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CARDIOVASCULAR DISEASES

Lower HDL-cholesterol among healthy middle-aged Japanese-Brazilians in São Paulo compared to Natives and Japanese-Brazilians in Japan

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Abstract. Blood lipid levels are determined by a combination of genetic and environmental factors. Higher than average values of high-density lipoprotein cholesterol (HDL-cholesterol) have been observed in people of Japanese ethnicity. The aim of this study was to investigate whether Japanese immigrants to Brazil and subsequent generations maintain the protective benefits associated with higher levels of HDL-cholesterol, and to examine the potential associations between HDL-cholesterol and a variety of other blood lipids, anthropometric and lifestyle factors. Healthy men and women aged 35 years and older who were Native Japanese (n = 198) or Japanese-Brazilians (JB) living in São Paulo, Brazil (n = 198) and in some Japanese cities (n = 246) were investigated. Anthropometric variables, blood lipids including HDL-cholesterol, and lifestyle factors were assessed. Serum HDL-cholesterol was observed to be lower for JB in São Paulo (both women and men) compared with Natives and JB in Japan. Among the groups, triglycerides, waist circumference, LDL-cholesterol, meat intake, stress, and smoking were observed to be independently negatively associated with HDL-cholesterol, whereas total cholesterol, fish intake, and physical activity were positively associated. Lower levels of HDL-cholesterol among both men and women of JB in São Paulo compared with both other groups were confirmed even after lifestyle adjustments. Our findings highlight the significantly lower levels of HDL-cholesterol among Japanese-Brazilians living in São Paulo city compared to Japanese-Brazilians and Native Japanese residing in Japan. Although several lifestyle factors were found to be significantly associated with HDL-cholesterol, they cannot adequately explain the role of the Brazilian cultural environment on HDL-cholesterol levels.

Key words: Cardiovascular disease, HDL-cholesterol, Lifestyle, Japanese immigrants, Japanese-Brazilian

Introduction

Epidemiological and clinical studies provide evidence that blood serum concentrations of high-density lipoprotein cholesterol (HDL-cholesterol) are independently associated with increased risks for coronary heart disease (CHD) [1–3]. Levels of HDL-cholesterol in the Japanese population are higher than those reported in Caucasian populations[4, 5]. This favorable lipid profile may be one of the explanations for the lower morbidity of CHD in Japanese populations [6]. Also, there is a growing consensus in support of high HDL-cholesterol as an additional therapeutic target to promote longevity [7]. Japanese have the longest life expectancy of the world, which may be associated with their lower mortality from CHD. Lipid profiles play an important role in overall health and protection from cardiovascular pathology [8]. The protective effect of HDL-cholesterol has been attributed to its role in reverse cholesterol transport, its effect on endothelial cells, and its antioxidant activity [9]. Other lipid abnormalities tend to accompany low HDL-cholesterol, such as increased triglycerides (TG) and low-density lipoprotein cholesterol (LDL-cholesterol) [2]. In many individuals, these characteristics occur as part of the metabolic syndrome, a constellation of risk factors for diabetes and CHD that also includes abdominal obesity, elevated fasting blood glucose levels, and hypertension [10].

Significant differences in serum lipid levels have been reported between various ethnic groups and nationalities which are likely a reflection of both environmental and genetic factors [11–13]. Environmental factors affecting serum HDL-cholesterol concentrations include physical activity, obesity, composition of diet, use of tobacco and alcohol, stress, and medication [1, 14–20]. Previous studies have shown unfavorable lipid profiles to be associated with increased prevalence of CHD among Japanese immigrants to Hawaii [21] and California [22] compared to Native Japanese. Likewise, lower levels of HDL-cholesterol were observed in Japanese-Americans in Seattle compared to Native Japanese, and it is suggested that the adoption of a westernized lifestyle may be harmful to people of Japanese ancestry who may have a greater propensity for the development of various metabolic abnormalities such as diabetes and hypercholesterolemia [13].

The Japanese immigration to Brazil has concentrated in and around São Paulo city. It has become the largest Japanese community outside of Japan. Previous studies of Japanese-Brazilians living in there found that several changes in lifestyle were related to an increased risk of developing chronic diseases [23]. The study reported lower levels of HDL-cholesterol in Japanese-Brazilians in Brazil compared to Natives. Furthermore, since twenty years ago a movement of back-immigration to Japan has been initiated, and nowadays a population of nearly 300 thousand Japanese-Brazilians is estimated to be living in Japan. However, there is little information about HDL-cholesterol and its association with other lipids and lifestyle factors among Japanese-Brazilians in Brazil, or among those who returned to live in Japan. With this in mind, this study investigated whether Japanese-Brazilians retained the increased HDL-cholesterol profile compared with Native Japanese, and examined the association between HDL-cholesterol levels and other lipids and lifestyle factors. This investigation clarifies our understanding of the impact of immigration on an important risk factor for CHD, a significant public health concern.

Methods

Study population

This cross-sectional study was undertaken in 2004 and 2005 to examine the serum lipid profiles and lifestyle factors of people aged 35 years and over in urban areas of Japan and Brazil. This study involved Native Japanese and Japanese-Brazilians (JB), with both parents of Japanese ancestry, who were raised in Brazil. The participants had no history of heart failure, stroke, angina pectoris, myocardial infarction, diabetes, or cardiac surgery, and were not under medication for dyslipidemia, heart failure or diabetes. Also, those with blood glucose levels above 126 mg/dl were excluded from this analysis. Consequently, two hundred fifty-two participants were excluded from the analysis (parents were not of Japanese ancestry in 85 cases, 17 cases displayed difficulties with blood assessment, 150 participants did not meet the above inclusion criteria regarding disease and medication). In total, 198 Natives Japanese (110 women and 88 men) and 444 Japanese-Brazilians (217 women and 227 men), ranging in age from 35 to 79 (52.9 ± 10.3) years were included in the study.

Native Japanese

Japanese natives were recruited through newspapers and local newsletters in three community centers located in Chiba (Sodegaura), Ibaraki (Tsukuba), and Mie (Shima) prefectures. Data were collected on weekends in October and November of 2005 and 198 participants (110 women and 88 men) were included in this group. None of the participants had lived in abroad for more than 3 months during their lifetime.

Japanese-Brazilians in Japan

Brazilians of Japanese ancestry residing in three different provinces in Japan (Oizumi in Gunma, Kamisato in Saitama, and Minokamo in Gifu) were recruited through Nippon-Brazilian community centers, Brazilian schools, restaurants, stores, newspapers, magazines, and local television stations. Data were collected during weekends in October and November of 2004. A total of 246 participants were included in this group (97 women and 149 men). The majority of JB in Japan were from the second generation (*nisei*) of Japanese descendents (73.2%, 68 women and 112 men), in addition, 2.5% (1 women and 5 men) from the first generation (*issei*), and 24.4% (28 women and 32 men) from the third generation (*sansei*). At the time of data collection, all participants in this group were living in Japan for a length of greater than 1 year, with 59.3% (56 women and 90 men) for a period of greater than 5 years.

Japanese-Brazilians in São Paulo

Data were collected in ten Nippon-Brazilian associations and cultural centers located in São Paulo city during March and April of 2005. A total of 198 participants were included in this group (120 women and 78 men). The majority of JB in São Paulo were *nisei* (61.6%, 49 men and 73 women), with 15.7% (13 men and 18 women) and 22.7% (17 men and 28 women) *issei* and *sansei*, respectively.

Protocol

The overall protocol was approved in Brazil by the Ethical Committee of the School of Medicine, University of São Paulo, and in Japan by the Human Investigation Review Committee at the School of Comprehensive Human Sciences, University of

Tsukuba. A statement of informed consent (available bilingually in Japanese and Portuguese) was obtained from all participants prior to initiation of the data collection. Data collection was carried out for all groups during mild seasons (spring or autumn), in order to avoid the influence of climatic factors on the variables measured in this study. The survey consisted of both quantitative clinical examinations and qualitative information assessed through self-administered questionnaires checked by trained researchers.

Data collection was conducted in the morning, following an at least 12 h fasting period in which no food or medication was taken by the participants. A sample of venous blood (approximately 10 cc) was drawn from each participant and collected in vacuum tubes. The blood samples in Japan were stored at 4°C until they were delivered to the laboratory for analysis (Kotobiken Medical Laboratories, Inc., Tsukuba, Japan). All analyses were conducted within 72 h of the blood collection. For samples collected in Brazil, blood tubes were immediately centrifuged to obtain plasma and serum, and frozen at −80°C. After the data collection in Brazil, frozen blood samples (approximately 5 cc) were transferred to Japan to be analyzed by the same procedure in the same laboratory. Serum total cholesterol (TC) was measured by the cholesterol oxidase HDAOS method (Wako Pure Chemical Industries, Ltd.), HDL-cholesterol using a modified enzymatic method (Kyowa Medex Co., Ltd.), and TG by a GPO-HDAOS method, a glycerol blanking method assay (Daiichi Pure Chemicals Co., Ltd.). The LDL-cholesterol was calculated according to the method of Friedewald et al [24]. The total/HDL-cholesterol ratio was calculated as TC divided by HDL-cholesterol (in mg/dl). A homogeneous method based on an innovative detergent technology (A&T Corporation) was used for the assessment of fasting plasma glucose.

Weight to the nearest 0.1 kg was measured using a digital scale balance (TBF-551, Tanita, Tokyo, Japan) and height to the nearest 0.1 cm using a wall-mounted stadiometer (YG-200, Yagami, Nagoya, Japan). Body mass index (BMI) was calculated as weight (kg) by squared height (m^2). Waist circumference (WC) was measured at the umbilical level (cm). A questionnaire on history of disease, medication and lifestyle, including personal data about immigration history for Japanese-Brazilians, was completed by each participant. Participants were classified into the three groups (Native, JB in Japan, JB in São Paulo) by residence and according to their history of immigration. A questionnaire examining smoking history was used to determine whether or not the participant was a current smoker and the number of cigarette smoked per day. For consumption of alcoholic beverages (wine, beer, liquor, Japanese *sake*, Brazilian *cachaça*, vodka, and others), fish (fillet, sticks, sushi, and others) and meat (hamburger, steak, roast beef, meatloaf, and others), participants were asked to report their usually weekly intake frequency. Physical activity in a typical week was assessed in four domains: (1) occupational (whether a participant's job was physically demanding); (2) household (cleaning, gardening, and cooking); (3) transportation (bicycle or walking as transportation for moving around the city); and (4) sports/recreation (regular physical exercise or leisure-time activity). Each domain was assessed separately, and those who reported moderate or high levels of physical demand were classified as ''active'', whereas those who reported none or low physical demand were classified as ''low active''. A physical activity index was established according to information from all four domains, and those reporting moderate or high physical demand in all domains were considered ''more active''. The assessment of stressful events in life was based on a previous study [25] which reported several stress items in life associated with increased prevalence of CHD. The stress variables included: concern about a family member (serious illness, death or other serious concern), divorce or separation, change in residence, concern about work (feelings of insecurity at work or forced to change job), serious financial trouble, legal problems, and having difficulties in sleeping. For the present study, those who reported ''never experienced'' or ''experienced temporally'' were grouped as ''no stress present'', whereas those that had experienced the stressful event item for ''some periods'', ''several periods'', or ''permanent stress'' during the past 5 years were categorized as ''presence of stress''. In addition to evaluating stress levels for each of the seven variables identified above, an index of overall stress was computed based on a participant's report of the ''presence of stress'' for at least one of the stressful life events. Lastly, hours of sleep in a typical day were also recorded.

Statistical analysis

Chi-square tests were used for the analyses of categorical variables, and post hoc tests were applied for the comparison between each pair of groups. Analyses of variance (ANOVA) and covariance (ANCOVA) were used in comparisons of metabolic risks among groups. Stepwise multiple regression analyses were performed to examine potential independent associations of waist circumference, blood lipids and lifestyle factors by gender, and their relative importance as determinants of HDL-cholesterol. Analyses of covariance were assessed as shown in Figure 1, adjusted by age (year), and the following selected lifestyle factors that were shown to significantly vary across groups: smoking (never and former = 0, current = 1), alcohol only for women (abstainer or former = 0, current = 1), fish and meat consumption (≤ 5 times/week = 0, >5 times/week = 1), physical activity index only for men (low active = 0, more

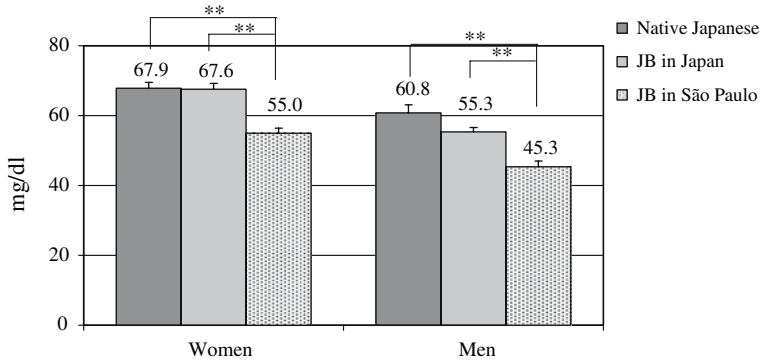

Figure 1. Mean and SE values of HDL-cholesterol adjusted for age and selected lifestyle factors. JB, Japanese-Brazilian. ** $p < 0.001$.

active = 1), and stress index (no stress presence = 0, stress presence = 1). All statistical analyses were performed using SPSS 13.0 for Windows and statistical significance was set at $p < 0.05$.

Results

Table 1 shows physical characteristics and lipid profiles of the participants. As significant differences between groups were observed in age, group differences were examined by ANCOVA with age as covariate. BMI was not significantly different among groups, ranging between 23.8 and 25.0 kg/m^2 in women, and between 24.3 and 25.3 kg/m^2 in men. Waist circumference in men from the JB in São Paulo group was significantly higher, followed by JB in Japan, and Native; whereas no significant difference was observed among women. The analyses for both men and women confirmed significantly lower means of serum HDL-cholesterol among JB in São Paulo (44.0 mg/dl) compared to Native (63.4 mg/dl) and JB in Japan (55.7 mg/dl). For men, JB in Japan HDL-cholesterol was also significantly lower than for Natives. Women showed slightly higher values than men, and women JB in São Paulo averaged values of 55.1 mg/dl, whereas Natives and JB in Japan showed 68.3 and 67.0 mg/dl, respectively. Among the other lipids investigated in men and women, the mean TC/HDL-cholesterol ratio and TG were also significantly higher for JB in São Paulo, however, JB in Japan showed higher TC and LDL-cholesterol compared to the other two groups.

Among lifestyle factors (Table 2), compared to Native Japanese, cigarette smoking was more frequently observed among participants in the JB in Japan group (21.6 and 32.96% in women and men, respectively), and JB in São Paulo (13.3 and 51.3% in women and men, respectively). Current alcoholic beverage consumption was more frequently observed among Native Japanese women (30%) and no differences were observed among men. Fish consumption was higher among Native Japanese women (23.6%) and men (16.3%); whereas consumption of meat was higher among JB in São Paulo (19.2 and 23.1% in women and men, respectively), and JB in Japan (18.6% and 24.8% in women and men, respectively). For women, JB in Japan reported more physically demanding occupational activities and lower sports/recreation activities, whereas Natives Japanese and JB in São Paulo reported higher household and sport/recreation activities. For men, JB in Japan reported higher physically demanding occupational activities, and higher household and transportation activities. Whereas Native Japanese and JB in Japan reported higher sports/recreation activities. The overall physical activity index was not significantly different among women (75.5% of Native Japanese reported to be active in all domains, 86.6% of the JB in Japan, and 75% of the JB in São Paulo). However, among men, JB in Japan were found to be significantly more active (77.9%), compared to JB in São Paulo (34.6%), and Native Japanese (36.7%). Native Japanese women and men self-reported lower presence of stress among all items investigated compared to JB in São Paulo and Japan. Therefore, the overall stress index was higher for JB in São Paulo (71.7% in women and 78.2% in men) and JB in Japan (68.0 and 61.7% in women and men, respectively) compared to Native Japanese (50.9 and 38.8% in women and men, respectively).

The stepwise regression model (Table 3) confirmed the independent association of lipids, anthropometric and lifestyle factors with HDL-cholesterol levels. For women, TG, LDL-cholesterol, meat intake and the stress index (trend) were negatively associated, whereas TC and fish intake were positively associated. For men, TG, waist circumference, LDL-cholesterol, the stress index and smoking (trend) were negatively associated, while TC and physical activity index were positively associated. Further analyses, stratifying subjects by Japanese ancestry, confirmed a significant negative association of living in São Paulo with elevated HDL-cholesterol, and this association remained even after adjustment for selected lifestyle factors (Figure 1). Men of JB in Japan also showed a

Table 1. Characteristic of the participants and lipid profile

	Native Japanese		JB in Japan		JB in São Paulo		*P*
	Mean ± SD	Adjusted* mean (95% CI)	Mean ± SD	Adjusted* mean (95% CI)	Mean ± SD	Adjusted* mean (95% CI)	
Participant, *n*							
Women	110		97		120		
Men	88		149		78		
Age, year							
Women	57.6 ± 9.6		46.9†‡ ± 7.3		54.1† ± 10.1		< 0.001
Men	57.1 ± 12.4		48.3†‡ ± 6.6		56.7 ± 10.2		< 0.001
Waist circumference, cm							
Women	83.4 ± 8.6	82.8 (81.2 to 84.5)	81.7 ± 9.4	82.5 (80.7 to 84.4)	82.1 ± 8.1	82.0 (80.4 to 83.5)	0.741
Men	83.2 ± 8.1	83.4 (81.6 to 85.3)	86.8 ± 8.9	86.5†‡ (85.0 to 87.9)	90.4 ± 8.5	90.7† (88.7 to 92.6)	< 0.001
Body mass index, kg/m^2							
Women	24.6 ± 4.8	24.2 (23.4 to 25.0)	24.4 ± 4.5	25.0 (24.2 to 25.9)	23.8 ± 3.2	23.8 (23.1 to 24.6)	0.128
Men	24.2 ± 3.3	24.3 (23.6 to 25.0)	24.9 ± 3.3	24.7 (24.1 to 25.3)	25.2 ± 3.3	25.3 (24.6 to 26.1)	0.142
Total cholesterol, mg/dl							
Women	216.1 ± 29.3	211.1 (204.7 to 217.5)	208.2 ± 38.2	215.6‡ (208.5 to 222.7)	203.2 ± 34.3	202.1 (196.2 to 207.9)	0.011
Men	202.5 ± 34.7	203.6 (196.1 to 211.1)	213.7 ± 34.5	212.5‡ (206.5 to 218.4)	196.5 ± 34.1	197.6 (189.7 to 205.4)	0.014
HDL-cholesterol, mg/dl							
Women	69.4 ± 15.3	68.3 (65.4 to 71.2)	65.5 ± 17.1	67.0‡ (63.8 to 70.3)	55.4 ± 12.4	55.1† (52.4 to 57.7)	< 0.001
Men	63.9 ± 18.7	63.4 (60.2 to 66.6)	55.2 ± 14.0	55.7†‡ (53.4 to 58.0)	44.4 ± 10.7	44.0† (40.6 to 47.4)	< 0.001
Total/HDL-cholesterol ratio							
Women	3.23 ± 0.72	3.17 (2.98 to 3.36)	3.35 ± 0.93	3.43‡ (3.22 to 3.64)	3.87 ± 1.17	3.86† (3.68 to 4.03)	< 0.001
Men	3.35 ± 0.88	3.41 (3.15 to 3.66)	4.15 ± 1.34	4.08†‡ (3.88 to 4.28)	4.63 ± 1.17	4.69† (4.42 to 4.96)	< 0.001
LDL-cholesterol, mg/dl							
Women	130.3 ± 27.0	127.4 (121.9 to 133.0)	125.2 ± 32.6	129.3†‡ (123.1 to 135.5)	118.1 ± 27.3	117.5† (112.4 to 122.6)	0.005
Men	113.4 ± 31.7	113.7 (105.9 to 121.5)	134.5 ± 33.4	134.2†‡ (128.7 to 139.7)	114.2 ± 28.1	114.6 (107.2 to 121.9)	< 0.001
Triglycerides, mg/dl							
Women	85.9 ± 36.3	81.2 (70.1 to 92.3)	88.1 ± 45.9	94.9 (82.6 to 107.3)	111.1 ± 75.7	110.1† (99.9 to 120.3)	0.001
Men	106.0 ± 69.7	108.4 (89.6 to 127.3)	127.1 ± 94.7	124.5 (109.7 to 139.4)	151.0 ± 89.7	153.3† (133.5 to 173.0)	0.004

JB, Japanese-Brazilian. *Age-adjusted.† Differ from Native Japanese, ‡Differ from JB in São Paulo.

Table 2. Lifestyle factors among groups by gender

	Women					Men				
	Native Japanese	JB in Japan	JB in São Paulo	χ^2	post hoc	Native Japanese	JB in Japan	JB in São Paulo	χ^2	post hoc
Participant, *n*	110	97	120			88	149	78		
Cigarette smoke, %										
Never	90.0	66.0	84.0	26.68**	†‡	46.1	40.3	39.7	24.64**	†‡§
Former	7.3	12.4	2.5			35.5	26.8	9.0		
Current	2.7	21.6	13.3			18.4	32.9	51.3		
Amount per day, mean SD	16.0 ± 6.6	12.8 ± 6.2	12.4 ± 6.1	NS		16.4 ± 9.5	15.0 ± 8.5	17.4 ± 11.4	NS	
Alcoholic beverage, %										
Abstainer	67.3	80.4	83.3	9.83*	†‡	30.6	45.6	48.7	9.43	
Former	2.7	2.1	2.5			8.2	3.4	0.0		
Current	30.0	17.5	14.2			61.2	51.0	51.3		
Fish intake > 5 days/week, %	23.6	7.2	5.0	21.89**	†‡	16.3	8.1	3.8	6.17*	†
Meat intake > 5 days/week, %	1.8	18.6	19.2	18.65**	†‡	0.0	24.8	23.1	14.93*	†‡
Physical activity[a], %										
Occupation	43.8	83.2	23.6	72.36**	†‡§	35.7	91.7	14.5	136.46**	†‡§
Household	98.2	93.8	93.3	3.37		28.3	67.1	29.5	39.23**	‡§
Transportation	37.3	40.2	40.0	0.25		20.8	43.0	20.5	15.44*	‡§
Sports/ recreation	52.7	19.6	53.3	31.14**	‡§	44.9	24.2	59.0	27.75**	‡§
Overall physical activity index [b]	75.5	86.6	75.0	5.26		36.7	77.9	34.6	50.81**	‡§
Stressful events in life[c], %										
Concern about family member	22.7	49.0	55.0	26.93**	†‡	6.1	38.6	52.6	28.38**	†‡§
Divorce or separation	0.9	8.3	2.5	8.72*	‡	2.0	1.4	0.0	1.37	
Change in residence	1.8	14.6	1.7	21.42*	‡§	2.0	6.9	1.3	4.59	
Concern about work	22.7	34.4	20.8	5.81*	‡§	18.4	27.6	28.2	1.86	
Serious financial trouble	20.9	19.8	26.7	1.74		12.2	19.3	28.2	5.00	
Legal problems	1.8	2.1	0.8	0.64		0.0	0.7	3.8	4.38	
Sleeping difficulties	20.9	33.3	36.7	7.30*	†‡	6.1	25.5	28.2	9.65*	‡§
Overall stress index [d]	50.9	68.0	71.7	11.85*	†‡	38.8	61.7	78.2	19.97**	†‡§
Sleeping (hour/day), mean ± SD	6.7 ± 0.9	6.5 ± 1.0	6.6 ± 1.1	NS		6.9 ± 1.1	6.6 ± 1.0	6.7 ± 1.1	NS	

[†]Native Japanese different from JB in São Paulo, [‡]Native Japanese different from JB in Japan, [§]JB in São Paulo different from JB in Japan. JB, Japanese-Brazilian. [a]Active, [b] Active in all items above, [c]Presence of stress, [d]Presence of stress in at least one of the above items. NS, non-significant. * $p < 0.05$, ** $p < 0.001$.

Table 3. Stepwise multiple regression for HDL-cholesterol as the dependent variable, and other blood lipids, waist circumference, and lifestyle factors as the independent variables

	Standardized Coefficients	t	*p*
Women			
Triglycerides	−0.746	−33.724	< 0.001
Total cholesterol	1.875	39.462	< 0.001
LDL-cholesterol	−1.568	−34.040	< 0.001
Fish intake	0.058	2.822	0.005
Meat intake	−0.045	−2.158	0.032
Stress index	−0.041	−1.959	0.051
Men			
Triglycerides	−0.799	−25.464	< 0.001
Waist circumference	−0.107	−3.865	< 0.001
Total cholesterol	1.842	27.479	< 0.001
LDL-cholesterol	−1.724	−26.047	< 0.001
Physical activity index	0.088	3.493	0.001
Stress index	−0.064	−2.533	0.012
Smoking	−0.048	−1.854	0.065

Independent variables included in the model: age, waist circumference, total cholesterol, LDL-cholesterol, triglycerides, smoking, alcohol, fish and meat intake, physical activity index, stress index, and sleeping hours.

significantly negative association with HDL-cholesterol; however, after selected lifestyle factor adjustments, the association disappeared. This finding was confirmed, as shown in Figure 1, with analysis of covariance adjusted for selected lifestyle factors.

Discussion

Regardless of immigration status, our study confirmed the presence of increased levels of HDL-cholesterol among healthy middle-aged men and women of Japanese descent, with average values above the cutoff point of 40 mg/dl proposed as a risk factor in metabolic syndrome. However, this study did find significant differences in serum HDL-cholesterol among people of Japanese ancestry living in São Paulo city and in Japan, suggesting that a variety of immigration factors including the cultural environment may play a role in influencing an individual's blood lipid profile. We have found that Japanese-Brazilians in São Paulo have significantly lower levels of HDL-cholesterol compared to Native Japanese and Japanese-Brazilians in Japan. Our findings support the hypothesis that the traditionally favorable lipid profiles of people of Japanese ethnicity may be negatively affected by immigration and exposure to a western cultural environment [13, 21–23].

The group of Japanese ancestry with lower HDL-cholesterol (JB in São Paulo) also showed higher waist circumference, TG and total/HDL-cholesterol ratio levels than the other two groups, but was not higher for BMI, TC and LDL-cholesterol. For women and men, HDL-cholesterol showed a significant negative association with TG and LDL-cholesterol, and positive association with TC. Conventionally, LDL-cholesterol is the first target of dyslipidemia therapy, [26] but a clear association between decreased HDL-cholesterol and increased CHD risk is also strongly supported by the Framingham Study, [27, 28] which confirms not only the apparent protective effect of elevated HDL-cholesterol, but the clear risk associated with low levels of HDL-cholesterol. As previously mentioned, Japanese people have the longest life expectancy among developed countries. Indeed, until recently, Okinawa (the most southern area of Japan) was known as the world's foremost prefecture for longevity. Previous studies have related more favorable HDL-cholesterol profiles of Okinawans to significantly lower atherogenic indices than those from people living on the mainland of Japan [29]. On the other hand, changes in lifestyle appear to promote increases in the incidence of CHD among Okinawans, which also seem to be associated with decreased HDL-cholesterol and increased TG levels [30]. One study of Okinawans in Brazil reported overall lower levels of HDL-cholesterol which was associated with a 1/3 decrease in the number of centenarians compared to Japan. According to the author of that study, changes in lifestyle (more calories and fewer fish and seafood products) are among the possible explanations for this finding [31].

In the present study, because all groups are originally from a similar Japanese genetic background, lifestyle changes are among the mechanisms proposed as possible explanations for the lower level of HDL-cholesterol among Japanese-Brazilians in São Paulo. In a stepwise multiple regression analysis including lifestyle, consumption of fish and meat, and stress were the factors most strongly associated with HDL-cholesterol among women. Likewise, physical activity, stress and smoking were found to be important factors associated with HDL-cholesterol among men. Although different mechanisms by which smoking decreases HDL-cholesterol have been reported by previous studies, these results confirm our findings that HDL-cholesterol has a negative association trend with smoking among men [32, 33]. For instance, a recent study on smoking habits and serum lipids in a large Japanese cohort confirmed the association of smoking with lower HDL-cholesterol in both genders at any age [34]. The hypolipidemic effect of dietary fish and fish oils has been associated with protection against CHD [19, 35, 36]. Results of a study with middle-aged Japanese-Americans in Hawaii and Natives Japanese showed a positive association of fish consumption with serum HDL-cholesterol, which may have been associated with reduced mortality due to CHD among the Native Japanese [21]. Our study identified significant associations between HDL-cho-

lesterol and consumption of fish (positive) and meat (negative) among women. Favorable effect of physical activity on increased levels of HDL-cholesterol has been observed [14, 18, 32, 37]. Previous studies accounted this mechanism by the increase lipoprotein lipase activity, concomitant rapid turnover of triglycerides-rich lipoproteins, [16] fat clearance, and increase reverse cholesterol transport from increase plasma lecithin cholesterol acyl trasnferase and cholesterol ester transfer protein activities [18]. Cross-sectional studies of physically active people have shown higher levels of HDL-cholesterol, but intervention studies in which non-athletes are encouraged to begin to exercise have often shown only moderate changes [38–40]. In our study, men with lower levels of physical activity were more likely to have lower levels of HDL-cholesterol than those who were more active. Another important factor associated with HDL-cholesterol was the higher presence of stress in life for Japanese-Brazilian (both men and women). Work stress and other forms of chronic stress have been found to be related with an unfavorable lipid profile [17, 20].

After adjusting for selected lifestyle factors in the covariance analysis, Japanese-Brazilian in São Paulo maintained a significant lower level of HDL-cholesterol. However, Japanese-Brazilian men living in Japan were no longer significantly different from Native Japanese after adjusted for selected lifestyle factors. For Japanese-Brazilian in Japan, smoking habits appear to be an important risk factor for decreased levels of HDL-cholesterol in men.

The present study has some limitations. First, as a population-based design, this study does not allow us to draw inferences about causal pathways. Second, significant differences in age were observed among groups. Despite the fact that participants were volunteers recruited using identical age inclusion criteria across all groups, it was not possible to precisely equalize the mean ages for each of the three groups. Due to cultural and logistic differences between countries there may have been small differences in exactly how participants were contacted. However, it is unclear to what extent this may have contributed to the age differences observed. An additional limitation to consider was that lifestyle factors were evaluated by non-standard methods. It is possible that our measurement instruments were not sensitive enough to assess significant associations between lifestyle factors and HDL-cholesterol.

In summary, we found substantial variation in serum HDL-cholesterol among people of Japanese ancestry, which we believe illustrates the heterogeneity of people of Japanese ancestry living under different cultural environments. Japanese-Brazilians in São Paulo showed lower levels of HDL-cholesterol, and, given the well-understood association of HDL-cholesterol and CHD, we would predict, a higher risk of developing CHD among Japanese-Brazilians in São Paulo. Maintaining high levels of HDL-cholesterol may also impact the risk of developing other morbidities for coronary disease, which is also important from a clinical and public health perspective. Also, our findings support the notion that the consumption of fish and maintaining a physically active lifestyle are important factors for increasing HDL-cholesterol levels. Furthermore, smoking, consumption of meat, and stress all negatively affected HDL-cholesterol levels. However, further investigations are necessary to elucidate the effects of cultural environment factors in Brazil on the lipid profiles of Japanese immigrants and subsequent generations.

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