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ORIGINAL ARTICLE

Socioeconomic status and incident cardiovascular disease in a developing country: findings from the Isfahan cohort study (ICS)

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Abstract
Objectives We evaluated the association between socioeconomic status (SES) and incident cardiovascular disease (CVD) in a sample of the Iranian population.
Methods We followed 6,504 participants who were initially free from CVD. At baseline, subjects were assessed for CVD risk factors and self-reported data were obtained for education, occupation, and income.
Results After 24,379 person-years of follow-up (median = 4.8 years), 276 incident cases of CVD were detected. There was no significant association between the level of education and the incidence of CVD. In univariate analysis, retired individuals showed a significantly higher incidence of CVD than individuals who were working, and subjects in the highest tertile of income were less likely to suffer CVD than those in the lowest tertile. However, the associations disappeared after adjusting for age and sex.
Discussion There was no detectable, independent association between the SES and incident CVD. The counterbalance of the higher exposure to CVD risk factors and better access to health-care services and more appropriate risk factor modification in higher socioeconomic classes might diminish the association of SES and CVD in developing countries.

Keywords Socioeconomic status · Ischemic heart disease · Stroke · Iran

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Introduction

Cardiovascular disease (CVD) has emerged as a global epidemic and is currently the major cause of death and disability worldwide (Lopez 1993; Yusuf et al. 2001; Lopez et al. 2006). At the beginning of the 20th century, CVD and its attendant consequences were originally more common in the affluent members of society and residents of developed countries. However, from mid-20th century onwards, the burden of disease shifted toward people at the lower end of socioeconomic hierarchy, and to less developed countries (Yusuf et al. 2001). Eighty-three percent of CVD mortality and 86% of CVD disability-adjusted life years (DALYs) took place in low- and middle-income countries (Lopez et al. 2006). Parallel with the increasing number of developing countries undergoing epidemiologic transition (shifting from infectious diseases to chronic diseases) and demographic transition (aging of population) (Omran 2005; Yusuf et al. 2001), the burden of CVD is bound to increase in the coming years. The status of Middle Eastern nations in this context is especially worrying, as they will face the greatest increment in the absolute burden of CVD in the world (Wild et al. 2004).

Socioeconomic status (SES) is a measure of an individual's social position relative to other members of a society (Clark et al. 2009). In other words, individuals are identified as belonging to members to low-, medium-, or high socioeconomic classes based on comparisons of SES indicators, such as educational qualifications, occupation, income, housing tenure, and household amenities.

An association between lower SES and poor health—the so-called "wealth-health gradient", has been observed for many years (Kaplan and Keil 1993). Although several studies from high-income countries have linked low SES to increased mortality from, and incidence of CVD (Deans et al. 2009; Nash et al. 2011; Diez-Roux et al. 1995), studies on the association of SES and incidence of CVD are scarce in low- and middle-income countries, particularly in the Middle East (Clark et al. 2009; Bahonar et al. 2011; Gupta et al. 2010). Furthermore, a weaker and more erratic relationship between SES indicators and health has been reported in the small number of studies from middle-income countries, compared to those from industrialized countries (Rosero-Bixby and Dow 2009; Smith and Goldman 2007). Hence, additional information has been called from developing countries to assess the association of SES with CVD (Clark et al. 2009).

With this in mind, we investigated the likely association between three SES indicators (i.e. education, occupation, and income) and incidence of CVD during the 5-year follow-up of the Isfahan cohort study (ICS), which includes a representative sample of Iranian adults who did not have CVD at baseline.

Methods

Study population

The ICS is a population-based, longitudinal ongoing study of 6,504 adults aged 35–75 years at baseline in 2001, living in urban and rural areas of three counties (Isfahan, Arak, and Najafabad) in Central Iran. Cohort study participants had participated in the Isfahan Healthy Heart Program (IHHP), a comprehensive integrated community-based program for CVD prevention and control (Sarrafzadegan et al. 2003) conducted by Isfahan Cardiovascular Research Center (ICRC), a World Health Organization (WHO) collaborating center in the eastern Mediterranean region. The methodology of ICS has been previously described in detail (Sarrafzadegan et al. 2010); briefly, between January and September 2001, subjects aged ≥35 years were recruited using multistage random sampling; those with history of CVD at baseline were excluded and the remaining subjects have been followed since then. The study protocol was approved by the Ethics Committee of ICRC and all subjects gave written informed consent.

Data collection

A full structured interview was conducted by trained health professionals using a validated questionnaire including questions on demographic characteristics, SES, knowledge, attitude and practice of subjects regarding lifestyle behaviors (including smoking, physical activity, and dietary habits) and CVD.

Three domains of SES, namely, education, occupation, and income were addressed by using self-report interview questions. Education was categorized into three levels: (1) Low (illiterate or primary) corresponding to ≤5 years of schooling, (2) Medium (Middle school and High school) corresponding to 5–11 years of schooling, and (3) High (University) corresponding to ≥12 years of schooling. Occupation was categorized into four main groups: housewife, manual, non-manual, and retired. Household income was categorized based on the income brackets identified by the Iranian Central Bank. It should be acknowledged that the self-reported responses about income might be unreliable; however, we assumed that any misclassification of income would apply to all income groups and would result in a non-differential bias.

After the interviews, the participants underwent full physical examination by trained physicians and nurses. Waist circumference was measured at the midpoint between the iliac crest and the rib cage at minimal respiration. Hip circumference was measured at the maximum protuberance of the buttocks, and the waist-to-hip ratio (WHR) was calculated. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Blood pressure was measured after 5 min of rest in sitting position and repeated by a trained person after at least 5 min. None of the participants had drunk tea/coffee or smoked within 30 min preceding the measurements. A 12-lead electrocardiogram was recorded for all participants.

Laboratory assays

Peripheral venous blood specimens were collected from an antecubital vein after 10–12 h fasting of subjects. All blood samples were kept frozen at −20°C to be assayed within 72 h at the central laboratory of ICRC, which meets the criteria of the National Reference Laboratory (a WHO-collaborating center) and is under external quality control of St. Rafael University, Leuven, Belgium. Fasting plasma glucose, total cholesterol (TC), and triglyceride (TG), were determined by enzyme colorimetric assay using an Eppendorf autoanalyzer (Eppendorf Corp., Hamburg, Germany). High-density lipoprotein-cholesterol (HDL-C) was measured using the precipitation-based method. Serum low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation (Friedewald et al. 1972) in subjects with triglycerides less than 400 mg/dL; otherwise, it was measured using standard kits.

Follow-up surveys

After the baseline survey in 2001, the participants were followed up biannually, through structured telephone interviews or home visits (15%) in 2003 and in 2005–2006. In telephone follow-up, at least five attempts were made to contact all the living participants or, if deceased, their first-degree relatives. If telephone interviews were unsuccessful, the participants would be visited at their home address.

In the event of death, hospitalization or neurological symptoms, the date of the events, the physician's diagnosis and the name of the hospital were obtained. A physician reviewed follow-up data from 1,032 (20%) participants or relative's of deceased participants; there were 92 reports (1.8%) of only neurological symptoms, and 528 (10.4%) of ischemic heart disease (IHD), including 132 (2.6%) deaths and 396 (7.8%) hospitalizations. Further investigations were carried out to authenticate documents, including medical records, death certificates, and verbal autopsies. A trained nurse carried out the verbal autopsies as a secondary interview with surviving family members using a defined questionnaire to elicit medical history, as well as signs and symptoms prior to out-of-hospital death. Unrelated reports included 82 (1.6%) other internal diseases, 235 (4.6%) elective surgery cases, 43 (0.8%) trauma patients, and 144 (2.8%) patients with other diseases.

Confirmation of end-points

The primary end-point of the study was the occurrence of CVD including IHD and stroke. Two separate expert panels of cardiologists and neurologists blinded to the subjects' risk factor profiles reviewed all relevant documents including death certificates to confirm the events. Although the in-hospital diagnoses of clinicians were considered, the final decisions of the panel were made independently.

IHD was defined as definite or probable acute myocardial infarction (AMI), unstable angina (UA), and sudden cardiac death. The criteria for ischemic heart disease were modified from those of the WHO Expert Committee (Sarrafzadegan et al. 2010). The diagnosis of acute MI was based on the presence of at least two of the following criteria: (1) typical chest pain lasting more than 30 min, (2) ST elevation >0.1 mV in at least two adjacent electrocardiograph leads and (3) an increase in the serum level of cardiac biomarkers. The definition of UA required typical chest discomfort lasting more than 20 min within the 24 h preceding hospitalization and a change in the usual pattern of angina or pain: occurring with a crescendo pattern, being severe and described as a frank pain. The diagnosis of UA might be new or based on dynamic ST-segment or T-wave changes in at least two adjacent electrocardiogram leads. Sudden cardiac death was defined as death within 1 h of onset, a witnessed cardiac arrest, or abrupt collapse not preceded by >1 h of symptoms.

Stroke was defined according to the WHO definition: a rapid-onset focal neurological disorder persisting for at least 24 h and of probable vascular origin (Sarrafzadegan et al. 2010). The diagnosis of incident stroke was made based on the clinical criteria.

Statistical analysis

The Kolmogorov–Smirnov test was applied to examine normal distribution. Continuous variables are expressed as mean ± SD and were compared by Student's *t* test. Categorical variables were compared using a Chi-square test and are presented as absolute frequencies with percentages. The predictive value of SES indicators including education, occupation, and income for CVD was assessed by Cox proportional hazards modeling with time to outcome as the dependent variable and the presence of defined risk factors as independent dichotomous variables. Individuals were censored at the first cardiovascular event. First, univariate regression analysis was used to assess the association of each of the three domains of SES education, occupation, and income with CVD (Model A). Then the effect was adjusted for potential confounders by consecutively adding the age and sex (Model B), smoking status (Model C), BMI and hypertension (Model D). For all analyses, the statistical package SPSS version 13.0 for Windows (SPSS Inc, Chicago, Illinois, USA) was used. All *p* values were 2-tailed with significance defined as $p \leq 0.05$.

Results

The response rate for house interviews was 98%, with 95% of the total subjects attending the examination clinic. Of a total 6,504 subjects (mean age of 50.7 ± 11.6 years) recruited to the ICS, 2,788 (51.9%) were men. Of the whole sample, 978 (15.0%) and 464 (7.1%) participants were lost in 2003 and 2005–2006 follow-ups, respectively. A major reason for the high rate of loss in follow-up was widespread changes in domestic telephone numbers, mainly due to government sponsored development projects. There were no significant differences between available participants and subjects lost in follow-up in respect of baseline characteristics and the prevalence of CVD risk factors.

After 24,379 person-years of follow-up (with median follow-up of 4.8 years; 4.6 and 5 years for the 25th and the 75th quartiles, respectively), 219 incident cases of IHD (125 in men and 94 in women) and 57 incident cases of stroke (28 in men and 29 in women) were documented. IHD consisted of 13 cases of fatal MI (8 in men) and 45 cases on non-fatal MI (30 in men), 113 UA cases (54 in men) and 48 cases of sudden cardiac death (33 in men). Absolute incidence of IHD was 8.9 (95% confidence intervals: 7.8–10.2) per 1,000 person-years for total participants, 10.6 (8.8–12.5) per 1,000 person-years for men and 7.4 (6.0–9.0) per 1,000 person-years for women. The respective incidence of ischemic stroke was 2.3 (1.7–3.0), 2.3 (1.6–3.3) and 2.3 (1.5–3.2) per 1,000 person-years.

The baseline clinical, socioeconomic and laboratory characteristics of the study participants are presented in Table 1. In general, participants who developed CVD were more likely to be urban men, to be older and to have higher rates of smoking, hypertension, diabetes mellitus, dyslipidemia, and obesity than those without CVD. Plasma levels of glucose, TG, TC and LDL-C were significantly higher in subjects who had cardiovascular events than those without events, whereas no significant difference was observed between the two groups with respect to HDL-C levels. Furthermore, patients with cardiovascular events were more likely to have lower educational achievements, to be retired and to have lower monthly income than those without cardiovascular events.

Table 2 shows the distribution of CVD events according to three SES indicators, namely, education, occupation, and income. Of the participants with <5 years of education, 5.6% developed CVD; among the participants with

Table 1 Baseline demographic, socioeconomic and clinical characteristics of study population

	Cardiovascular disease		
	Present (n = 276)	Absent (n = 5,099)	p
Demographic and clinical characteristics			
Age (year)	58.81 ± 11.20	50.23 ± 11.49	<0.0001
Male sex, n (%)	153 (55.4)	2,464 (48.3)	0.021
Urban residence, n (%)	217 (78.6)	3,680 (72.2)	0.019
Diabetes mellitus, n (%)	59 (21.8)	459 (9.1)	<0.0001
Systemic hypertension, n (%)	165 (59.8)	1,395 (27.4)	<0.0001
Dyslipidemia, n (%)	252 (92.3)	4,355 (86.9)	0.009
Reformed ever-smoking[a], n (%)	71 (25.7)	1,050 (20.6)	0.041
Body mass index (kg/m^2)	27.28 ± 4.83	26.65 ± 4.44	0.024
Waist circumference (cm)	97.65 ± 12.58	94.53 ± 12.25	<0.0001
Waist-to-hip ratio	0.95 ± 0.07	0.93 ± 0.07	<0.001
Biochemical profile			
LDL-C (mg/dL)	139.84 ± 45.91	127.39 ± 41.93	<0.001
HDL-C (mg/dL)	46.51 ± 10.35	46.91 ± 10.36	0.534
Total cholesterol (mg/dL)	227.47 ± 52.33	211.27 ± 49.08	<0.0001
Triglycerides (mg/dL)	218.28 ± 118.39	188.88 ± 102.43	<0.0001
Fasting glucose (mg/dL)	100.42 ± 46.89	87.92 ± 31.74	<0.0001
Socioeconomic profile			
Education, n (%)			0.041
0–5 year	215 (77.9)	3,605 (70.8)	
6–12 year	48 (17.4)	1,172 (23.0)	
>12 year	13 (4.7)	314 (6.2)	
Occupation, n (%)			<0.0001
Housewife	118 (42.7)	2,450 (48.1)	
Manual	56 (20.3)	1,238 (24.3)	
Non-manual	48 (17.4)	980 (19.2)	
Retired	54 (19.6)	430 (8.4)	
Income, n (%)			0.001
1st tertile	103 (39.0)	1,469 (29.7)	
2nd tertile	91 (34.5)	1,716 (34.7)	
3rd tertile	70 (26.5)	1,764 (35.6)	

All plus-minus values are mean ± SD

LDL-C low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol

[a] Ever-smoking means a positive history of smoking at any time in the life

Table 2 Distribution of CVD among the study population by socioeconomic status

SES category	Incidence rate of CVD[a]	Incidence of CVD (%)
Education		
0–5 year	12.41	5.6
6–12 year	8.72	3.9
>12 year	8.58	4.0
Occupation		
Housewife	10.11	4.6
Manual	9.51	4.3
Non-manual	10.17	4.7
Retired	25.84	11.2
Income		
1st tertile	14.73	6.6
2nd tertile	10.99	5.0
3rd tertile	8.35	3.8

[a] Cases per 1,000 person-year

[b] 1st tertile: Monthly income <500,000 Rials, 2nd tertile: Monthly income 500,000–800,000 Rials, 3rd tertile: Monthly income >800,000 Rials

6–12 years and >12 years of education, 3.9 and 4.0% were found to have CVD, respectively. As expected, retired subjects displayed the highest rates of CVD (25.84 cases/1,000 person-years) compared to working individuals. Moreover, participants with monthly income below the lowest tertile were more likely to have cardiovascular events (14.73 cases/1,000 person-years), followed by those falling in the second tertile of monthly income (10.99 cases/1,000 person-years).

In univariate analysis (Model A) shown in Table 3, the incidence of CVD in retired subjects was about 2.7 times the incidence in housewives (HR = 2.69, 95% CI = 1.91–3.79, $p < 0.0001$). In addition, among subjects with monthly incomes over the third tertile, the incidence of CVD was 32% less than subjects whose monthly incomes were less than the lowest tertile (HR = 0.68, 95% CI = 0.48–0.96, $p = 0.03$). However, after adjustment for age and sex (Model B), the associations of occupation and income with the incidence of cardiovascular event were no further significant. After consecutively adding other potential confounders, including smoking status (Model C), BMI, and hypertension (Model D), the strengths of the associations were further attenuated (Table 3).

Discussion

In this representative cohort of the Iranian population, we observed that the incidence of CVD in retired individuals was higher than in housewives (HR = 2.69, $p < 0.0001$). However, the association was no longer significant after adjustment for age and sex ($p = 0.59$), and consecutively adding other potential confounders to regression model did not change the model significantly ($p = 0.42$). We also observed that subjects in the highest tertile of income had significantly lower incidence of CVD than those in the lowest tertile (HR = 0.68, $p = 0.03$). However, the association disappeared by simultaneous adjustment for age and sex ($p = 0.75$). In addition, there was no detectable

Table 3 Hazard ratios of categories of socioeconomic status for cardiovascular events: ICS, 2001–2006 ($n = 5,375$)

	Model A			Model B			Model C			Model D		
	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*
Education												
0–5 year	R	R		R	R		R	R		R	R	
6–12 year	0.76	0.53–1.08	0.13	1.20	0.83–1.75	0.33	1.10	0.75–1.60	0.62	1.15	0.78–1.68	0.48
>12 year	0.72	0.38–1.35	0.31	1.08	0.57–2.05	0.81	0.95	0.50–1.81	0.89	1.01	0.53–1.92	0.99
Occupation												
Housewife	R	R		R	R		R	R		R	R	
Manual	0.99	0.72–1.39	0.99	0.58	0.21–1.63	0.30	0.82	0.29–2.34	0.71	0.84	0.29–2.39	0.75
Non-manual	1.29	0.88–1.88	0.19	0.65	0.23–1.83	0.42	0.87	0.31–2.48	0.80	0.86	0.30–2.44	0.77
Retired	2.69	1.91–3.79	<0.0001	0.75	0.26–2.15	0.59	0.62	0.21–1.78	0.37	0.65	0.22–1.86	0.42
Income												
1st tertile	R	R		R	R		R	R		R	R	
2nd tertile	0.79	0.59–1.07	0.12	0.97	0.72–1.31	0.85	0.95	0.71–1.28	0.73	0.89	0.66–1.21	0.47
3rd tertile	0.68	0.48–0.96	0.03	0.94	0.66–1.35	0.75	0.90	0.63–1.29	0.58	0.85	0.59–1.23	0.40

Model A unadjusted model, *Model B* adjusted for sex and age, *Model C* adjusted for sex, age, and smoking status, *Model D* adjusted for sex, age, smoking status, body mass index, and hypertension

HR hazard ratio, *CI* confidence interval, *R* reference category association between the level of education and the incidence of CVD in the studied population.

Our findings support and expand the evidence that the relationship between SES and incidence of CVD is likely to vary across cultural and socioeconomic settings (Goldman et al. 2011; Mackenbach et al. 2000). There are multiple studies from developed countries, which are consistently reporting an inverse association between SES and incidence of CVD and mortality (Diez-Roux et al. 1995; Feldman et al. 1989; Marmot et al. 1991; Rose and Marmot 1981; Kaplan and Keil 1993; Clark et al. 2009). In contrast, recent data linking SES with CVD in low- and middle-income countries are both limited and controversial. Few studies from developing countries have shown higher prevalence of IHD among subjects with higher SES (Reddy 1993; Terris 1999). In a study by Chadha et al. (1990) on the urban population of Delhi, the prevalence of IHD was 6.1% in males and 3.0% in females in higher socioeconomic groups as compared with 2.0% in males and 0.9% in females in lower socioeconomic groups. Rosero-Bixby and Dow (2009) performed an analysis on data from 8,000 elderly Costa Ricans and observed a trend toward better situation in mortality and CVD risk factors including high blood pressure, obesity, high epinephrine, TG, and low dehydroepiandrosterone-sulfate (DHEA-S) levels, as well as the metabolic syndrome in more affluent subjects than in those with high-SES. In concordance with our findings, Smith and Goldman (2007) performed an investigation in a nationally representative sample of elderly Mexicans and observed a weaker and more erratic association between SES and health indices than in developed countries. In contrast to our data, Gupta et al. (2010) reported that urban Indian subjects with low and middle educational status are at a greater cardiovascular risk (as measured by the Framingham risk score) than highly educated individuals.

Such disparity in study results from developing countries might be due to the fact that these countries are currently experiencing a transitional phase from positive SES-CVD relationship toward negative one (Clark et al. 2009). In other words, in parallel with the economic growth, the pattern of SES-CVD in developing countries is replicating that in developed countries (Clark et al. 2009), where CVD were more frequent in higher-SES subjects until the 1960s and later shifted towards the poor (Yusuf et al. 2001). Hence, it might be implied that the different results obtained in studies from low- and middle-income countries might be due to the relative status of the studied societies in the transition process. The conflicting results in the aforementioned studies from developing countries may also be related to the differences in the measured health-related outcomes. For example, Rosero-Bixby and Dow (2009) assessed the all-cause mortality and the prevalence of CVD risk factors, Smith and Goldman (2007) evaluated the self-reported health and physical functioning, Gupta et al. (2010) measured the incidence of CVD using the Framingham risk score, and Chadha et al. (1990) measured the prevalence of IHD in low-SES and high-SES subjects. In this study, we evaluated the relationship of SES indicators with the risk of incident CVD in a longitudinal study; to the best of our knowledge, ICS is the first longitudinal study of incidence of CVD from any eastern Mediterranean country that is being conducted in a geographic area with a large, well-defined population living in urban and rural areas, and has a relatively high participation rate using valid case ascertainment.

The negligible association of CVD with SES in developing countries compared to rich countries may also be attributed to the complex pattern of distribution of risk factors across socioeconomic classes in these countries. Wealthy citizens in poor countries tend to have more behavioral risk factors than do poor citizens (Okrainec et al. 2004). Data from International Clinical Epidemiology Network (INCLEN) found a positive association between the level of education and obesity among the Asian populations studied (body mass index and cardiovascular disease risk factors in seven Asian and five Latin American centers: data from the International Clinical Epidemiology Network INCLEN (1996). A study in Nigeria documented increased meat consumption, serum lipids, blood pressures, insulin levels, and obesity among those with higher SES when compared to those with lower SES (Yeh et al. 1996). In agreement with the aforementioned studies, in a recently published study by our group (Bahonar et al. 2011), we observed that highly educated subjects were more likely to be obese and to have higher levels of TG, TC, and LDL than those with lower educational qualification. A similar pattern was also observed in subjects with higher monthly income than in those with lower income. In developing countries, higher socioeconomic classes are often the first to adopt a Western lifestyle because of wealth and exposure. However, because they are also more educated, they are more likely to have higher incomes and better access to health-care services; also they are primed to learn about the negative aspects of their lifestyle choices and to make appropriate behavior modifications (Clark et al. 2009; Okrainec et al. 2004). Hence, the counterbalance of the higher exposure to CVD risk factors and better access to health-care services and more appropriate risk factor modification might diminish and even eliminate the association of SES and CVD in developing countries.

Our study has a potential limitation; some unreliable self-reported income data might have confounded our results, hence interpretation of our findings on the relationship of income and incidence of CVD warrants caution.

In conclusion, we found that three dimensions of SES, namely education, occupation and income, were not significantly associated with the incidence of CVD in the Iranian population. The similar incidence of CVD alongside the high prevalence and complex distribution of CVD risk factors across different socioeconomic classes in developing countries (Bahonar et al. 2011), underscores the necessity of intensive interventions on entire populations of these countries for prevention and control of CVD.

Disclosure We declare that this study was performed in accordance with the declarations of Helsinki and Tokyo and the current laws of the Islamic Republic of Iran regarding Human Studies and the study protocol was approved by the Ethics Committee of ICRC.

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Conflict of interest The authors declare that they have no conflict of interest.

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