The impact of migration on cardiovascular disease and its risk factors among people of Indian origin

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The overall burden of cardiovascular disease (CVD) continues to grow in both developed and developing countries. The expected rate of increase in CVD in developing countries in the next two decades is likely to be almost twice that in the developed countries. Furthermore, Indians tend to have premature CVD, at least a decade or so earlier than their counterparts in the developed countries and also have higher case fatality rate. It is becoming increasingly apparent that rapid transition of lifestyle in the era of globalization can have a significant impact on health, in particular the incidence of CVD risk factors and related events. Studying the impact of migration on CVD and its risk factors is helpful in understanding the lifestyle induced or ethnic differences in the relative incidence of CVD in different populations. In this article we systematically review migration-related studies on the Indian population with respect to CVD and discuss the relative importance of these findings in the prevention of CVD in this population. The review summarizes that the different rates of CVD in various ethnic groups represent a complex interaction of classical and novel cardiovascular risk factors in varying environments. However, a significant proportion of the excess risk of CVD in Indians of South Asian origin is explained by environmental, nutritional and lifestyle factors. It is important to validate the threshold levels for all conventional risk factors in this population and future work is necessary to understand the precise environmental mechanisms and possible genetic interactions underlying the increased CVD risk among South Asians.

Keywords: Cardiovascular disease, ethnic groups, lifestyle, migration, risk factors.

Introduction

CARDIOVASCULAR disease (CVD) is the single largest cause for mortality and morbidity in the world[1]. The overall burden continues to grow in both developed and developing countries, but there are distinct differences in the pattern of growth between the two, as the expected rate of increase in CVD in developing countries in the next two decades is likely to be almost twice that in the developed countries[2]. In India almost 2.6 million individuals are predicted to die due to coronary heart disease (CHD)[3], constituting nearly 54% of all CVD deaths by 2020. In addition, Indians tend to have premature CHD, at least a decade or so earlier than their counterparts in the developed countries and also have higher case fatality rate[4]. It is most likely that the rapid demographic and health transitions currently occurring in India make a major contribution to gene–environmental interactions and early life influences of foetal malnutrition that may be a cause of increased CVD in India[5,6].

Migration is defined as a permanent or semi-permanent change in residence across administrative boundaries for a period greater than one year. Major reasons for migration can be clubbed as 'push' factors encompassing factors like rural instability, low employment and demographic pressure. 'Pull' factors like better employment market, better services and low barriers also contribute to migration, especially of the young and productive group (18–35 years). While least developed countries are in the initial stage, most of the developing countries, including India are in the transition stage and developed countries in the terminal stage of migration, classified based on the proportion of urban population. Studying the impact of migration-induced differences on CVD risk factors and events is helpful in understanding the relative strength of association of various exposures in the home environment and that in the adopted environment. For example, among South Asian Indian migrant overseas communities, relatively high levels of CHD and of coronary and diabetic risk factors have been consistently noted, compared to their counterparts in India[7]. In this article, we review migration-related studies on the Indian population

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with respect to CVD and its risk factors. We will also discuss the various designs of migration studies on CVD, their strengths and weaknesses with specific examples.

Types of migration studies on CVD

Simple urban–rural comparison studies

Simple comparison based on geographical locations can provide only weak evidence on migration-induced disease outcomes. Often, simple comparison studies ignore the cultural, genetic and lifestyle backgrounds and migration status of the comparison groups[8]. However, the relative strength of association of various exposures and disease outcomes in urban–rural comparison studies is useful in generating research hypothesis for controlled comparison studies. For example, such comparison studies have highlighted urban–rural differences in CVD risk factors and their relative influence on CVD outcomes[9–11]. Another utility of such simple comparison studies, especially when repeated, is that they have the potential to evaluate temporal changes in CVD risk factor burden and compare the differences between rural and urban populations[12].

Within-country migration studies

Comparison of migrants who have moved from a rural origin to urban locations (rural to urban migrants) and the population from the original rural location is often interesting and provides epidemiological leads related to the causal pathway of various disease outcomes. The rural to urban migrants are expected to acquire the high risk of the urban population if the disease is largely environmentally determined. Sib-comparison studies of rural to urban migrants (comparison of rural–urban migrants and their siblings living in the rural area) allow us to overcome the inherent problems of conventional rural–urban comparisons by controlling partially for the cultural and genetic variation. However, such comparisons do not necessarily examine the interaction of migration with baseline risk levels, since those who migrate may be at a higher or lower risk than the non-migrant population. For example, in a longitudinal follow-up study on rural to urban migration and CVD risk factors in young Gautemalan adults, Torun *et al.*[13] showed migration-induced differences in undesirable eating habits, physical inactivity, higher body fat percentage and adverse lipid profile among rural to urban migrants compared to non-migrants. The effects of within-country migration process on CVD and its risk factors have been explored in only a limited way so far.

Cross-sectional comparison studies using country of birth as ethnic origin within a population

Migrants from a country with relatively low exposure to CVD risk factors are expected to acquire the high risk behaviours of the host country population. However, the outcomes of same level of exposure to risk factors may be different in genetically different individuals/populations. A study on the influence of country of birth on mortality from CVDs in Sweden revealed significantly higher CHD mortality rate among women born in Finland or Eastern Europe compared to the native Swedish population[14]. However, such comparison studies often yield unpredictable results. For example, when South Asians were compared to the local population in the United Kingdom, conventional risk factors did not explain the high propensity to CVD in South Asians[15]. This is mainly because the comparison was essentially of individuals belonging to different gene pools living in the same environment. Such studies often have the potential to nullify or dilute environmental factors and magnify the role of non-environmental factors. Moreover, comparison of ethnic minority groups against the whole population in the host country is not recommended, as in most of the cases both the groups are not comparable based on duration of exposure to various risk factors. The use of carefully chosen comparison populations, not necessarily the whole population originally from the host country, would sharpen ethnic variations. While structuring such comparisons in a well-designed study, it is important to make provisions for adjustment of temporal lifestyle and exposure trends that will have affected both the migrant population and the comparison group.

Inter-country migration studies comparing migrants and non-migrants

Similar to within-country migration studies, it is worthwhile to compare the disease outcomes in migrants living in a country with relatively high exposure to risk factors and to their counterparts living in the country of origin with relatively low levels of exposure to risk factors. The classic example is the study on risk factors of diabetes in Japanese migrants, comparing the risk of diabetes amongst Japanese living in Hawaii, Los Angeles and Japan[16]. The risk of diabetes in Japanese living in Hawaii and Los Angeles was 2–3 times higher than Japanese living in Japan. Similarly, the Tokelau islanders who migrated to New Zealand had a higher risk of diabetes and were more obese compared to non-migrants[17–19]. Similar to the within-country migration studies, if we use sib-comparison studies we can overcome the inherent problems of ethnicity comparison studies by controlling partially the genetic and cultural variation. The Boston–Irish Diet Heart Study, a study of the effects of Irish migration to USA,

Table 1. Number and type of studies selected for the review

Total number of studies	
Total number of studies obtained in the literature search	$n = 74$
Studies related to the review topic (CVD and its risk factors in Asian Indians)	$n = 36$
Type of study	
Simple urban–rural comparison studies	$n = 06$
Within-country migration studies	$n = 03$
Comparison studies using country of birth as ethnic origin within a population	$n = 24$
Inter-country migration studies comparing migrants and non-migrants	$n = 03$

Table 2. Mortality from CHD in South Asians overseas

	Groups contrasted		Age (yrs)	CHD mortality ratio
Singapore[21]	1980–88	South Asian/Chinese	30–69	3.8
Fiji[22]	1980–91	Indian/Melanesian	30–69	1.3
Trinidad[23]	1977–86	South Asian/African	35–69	2.4
South Africa[24]	1985	South Asian/European	35–74	1.4
England[25]	1979–83	South Asian/European	20–69	1.5
England[26]	2001–03	Indian/European	20-plus	1.5
Canada[27]	1979–93	South Asian/European	35–74	1.1
The United States[28]	1996–2000	Asian Indians/Whites	20-plus	1.3
California[29] (The Unites States)	1990–2000	Asian Indians/Hispanics	25–84	1.2

used sib-comparison methodology and highlighted the role of key dietary factors attributable to relatively high burden of CHD[20].

Migrants studies and CVD in Asian Indians

Review methodology

A literature search was carried out using various medical search engines, including 'Pubmed', 'OVID' and 'MDconsult' over the last 25 years using keywords 'South Asian (text)' or 'Indians (text)', or 'migrants (text)' and 'coronary heart disease (MeSH)' or 'Cardiovascular Diseases (MeSH)', or 'Diabetes Mellitus (MeSH)' or 'Metabolic Syndrome X (MeSH)' or 'Insulin Resistance (MeSH)'. The publications obtained through these literature searches signifying migration-induced differences were reviewed systematically and the key findings are summarized below. The search yielded 74 studies, out of which 36 were relevant to the review. Types of studies selected for the review are summarized in Table 1.

Studies with main outcome measurement as cardiovascular deaths/events

South Asians have emigrated in large numbers all over the world in the last 150 years. South Asians worldwide have been demonstrated to have a higher standardized mortality ratio when compared to other ethnic populations. This is clearly evident from 'migrant' studies which report a 1.1 : 3.8 CHD mortality ratio among migrants from the Indian subcontinent compared to the local populations (Table 2)[20–29]. Although Indian Asians are more likely than Europeans to seek medical advise for symptoms suggestive of angina, Chaturvedi *et al.*[30] demonstrated that they may be less likely to be referred for exercise testing, wait longer to be seen by a cardiologist, wait longer for angiography, and are less likely to receive thrombolysis for ST segment elevated myocardial infarction. South Asians also have high risk of stroke that is raised 1.5-fold compared to Europeans in the UK[31]. However, stroke has been less studied in South Asians compared to CHD.

Prevalence studies using country of birth as the ethnic identifier also reported higher CHD prevalence rate among South Asians compared to Europeans[15–32]. With respect to the within-country situation, higher prevalence rate of CHD in Indians living in highly urban areas compared with rural Indians has been documented[33–35].

Studies on determinants of CVD

Ethnic differences in exposure to various CVD risk factors and their related outcomes have been studied extensively. Studies on determinants of CHD involving the Asian Indian population[27,34,36–55] are summarized in the Table 3. It has been documented that classic risk factors, such as smoking, blood pressure, obesity and cholesterol vary substantially between subgroups of South Asians, such that in some cases levels are equivalent to, or significantly lower than, or significantly higher than the

Table 3. Migrant studies and CVD risk factors in South Asian Indians

Author	Identified risk factor
Migrant studies (highlighting non-conventional risk factors)	
McKeigue *et al.*[36,37]	Central obesity, hyperinsulinemia glucose intolerance (diabetes + IGT)
Hayes *et al.*[56]	Dyslipidemia (decrease HDL-cholesterol and increase triglycerides)
Enas and Mehta *et al.*[38] Anand *et al.*[39] Huogeveen *et al.*[40] Sandholzer *et al.*[41]	Elevated lipoprotein 'a'
Chambers *et al.*[42] Chandalia *et al.*[43] Anand *et al.*[44]	CRP
Bhalodkar *et al.*[45]	Particle size (HDL-c and LDL-c)
Liew *et al.*[46]	Leptin
Raji *et al.*[47]	Adiponectin
Anand *et al.*[27]	
Chambers *et al.*[48]	Elevated homocysteine
Migrant studies (highlighting conventional risk factors)	
Bhatnagar *et al.*[49] Shaukat *et al.*[50] Bhopal *et al.*[51]	Conventional risk factors are important and have been underestimated
Patel *et al.*[52]	Conventional factors: body mass index, blood pressure and fasting serum total cholesterol. Emerging factors: higher apolipoprotien B, triglycerides, non-esterified fatty acids and C-reactive protein
Urban–rural prevalence studies within India	
Mohan *et al.*[53]	Emphasis on conventional risk factors. High prevalence of IGT
Singh *et al.*[54]	Emphasis on conventional risk factors
Chadha *et al.*[34]	Emphasis on conventional risk factors
Gupta *et al.*[55]	Hypertension
Reddy *et al.*[58]	Obesity and overweight
Prabhakaran *et al.*[59]	Metabolic syndrome

comparison population[8,51]. In earlier studies comparing lipid parameters, the total cholesterol levels have been reported to be normal or low among the South Asian population compared to Europeans[49–52] and non-traditional risk factors like glucose intolerance, central obesity as measured by waist to circumference or waist to hip ratio, fasting triglycerides levels, free fatty acid level and insulin were uniformly elevated compared to Europeans[36,37]. Available data on physical activity levels among migrant Asian Indians, particularly among women, suggest that they have lower levels of physical activity compared with both Europeans and non-migrant Indian Asians[56]. Asian Indian migrants are more likely to live in areas with increased social and economic deprivation, which itself is suggested as a determinant of increased CHD rates in this population[57].

McKeigue *et al.*[15], in a study on early onset of CHD in South Asian men, suggested that higher insulin resistance among South Asian could provide a causal link. Studies among urban residents of India also suggest matching levels of insulin resistance and hyperinsulinemia as in migrant Indians[58]. Several simple urban–rural comparison studies also documented significantly higher levels of traditional as well as non-traditional risk factors in highly urban Indian localities[34,53–55,58,59]. In a sib-comparison within-country migration study conducted on a pilot basis in India, the prevalence of diabetes was higher in urban participants than in rural sibs[60]. A case report analysing the pedigree of a family who migrated from rural to urban areas also suggests that migration can accelerate the development of metabolic syndrome[61]. While an excess of CHD risk has been clearly demonstrated in Indians at home and abroad, with a gradient of increasing risk from rural to urban to emigrant subjects, follow-up studies that have examined the change in risk of South Asian Indians on migration are limited or none.

In our literature search we could find only three studies related to the inter-country migration influences that have examined free-living subjects in India compared to their counterparts who have migrated. This includes the study carried out by our group[49], in which Indian migrants living in West London were compared with their siblings in Punjab, India (sib-comparison). In this study the migrants from India had a less favourable risk profile compared to their siblings who did not migrate. In another similar study, Patel *et al.*[52] compared Gujratis (Indians) in Britain and their contemporaries in villages of origin in India and concluded that exposure to increased fat intake and obesity induced by migration is likely to explain the disproportionate combination of established risk factors (higher mean body mass index, greater dietary energy intake, fat intake, blood pressure and fasting serum total cholesterol)

and emerging risk factors (higher apolipoprotien B, triglycerides, non-esterified fatty acids and C-reactive protein) prevalent in Gujratis in Britain. However, in a study of healthy volunteers of Indian migrants in Sydney and their nominated relatives in India, Mahajan and Bermingham[62] found that the group in Australia had a more favourable disease risk profile than that in India. All these studies on determinants of CVD indicate that environmental factors are more responsible for higher incidence of CVD in Indians.

With regard to non-conventional risk factors a few interesting patterns have been observed. Novel risk factors such as C reactive protein, homocysteine and lipoprotein(a) are higher among Indian Asians compared with Europeans and may contribute to part of the excess cardiovascular risk in South Asians[39–48]. Similarly, the particle size of LDL and HDL cholesterol was lower in South Asians compared to people from other ethnicities[45]. Raji *et al.*[47], in a study comparing the ethnic differences in Asian migrant Indians and Whites, demonstrated significantly lower levels of adiponectin in Asian Indians that corresponds to increased insulin resistance, impaired fibrinolysis and altered endothelial function in this population.

Migrant studies and implication for prevention of CVD

Migration provides a naturally occurring experiment which may establish the etiological importance of factors acting at difference points in the life course[63]. If the risk of CHD among people migrating from a low incidence to a high incidence country increases with time, it is highly probable that factors acting later in life following migration are of etiological importance. On the other hand, if migrants retain the risk of their country of origin, then it is likely that genetic characteristics or factors operating early in life exert a greater influence than exposure later on.

Different rates of CHD among ethnic groups represent complex interactions of classical and novel cardiovascular risk factors in varying environment. Acculturation is the process by which immigrants acquire the behavioural patterns, values and attitudes of a new society and the major reason for migration-induced differences in risk-factor exposure and disease outcome among immigrants. It is becoming increasingly apparent that rapid transition of lifestyle in the era of globalization in certain ethnic groups can have a significant impact on health, in particular the incidence of cardiovascular diseases risk factors and related events. The information derived from follow-up studies comparing the migration-induced differences in risk-factor exposures and disease outcomes will be helpful in understanding the relationship among genes, the environment, society and culture that work together to accelerate morbidity and mortality attributable to CVD.

South Asians may have a genetic predisposition to CHD; however, environmental, nutritional and lifestyle factors are responsible for much of the population attributable risk. The South Asian arm of the INTERHEART study, a case control comparison of acute myocardial infarction and healthy controls, depicts similar population attributable risk (PAR) among South Asians for nine selected modifiable risk factors as in other ethnic populations. The combined PAR for the nine selected risk factors was 93% in young men and 96% in young women[64]. These risk factors included smoking, raised apolipoprotien B/apolipoprotien A1 ratio, hypertension, diabetes mellitus, abdominal obesity and psychosocial stress. Protective factors included daily consumption of fruits and vegetables, moderate alcohol consumption and regular physical activity. The known association of conventional risk factors with CVD supports a call for increased public health action to address these risk factors and prevent an inordinate increase of such diseases.

Aspects of primary prevention differ in some respects in ethnic minority groups compared to the general population. For the South Asian ethnic group obesity control via dietary intervention and increased physical activity are likely to be critical in reducing CVD risk. However, it is important to recognize that definitions of obesity derived in European populations may be inappropriate for ethnic minority groups, where the difference in obesity phenotype invalidates conventional thresholds[65–68]. Therefore, the awareness of ethnicity as a potential independent risk factor for CVD has clinical importance. Lower threshold should be considered for primary prevention strategies in South Asians. In addition, culturally sensitive and healthy lifestyle advice should be targetted to specific groups from an early age in an attempt to delay or prevent premature morbidity and mortality.

Migrant studies also emphasize the importance of health systems in being proactive in seeking out and treating individuals with cardiovascular risk factors.

Future directions

Future work is necessary to understand the precise environmental mechanisms and possible genetic interactions underlying the increased CHD risk among South Asians. The failure to explain increased CHD risk among South Asians at relatively younger ages and at lower levels of conventional risk factors explains the need for prospective population studies in South Asian ethnic groups. Well-designed prospective population studies in this ethnic group will help us to develop suitable models for risk prediction and risk reduction.

Migration studies provide an opportunity to test Forsdahl's hypothesis that poverty in early life followed by later affluence increases the risk of CHD[63]. According to this hypothesis, migrants who encounter prosperity in

adult life, having experienced relative deprivation during childhood, should face an even greater risk of CHD than long-term residents of the country they migrate to. However, early deprivation may not be the only explanation for high CHD rates in South Asians in the UK, since Afro-Caribbeans and others who have migrated from less developed regions have low CHD mortality rates[7]. Well-designed follow-up studies among Indian migrants will give key leads to prove this hypothesis in the Indian population.

Limited data are available describing the pattern of vascular dysfunction in South Asians, and the mechanisms underlying these abnormalities are yet to be established. The use of valid surrogate markers is important in understanding the nature of ethnic and geographic differences in the incidence of CHD. This is highly relevant in the South Asian Indian population as it is considered to be at high risk of developing CHD. Answers to questions about ethnic differences in CVD can be generated from large longitudinal studies of multi-ethnic cohorts specifically designed to assess the relative contributions of risk factors to subclinical atherosclerosis and incidence of individual cardiovascular disease outcomes. Future studies are vital both to identify appropriate targets of cardiovascular risk reduction depending on ethnicity and also to understand the genotype–phenotype–environmental interactions.

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