subjects in the study, 4532 (91%) participated in the study. The prevalence of diabetes was found to be 12.6% ($n = 536$), 36% of whom were undiagnosed previously.[35] Prevalence of diabetes was higher in the urban population (16.4%) compared to rural population (8.7%). The prevalence of smoking among adults in Sri Lanka was 18.3% (17.2% in urban population and 18.5% in rural population) while the prevalence of hypertension was 23.7%.[36,37] In terms of obesity (BMI ≥ 27.5 kg/m^2), 9.2% of the study population was found to be obese.[38]

An analysis from SLDCS that examined the correlates and patterns of metabolic syndrome in the Srilankan adults showed that female gender (OR:1.7, 95% CI: 1.3–2.2), increasing age, urban living (OR:1.7, 95% CI: 1.4–2.0), secondary (OR:1.5, 95% CI:1.1–1.9) and tertiary levels of education (OR:2.3, 95% CI:1.8–2.3), and physical inactivity (OR:1.6, 95% 1.3–1.9), were significantly associated with metabolic syndrome.[39] Another study that evaluated physical activity levels among participants in the study found that the rural population had higher activity levels (mean physical activity: 5175 ± 4583 MET minutes/week) compared to the urban population (2956 ± 2847 MET minutes/week, $p < 0.001$).[40] Patients with hypertension had lower physical activity levels (3627 ± 600 MET minutes/week) compared to those without hypertension (5107 ± 4555 MET min/week, $p < 0.001$). Similarly, patients with diabetes had lower physical activity levels (3037 ± 3095 MET min/week) than those without diabetes (4929 ± 4467 MET min/week, $p < 0.001$). Overall, 11.0% of the study population (14.6% of males, 8.7% females; $p < 0.001$) was found to be physically 'inactive' (those who do not perform any physical activity or (i) <3 days/week of vigorous-intensity activity of 20 min/day or (ii) <5 days of moderate-intensity activity per week or walking <30 min/day or (iii) <5 days of any combination of walking, moderate-intensity or vigorous-intensity activities achieving a total physical activity of 600 MET-min/week).

The SLDCS was one of the few studies in our search that examined the Sri Lankan population. The inability to recruit participants from war torn Northern and Eastern provinces does limit the applicability to those parts. The study is further limited by its cross-sectional design.

3.7. New Delhi Birth Cohort study

Early phases of the New Delhi Birth Cohort study targeted data collection regarding pregnancy outcomes and childhood growth.[41,42] Between December 1st 1969, and November 30th 1972, all families living in a defined area of 12 km^2 South Delhi were identified. Women from this population who became pregnant and their newborns were assessed periodically. Later phases of the study, however, switched focus to cardiovascular diseases.[41] The number of participants reduced from 8181 live births (original cohort) to 1100 participants for this phase of the study. Baseline information (medical history, family medical history, medication use, material possessions, tobacco use, and alcohol consumption) were collected through home visits. Study personnel measured participants' blood pressure, weight, height, and waist and hip circumferences during these visits. In addition, glucose tolerance tests and lipid panels were also checked. The participants were followed for a mean period of 6.9 years (±1.0 years). The study found that the mean age of the participants was 29 years (±1 years) at the start of the study. Obesity (BMI > 30 kg/m^2) increased from 9% in men and 13% in women to 21% in men and 25% in women ($p < 0.05$). Similarly, the prevalence of hypertension (systolic blood pressure [SBP] of ≥140 mmHg, a diastolic pressure (DBP) of ≥90 mmHg, or being on drug treatment for hypertension) rose from 11% to 34% in men and from 5% to 15% in women while the prevalence of diabetes (fasting plasma glucose concentration ≥126 mg/dl or glucose concentration of ≥200 mg/dl 2 h after 75 g glucose) rose from 5% to 12% in men and from 3.5% to 7% in women ($p < 0.05$ for all). LDL-C levels did not change significantly (from 122.1 ± 35.7 mg/dl to 122.7 ± 41.2 mg/dl in men and from 115.8 ± 33.8 mg/dl to 116.8 ± 32.7 mg/dl in women). The study, through its prospective design, highlights the high incidence of cardiovascular factors among South Asians at a young age. The study however, selectively examined a specific age group in an urban setting and had a high loss to follow-up rate.

3.8. Health Effects of Arsenic Longitudinal Study (HEALS)

The HEALS is a large prospective cohort study in Bangladesh that was initiated in 2011 in Arahizar, Bangladesh to evaluate health outcomes associated with arsenic exposure from groundwater.[43] Within this design, data for cross sectional studies that looked at exposures and outcomes unrelated to arsenic exposure was also collected. Between 2000 and 2002, 11746 married participants aged between 18 and 75 years old were recruited from the area. The study was expanded between 2006 and 2008 to include an additional 8287 individuals from the same location. Participants are followed up once every 2 years. Of those recruited at baseline, 35.4% of men and 3.5% of women smoked less than 10 sticks of cigarettes/*bidi* daily while 28.0% of men and 0.2% women smoked more than 10 sticks daily. Similarly, 1.5% of men and 0.2% of women smoked hookah less than 5 times a day while 1.4% of men and 0.1% of women smoked hookah more than 5 times daily. The prospective study by Wu et al. evaluated the association between tobacco smoking and mortality in the 11,746 participants who were recruited in the initial phase.[44] Person years of follow up were calculated from baseline to date of death from any cause. At the end of the study, there was a total of 151,641 person years of follow up in which 734 deaths occurred, 60% of which were related to CVD. Among men, current cigarette/*bidi* smokers (HR 1.30, 95% CI 0.88–1.91) and ever cigarette/*bidi* smokers (HR 1.18, 95% CI 0.81–1.71) both had a positive association with death related to CVD although these numbers were not statistically significant. A similar association was observed with hookah smoking and cardiovascular death. Current male cigarette/*bidi* smokers (HR 1.94, 95% CI 1.08–3.49) were also at a higher risk of ischemic heart disease related death while the association was not significant between ever hookah smoking and ischemic heart disease related death. The study thus illustrated the harmful effects of cigarette/*bidi* smoking on cardiovascular health in a Bangladeshi population.

In another study, the association of betel quid chewing with hypertension was studied in 8287 participants recruited in the second phase.[45] It was found that 33.2% (35.5% men, 31.6% women) of the population actively chewed quid at the time of baseline data collection, 82.5% of whom chewed it with tobacco. Multivariate analysis showed that betel quid chewing was associated with women, older adults, those with no formal education, those employed in business, tobacco smokers and persons who did not own land. At the time of follow up, betel quid chewing without tobacco was significantly associated with systolic hypertension (OR 1.55, 95% CI 1.01–2.37) hence demonstrating the harmful effects of betel quid chewing on cardiovascular health.

In another study, Chen et al studied the correlation of dietary patterns with cardiovascular disease.[46] A food frequency questionnaire, validated in the local population, was administered to all participants recruited in the study. Each food item was correlated with a diet pattern through a coefficient known as factor loading. This coefficient was used to calculate a composite factor score for each dietary pattern for each participant to assign them into one of three dietary patterns: animal protein (eggs, milk, red meat etc.), gourd and root vegetable diet (radishes, sweet potato, spinach etc.) and balanced (rice, red meat, fish, fruit, vegetables etc.). Cardiovascular mortality was used as the outcome of interest. There was a positive association between animal protein diet and risk of death from both disease of the circulatory system (1.13, 95% CI, 1.00–1.28) and heart disease (HR 1.17, 95% CI 0.99–1.38) in relation to one standard deviation increase in the factor scores for the animal protein diet pattern. Balanced diet, on the other hand, was found to be protective for diseases of the circulatory system (HR 0.86, 95% CI 0.73–1.01) and heart disease (HR 0.86, 95% CI 0.69–1.08) in relation to each standard deviation increase in the balanced diet pattern. Increased SBP (116.9 vs 113.1 mmHg, p for trend = 0.08), DBP (74.5 vs 72.7 mmHg, p for trend = 0.09) and BMI (20.7 vs 19.3 kg/m^2, p for trend = 0.19) were also found to be correlated with higher quartiles of animal protein pattern compared to the lowest quartile of animal protein pattern but they were not statistically significant.

3.9. Data from the Bangladesh Demographic and Health Survey

The 2011 Bangladesh Demographic and Health Survey was conducted as part of the Demographic and Health Surveys in multiple countries throughout the world.[47,48] Among the many objectives of the survey were to collect data regarding lifestyle and socioeconomic characteristics and the measurement of blood pressure and blood glucose for men and women greater than 35 years old. The above-mentioned data was available for 8834 participants (4311 women and 4523 men) which was then used by Harshfield et al to find the association of HTN and hyperglycemia with socioeconomic contexts.[49] The socioeconomic status indicators used were wealth, education and geographical location. While education was, self-reported and divided into 6 quantiles (no education, incomplete primary education, complete primary education, incomplete secondary education, complete secondary education and higher education), wealth was calculated using a wealth index derived from principle component analysis of household assets. Geographical location was either rural or urban as determined in the survey. The study showed that men had lower SBP (117.0 vs 122.6 mmHg, $p < 0.001$) and DBP (76.4 vs 79.7 mmHg, $p < 0.001$) compared to women. The study also concluded that higher wealth levels were associated with increased likelihood of having hypertension ($SBP \geq 140$ or $DBP \geq 90$ mmHg). The wealthiest quintile had twice the likelihood (OR 2.83, 95% CI: 2.32–3.44 for men and 2.25, 95% CI: 1.90–2.67 for women) of having hypertension compared with those in the lowest quintile. Similarly, individuals with more than secondary education (highest level of education) were associated with increased likelihood of having elevated BP ($SBP \geq 130$, $DBP \geq 85$) compared to those with the lowest levels of education (ORs were 2.55, 95% CI: 2.06–3.16 for men and 1.42, 95% CI: 0.99–2.03) for women. Trends were similar for hyperglycemia where the richest households were more than four times more likely to have hyperglycemia than individuals in the poorest households (ORs were 6.48, 95% CI: 5.11–8.22 for men and 4.77, 95% CI: 3.72–6.12 for women). With education, the most educated had at least a 4-fold greater likelihood of having hyperglycemia (OR 4.68, 95% CI: 3.56–6.15 for men and 5.02, 95% CI: 3.30–7.64 for women). This would suggest that with increasing wealth and education and hence a change in lifestyle, that comes with better socio-economic position in the society, participants were at a higher risk of white collar diseases like HTN and diabetes.

Rahman et al also utilized data from the Bangladesh Demographic Health Survey but only included hypertensive participants for whom both, BP and blood glucose data was available (n = 1620).[50] Hypertensives were defined as those with a diagnosis of HTN or with $SBP \geq 140$ or $DBP \geq 90$ mmHg. Cardiovascular risk was calculated using WHO guidelines to calculate 10-year risk of stroke or MI. The study showed that 21.8% of the participants had a high risk (>20%), 17.3% had a medium risk (15%-20%) and 61% of respondents had a low (<15%) 10-year risk of stroke or myocardial infarction. After adjustment, having female- versus male head households (AOR.1.85, 95% CI.1.16, 2.86); urban residence (AOR.1.32, 95% CI.1.00, 1.75), being overweight/obese versus underweight (AOR.1.80, 95% CI.1.14, 2.82); and being aged 55–69 years (AOR.1.95, 95% CI.1.48, 2.59) or >70 years (AOR.2.87, 95% CI.2.00, 4.12) versus 35–54 years were significant predictors of high 10-year risk of CVD versus the combined medium and low categories.

4. Other studies

The Diabetic Association of Bangladesh (BADAS) Eye Care Project was started in 2008 as a prospective survey to identify the burden of diabetic retinopathy and associated risk factors from a rural population. The study was conducted in a sub-district in Thankurgaon district called Pirganj in Northwestern Bangladesh. In 2011, Fatema et al., under the North Bengal Non-Communicable Disease Programme of Bangladesh University of Health Sciences, assessed a subset of the original cohort for the presence of cardiovascular symptoms.[51] Participants were aged between 31 and 74 and their risk was assessed via face–face interviews using the multiple risk assessment questionnaire of the WHO Risk Management Package. The questionnaire consists of 8 questions to determine probable angina, heart attack, stroke and TIA. Those who had probable stroke, angina, transient ischemic attack or MI based on responses to the questions were considered high risk participants. The study showed that 1170 or 1.84% of the participants enrolled in the study were high risk. High risk participants were significantly more likely to have lower education levels, lower income and more likely to be female. They also had a lower proportion of HTN (4.4% vs 9.0%) but higher prevalence of smoking (11.1% vs 9.8%, $p = 0.151$) and marginally higher prevalence of diabetes (0.7% vs 0.5%, $p = 0.482$). On multivariate analysis, being unemployed (OR 0.32, 95% CI 0.17–0.60) and being underweight ($BMI < 18.5\ kg/m^2$) (OR 0.60, 95% CI 0.47–0.77) was protective against high risk of CVD while obesity ($BMI > 27.51\ kg/m^2$) (OR 1.82, 95% CI 1.20–2.74), central obesity (>90 cm in male, >80 cm in female) (OR 1.32, 95% CI 1.06–1.66) and living in a tin-shed house compared to a brick house (OR 1.88, 95% CI 1.45–2.44) were associated with high risk of CVD. These numbers all suggest lower burden of CVD in this rural setting in Bangladesh compared with findings from other studies.

Noncommunicable disease Initiatives and Research at AMrita (NIRAM) study is an ongoing longitudinal, population based cohort study being conducted in Kochi, India.[52] The cohort enrolled 4507 participants between February 2015 and February 2016 and collected data relating to demographics, prevalence of CVD risk factors (example, alcohol use, tobacco use, physical activity), dietary patterns and baseline incidence of NCDs (history of known HTN, DM, dyslipidemia, corornary artery disease [CAD] requiring medications). CVD risk was calculated using 10 year and lifetime atherosclerotic cardiovascular disease (ASCVD) risk scores. Participants were stratified first by age into 18–39 years, 40–59 years and then 60–79 years. They were further stratified into low risk and high risk based on the 10 year ASCVD score (ASCVD score <7.5% and ≥7.5%) in the 40–59 year and 60–79 year groups and into low (<39%) and high risk (>39%) based on the ASCVD lifetime risk score in the 18–39 year and 40–59 year groups. Preliminary analysis showed that around 25.5% of participants had HTN, 20% had DM and 30.6% had hyperlipidemia. Less than recommended fruit and vegetables intake was found in 96.2% participants. $BMI > 25\ kg/m^2$ and regular use of alcohol were found to be significantly associated with HTN, dyslipidemia and DM. Of the subjects in the 18–39-year group, 45.1% females and 70.9% males had a low lifetime risk of ASCVD events (first occurrence of nonfatal myocardial infarction, coronary heart disease [CHD] death, or fatal or nonfatal stroke). In the 40–59-year group 2.3% females and 32.0% males had a high 10-year risk while 73.5% females and 81.1% males had a high lifetime risk of ASCVD events. In the 60–79-year group, 53% females and 97.4% males had a high 10-year predicted risk of ASCVD events. On multivariate analysis, occasional and regular drinking, obesity and low intake of fruits and vegetables were associated with high lifetime risk of ASCVD. The data helps identify "at-risk" subjects who may be targeted for primary prevention strategies.

The Urban Rural Chronic Diseases Study (URCDS) is a population based, cross sectional study in Pakistan that recruited apparently healthy individuals aged between 30 and 75 years from Faisalabad and one of its peripheral rural areas. This was established to investigate risk factors and their association with CVD and other NCDs. Participants were interviewed by trained nurses at participating hospitals. Data collected included demographic details, occupational and lifestyle information, medical history and their location of residence. Fasting blood glucose and lipid panels and blood pressure measurements were also obtained.

The baseline data of the study was used by Tareen et al to compare geographical location and social class as determinants of hypertension and diabetes.[53] Social class was defined based on occupation: unskilled workers (laborers, farmers) were labeled lower class, skilled individuals were labeled as middle class and those with 'executive' or government jobs were labeled as upper class. Women, if unemployed, were labeled according to the social class of their spouse. Geographical location was either rural or urban as determined by the location of their residence. The study found that living in an urban setting (adjusted odds ratio (aOR): 3.03, 95% CI 2.41–3.82), male sex (aOR: 1.88, 95% CI: 1.48–2.37) and obesity (aOR: 3.38, 95% CI 2.55–5.81) were independently associated with hypertension. Similarly, living in an urban setting (aOR: 1.77, 95% CI 1.37–2.29), male sex (aOR: 1.53, 95% CI: 1.18–1.98) and obesity (aOR: 2.85, 95% CI 1.81–4.47) were independently associated with DM. There were no significant associations between social class and hypertension or DM, hence suggesting that location of residence rather than social class is a stronger determinant of cardiovascular risk factors in Pakistan.

Data from URCDS was also used by Shafique et al. to determine the association of water-pipe smoking and metabolic syndrome.[54] From a total of 2700 participants in URDCS, 2032 were included in the study after excluding participants with missing data. A total of 325 individuals or 16.0% of participants were found to be waterpipe smokers. Manual workers (12.8%) were less likely to smoke than skilled workers (17.2%) and professionals (22.0%). Water-pipe smokers had more central obesity (waist circumference 84.7 cm vs 80.6 cm), higher SBP (129.9 mmHg vs 124.4 mmHg), higher DBP (74.3 mmHg vs 71.9 mmHg), higher fasting glucose levels (5.2 mmol/L vs 4.9 mmol/L) and higher TG levels (1.6 mmol/L vs 1.4 mmol/L, $p < 0.01$ for all) compared with non-smokers. The study hence showed the association of water-pipe smoking with multiple components of metabolic syndrome and risk factors of CVD.

Rastogi and colleagues in their case-control study recruited patients aged between 21 and 74 years from 8 urban hospitals in Bangalore in Delhi who were admitted with a diagnosis of a first incident of an MI from 1999 to 2000.[55–57] Controls were selected were selected from the same hospital from an inpatient or outpatient setting and were matched in terms of age and sex. The study was designed to evaluate risk factors of ischemic heart disease (IHD). Of the 1050 participants (350 cases, 700 controls) enrolled in the study, history of hypertension (30.3% vs 16.3%) and high cholesterol (2.6% vs 0.6%), prevalence of cigarette (30.0% vs 13.3%) and *bidi* smoking (25.4% vs 11.4%), history of diabetes (17.4% vs 13.0%) and family history of IHD (41.7% vs 31.1%, $p < 0.01$ for all) were all higher in the group who had myocardial infarction. Alcohol intake (0.28 servings/day 0.16 servings per day) was also higher in cases while physical activity (66.29 MET-min/day vs 98.67 MET-min/day) was lower. Multivariate-adjusted analyses showed cigarette (Risk Ratio (RR) 7.5, 95% CI: 40–14.0) and *bidi* (RR 6.7, 95% CI 3.7–12.3) smoking, body mass index ($BMI \geq 25$ vs $BMI < 25$) (RR 2.6, 95% CI 1.4–4.7), waist-to-hip ratio (waist to hip ratio >1.0 vs ≤0.9) (RR 2.5, 95% CI 1.3–4.8), leisure-time physical exercise (≥145 MET-min/day vs non-exerciser), family history of IHD (RR 2.3, 95% CI 1.6–3.5) and history of hypertension (RR 2.0, 95% CI 1.5–3.5) to be significant predictors of IHD. The authors evaluated vegetable intake among participants using a food frequency questionnaire and observed an inverse relationship between vegetable intake and ischemic heart disease risk. In comparison with persons consuming a median of 0.8 servings/d, persons consuming 3.5 servings of vegetables/day had a RR of 0.33, (95% CI: 0.13–0.82, p for trend = 0.006).

5. Conclusion

Several cross-sectional and prospective cohorts have been established in recent times to evaluate cardiovascular disease and its risk factors in South Asia. Many of these studies have been performed in collaboration with the West. Much of the data are derived from India followed by Pakistan and Bangladesh with Dhulikhel Heart Study being the lone large cohort from Nepal. Other South Asian countries (Sri Lanka, Maldives, Bhutan) need to follow the footsteps of these countries by setting up similar cohorts. These studies have allowed looking at risk factors indigenous to the South Asian population such as *bidi* and *hookah* smoking and betel quid chewing which highlights the importance of these cohorts. It is imperative that these studies provide long term findings to add meaningful context that to already published baseline data. Finally, culturally sensitive interventions geared towards treating risk factors identified in these studies are needed to fully realize the true potential of these epidemiologic studies.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Roth GA, Huffman MD, Moran AE, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. *Circulation*. 2015;17:667–67810.1161/CIRCULATIONAHA.114.008720.
2. World Health Organization. *Global Status Report on Noncommunicable Diseases 2014*. .
3. Roth GA, Forouzanfar MH, Moran AE, et al. Demographic and epidemiologic drivers of global cardiovascular mortality. *N Engl J Med*. 2015;372(14):1333–134110.1056/NEJMoa1406656.
4. O'Flaherty M, Buchan I, Capewell S. Contributions of treatment and lifestyle to declining CVD mortality: why have CVD mortality rates declined so much since the 1960? *Heart*. 2013;99(3):159–16210.1136/heartjnl-2012-302300.
5. Institute for Health Metrics and Evaluation, Human Development Network TWB. *The Global Burden of Disease: Generating Evidence, Guiding Policy –South Asia Regional Edition*. [Seattle, WA].
6. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *JAMA*. 2007;297(3):286–29410.1001/jama.297.3.286.
7. Teo K, Chow CK, Vaz M, Rangarajan S, Yusuf S. The Prospective Urban Rural Epidemiology (PURE) study: examining the impact of societal influences on chronic noncommunicable diseases in low-, middle-, and high-income countries. *Am Heart J*. 2009;158(1)1–710.1016/j.ahj.2009.04.019 [e1].
8. Corsi DJ, Subramanian SV, Chow CK, et al. Prospective Urban Rural Epidemiology (PURE) study: baseline characteristics of the household sample and comparative analyses with national data in 17 countries. *Am Heart J*. 2013;166(4)636–64610.1016/j.ahj.2013.04.019 [e4].
9. Yusuf S, Rangarajan S, Teo K, et al. Cardiovascular risk and events in 17 low-, middle-, and high-income countries. *N Engl J Med*. 2014;371(9):818–82710.1056/NEJMoa1311890.
10. McGorrian C, Yusuf S, Islam S, et al. Estimating modifiable coronary heart disease risk in multiple regions of the world: the INTERHEART Modifiable Risk Score. *Eur Heart J*. 2011;32(5):581–58910.1093/eurheartj/ehq448.
11. Chow CK, Teo KK, Rangarajan S, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. *JAMA*. 2013;310(9):959–96810.1001/jama.2013.184182.
12. Miller V, Yusuf S, Chow CK, et al. Availability, affordability, and consumption of fruits and vegetables in 18 countries across income levels: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet Glob Heal*. 2016;4(10):e695–70310.1016/S2214-109X(16)30186-3.
13. Khatib R, McKee M, Shannon H, et al. Availability and affordability of cardiovascular disease medicines and their effect on use in high-income, middle-income, and low-income countries: an analysis of the PURE study data. *Lancet (London, England)*. 2016;387(10013):61–6910.1016/S0140-6736(15)00469-9.
14. Duong M, Rangarajan S, Zhang X, et al. Effects of bidi smoking on all-cause mortality and cardiorespiratory outcomes in men from south Asia: an observational community-based substudy of the Prospective Urban Rural Epidemiology Study (PURE). *Lancet Glob Heal*. 2017;5(2)10.1016/S2214-109X(17)30004-9 [e168-e176].
15. Chow CK, Corsi DJ, Gilmore AB, et al. Tobacco control environment: cross-sectional survey of policy implementation, social unacceptability, knowledge of tobacco health harms and relationship to quit ratio in 17 low-income, middle-income and high-income countries. *BMJ Open*. 2017;7(3)10.1136/bmjopen-2016-013817 [e013817].
16. Teo K, Lear S, Islam S, et al. Prevalence of a healthy lifestyle among individuals with cardiovascular disease in high-, middle- and low-income countries: the Prospective Urban Rural Epidemiology (PURE) study. *JAMA*. 2013;309(15):1613–162110.1001/jama.2013.3519.
17. Koju RP, Karmacharya BM, Shrestha A, et al. Design of the Dhulikhel Heart Study (DHS): The epidemiology of emerging cardiovascular disease in Nepal. *Ann Glob Heal*. 2014;80(3):204–20510.1016/j.aogh.2014.08.119.
18. Shrestha A, Koju RP, Beresford SAA, Gary Chan KC, Karmacharya BM, Fitzpatrick AL. Food patterns measured by principal component analysis and obesity in the Nepalese adult. *Heart Asia*. 2016;8(1):46–5310.1136/heartasia-2015-010666.
19. Karmacharya BM, Koju RP, LoGerfo JP, et al. Awareness, treatment and control of hypertension in Nepal: findings from the Dhulikhel Heart Study. *Heart Asia*. 2017;9(1):1–810.1136/heartasia-2016-010766.
20. Nair M, Ali MK, Ajay VS, et al. CARRS Surveillance study: design and methods to assess burdens from multiple perspectives. *BMC Public Health*. 2012;12:70110.1186/1471-2458-12-701.
21. Deepa M, Grace M, Binukumar B, et al. High burden of prediabetes and diabetes in three large cities in South Asia: the center for cArdio-metabolic risk reduction in South Asia (CARRS) study. *Diabetes Res Clin Pract*. 2015;110(2):172–18210.1016/j.diabres.2015.09.005.
22. Ali MK, Bhaskarapillai B, Shivashankar R, et al. Socioeconomic status and cardiovascular risk in urban south asia: the CARRS study. *Eur J Prev Cardiol*. 2016;23(4):408–41910.1177/2047487315580891.
23. Berg CJ, Ajay VS, Ali MK, et al. A cross-sectional study of the prevalence and correlates of tobacco use in Chennai, Delhi, and Karachi: data from the CARRS study. *BMC Public Health*. 2015;15:48310.1186/s12889-015-1817-z.
24. Patel SA, Shivashankar R, Ali MK, et al. Is the south asian phenotype unique to south asians?: comparing cardiometabolic risk factors in the CARRS and NHANES studies. *Glob Heart*. 2016;11(1)89–9610.1016/j.gheart.2015.12.010 [e3].
25. Saleheen D, Zaidi M, Rasheed A, et al. The Pakistan Risk of Myocardial Infarction Study: a resource for the study of genetic, lifestyle and other determinants of myocardial infarction in South Asia. *Eur J Epidemiol*. 2009;24(6):329–33810.1007/s10654-009-9334-y.
26. Ahmad S, Zhao W, Renstrom F, et al. Physical activity, smoking, and genetic predisposition to obesity in people from Pakistan: the PROMIS study. *BMC Med Genet*. 2015;16:11410.1186/s12881-015-0259-x.
27. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature*. 2015;518(7538):197–20610.1038/nature14177.
28. Saleheen D, Haycock PC, Zhao W, et al. Apolipoprotein(a) isoform size, lipoprotein(a) concentration, and coronary artery disease: a mendelian randomisation analysis. *Lancet Diabetes Endocrinol*. 2017;5(7):524–53310.1016/S2213-8587(17)30088-8.
29. Thanikachalam S, Harivanzan V, Mahadevan MV, et al. Population study of urban, rural, and semiurban regions for the detection of endovascular disease and prevalence of risk factors and holistic intervention study: rationale, study design, and baseline characteristics of PURSE-HIS. *Glob Heart*. 2015;10(4):281–28910.1016/j.gheart.2014.11.002.
30. Ravi S, Bermudez OI, Harivanzan V, et al. Sodium intake, blood pressure, and dietary sources of sodium in an adult south indian population. *Ann Glob Heal*. 2016;82(2):234–24210.1016/j.aogh.2016.02.001.
31. Must A, Thanikachalam M, Begum M, et al. The components of metabolic syndrome in relation to weight status in South Indians. *FASEB J*. 2013;27(1 Suppl) [1055. 15–1055.15. http://www.fasebj.org/content/27/1_Supplement/1055.15.abstract.
32. Chomitz VR, Prabhu SS, Thanikachalam S, et al. Physical activity and sedentary behavior in South Indian adults: urbanicity, gender, and obesity. *FASEB J*. 2013;27(1 Suppl) [1055. 27–1055.27. http://www.fasebj.org/content/27/1_Supplement/1055.27.abstract.
33. Thanikachalam M, Harivanzan V, Baliga RR, Abraham WT, Thanikachalam S. Abstract 200: geographical location and gender are predictors of elevated high sensitive C-Reactive protein (hsCRP) levels and the levels strongly correlate with metabolic syndrome (MetS) in a south asian population. *Arterioscler Thromb Vasc Biol*. 2015;33(Suppl. 1) [A200 LP-A200. http://atvb.ahajournals.org/content/33/Suppl_1/A200.abstract].
34. Thanikachalam M, Bai S, Harivanzan V, Shoben A, Baliga RR, Thanikachalam S. Gender-specific plasma triglyceride/high-density lipoprotein cholesterol concentration ratio levels to identify insulin resistance and associated cardio-metabolic risk factors in a south asian population. *Can J Cardiol*. 2017;29(10):S319–S32010.1016/j.cjca.2013.07.537.
35. Katulanda P, Constantine GR, Mahesh JG, et al. Prevalence and projections of diabetes and pre-diabetes in adults in Sri Lanka–Sri Lanka Diabetes, Cardiovascular Study (SLDCS). *Diabet Med*. 2008;25(September (9)):1062–1069.
36. Katulanda P, Ranasinghe P, Jayawardena R, Constantine GR, Rezvi Sheriff MH, Matthews DR. The prevalence, predictors and associations of hypertension in Sri Lanka: a cross-sectional population based national survey. *Clin Exp Hypertens*. 2014;36(7):484–491.
37. Katulanda P, Wickramasinghe K, Mahesh JG, et al. Prevalence and correlates of tobacco smoking in Sri Lanka. *Asia-Pac J Pub Heal*. 2011 Nov;23(6):861–869.
38. Katulanda P, Jayawardena MAR, Sheriff MHR, Constantine GR, Matthews DR. Prevalence of overweight and obesity in Sri Lankan adults. *Obes Rev*. 2010;11(November (11)):751–756.
39. Katulanda P, Ranasinghe P, Jayawardana R, Sheriff R, Matthews DR. Metabolic syndrome among Sri Lankan adults: prevalence, patterns and correlates. *Diabetol Metab Syndr*. 2012;4(May (1)):24.
40. Katulanda P, Jayawardena R, Ranasinghe P, Rezvi Sheriff MH, Matthews DR. Physical activity patterns and correlates among adults from a developing

country: the Sri Lanka Diabetes and Cardiovascular Study. *Public Health Nutr*. 2013;16(September (9)):1684–1692.
41. Huffman MD, Prabhakaran D, Osmond C, et al. Incidence of Cardiovascular Risk Factors in an Indian Urban Cohort: Results From the New Delhi Birth Cohort. *J Am Coll Cardiol [Internet]*. 2011;57(April (17)):1765–1774.
42. Bhargava SK, Sachdev HS, Fall CHD, et al. Relation of serial changes in childhood body-mass index to impaired glucose tolerance in young adulthood. *N Engl J Med*. 2004;350(February (9)):865–875.
43. Ahsan H, Chen Y, Parvez F, et al. Health Effects of Arsenic Longitudinal Study (HEALS): description of a multidisciplinary epidemiologic investigation. *J Expo Sci Environ Epidemiol*. 2006;16(2):191–20510.1038/sj.jea.7500449.
44. Wu F, Chen Y, Parvez F, et al. A prospective study of tobacco smoking and mortality in Bangladesh. *PLoS One*. 2013;8(3):e5851610.1371/journal.pone.0058516.
45. Heck JE, Marcotte EL, Argos M, et al. Betel quid chewing in rural Bangladesh: prevalence, predictors and relationship to blood pressure. *Int J Epidemiol*. 2012;41(2):462–47110.1093/ije/dyr191.
46. Chen Y, McClintock TR, Segers S, et al. Prospective investigation of major dietary patterns and risk of cardiovascular mortality in Bangladesh. *Int J Cardiol*. 2013;167(4):1495–150110.1016/j.ijcard.2012.04.041.
47. Corsi DJ, Neuman M, Finlay JE, Subramanian SV. Demographic and health surveys: a profile. *Int J Epidemiol*. 2012;41(6):1602–161310.1093/ije/dys184.
48. National Institute of Population Research and Training (NIPORT), Mitra and Associates, ICF International. Bangladesh Demographic and Health Survey 2011. Dhaka.
49. Harshfield E, Chowdhury R, Harhay MN, Bergquist H, Harhay MO. Association of hypertension and hyperglycaemia with socioeconomic contexts in resource-poor settings: the Bangladesh Demographic and Health Survey. *Int J Epidemiol*. 2015;44(5):1625–163610.1093/ije/dyv087.
50. Rahman M, Nakamura K, Seino K, Kizuki M. Sociodemographic factors and the risk of developing cardiovascular disease in Bangladesh. *Am J Prev Med*. 2015;48(4):456–46110.1016/j.amepre.2014.10.009.
51. Fatema K, Zwar NA, Milton AH, Rahman B, ASMN Awal, Ali L. Cardiovascular risk assessment among rural population: findings from a cohort study in a peripheral region of Bangladesh. *Public Health*. 2016;137:73–8010.1016/j.puhe.2016.02.016.
52. Menon VP, Edathadathil F, Sathyapalan D, et al. Assessmentof 2013 AHA/ACC ASCVD risk scores with behavioral characteristics of an urban cohort in India: preliminary analysis of Noncommunicable disease initiatives and research at AMrita (NIRAM) study. *Medicine (Baltimore)*. 2016;95(49)10.1097/MD.0000000000005542 e5542.
53. Tareen MF, Shafique K, Mirza SS, Arain ZI, Ahmad I, Vart P. Location of residence or social class, which is the stronger determinant associated with cardiovascular risk factors among Pakistani population? A cross sectional study. *Rural Remote Health*. 2011;11(3):1700.
54. Shafique K, Mirza SS, Mughal MK, et al. Water-pipe smoking and metabolic syndrome: a population-based study. *PLoS One*. 2012;7(7)10.1371/journal.pone.0039734 [e39734].
55. Rastogi T, Reddy KS, Vaz M, et al. Diet and risk of ischemic heart disease in India. *Am J Clin Nutr*. 2004;79(4):582–592.
56. Rastogi T, Vaz M, Spiegelman D, et al. Physical activity and risk of coronary heart disease in India. *Int J Epidemiol*. 2004;33(4):759–76710.1093/ije/dyh042.
57. Rastogi T, Jha P, Reddy KS, et al. Bidi and cigarette smoking and risk of acute myocardial infarction among males in urban India. *Tob Control*. 2005;14(5):356–35810.1136/tc.2005.011965.