Serum Total Homocysteine Levels and the Prevalence of Folic Acid Deficiency and C677T Mutation at the MTHFR Gene in an Indigenous Population of Amazonia: The Relationship of Homocysteine with Other Cardiovascular Risk Factors

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Hyperhomocysteinemia is a risk factor for cardiovascular disease. C677T mutation at the MTHFR gene and deficiencies of folic acid and vitamin B-12 may account for elevation of total homocysteine (tHcy). Ninety Brazilian Parkatêjê Indians (90.0% of the population without admixture, aged ≥20 years) were studied. Hyperhomocysteinemia was observed in 26.7% of the Indians. No case of vitamin B-12 deficiency was detected. Folic acid deficiency was found in 43.3% of the subjects. Rates of mutated allele 677T and TT genotype were 40.7% and 14.0%, respectively. Prevalence of hypertension, dyslipidemia, smoking, WHR ≥0.9, BMI ≥25 kg/m^2 and chronic alcohol use were 4.4%, 44.4%, 25.6%, 72.2%, 67.8%, and 0.0%, respectively. All creatinine values were normal. Natural logarithmic (ln) tHcy showed no correlation with age, but was positively correlated with systolic (r=0.22) and diastolic (r=0.21) blood pressure and triglycerides (r=0.39) and inversely correlated with folic acid (r=−0.40) adjusted for age and sex. Total homocysteine (tHcy) was higher among TT genotype (P<.001). The multiple linear regression model, containing variables for sex, folic acid, TT genotype, and triglycerides, explained 50.0% of the variation of the ln tHcy. In summary, high rates of cardiovascular risk factors were discovered. C667T mutation and folic acid deficiency can explain, at least in part, the observed hyperhomocysteinemia. (*Ethn Dis*. 2004;14:49–56)

Key Words: Brazilian Indians, C677T Mutation, Cardiovascular Risk Factors, Folic Acid, Homocysteine, MTHFR, Vitamin B-12

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Introduction

Hyperhomocysteinemia is an independent risk factor for cardiovascular disease.[1,2] Total homocysteine (tHcy) concentrations are determined by a myriad of genetic, physiologic, pathologic and nutritional factors.[2] Genetic factors include a common mutation (C677T) in the methylenetetrahydrofolate reductase (MTHFR) gene. This common mutation (C677T) may account for reduced enzyme activity causing mildly increased tHcy levels among the homozygotes, if their folic acid intake is insufficient.[3–5] The frequency of homozygotes for the mutation varies greatly among different ethnic groups and also among different Indian groups.[6] Blood levels of folic acid, vitamin B-12, and vitamin B-6 are inversely related to tHcy levels.[7] Total homocysteine (tHcy) levels are higher in men than in women and increase with age.[8,9] Elevated tHcy levels are associated with smoking, high blood pressure, elevated cholesterol and triglycerides levels, lack of exercise, renal impairment and chronic alcohol intake.[8,10–12]

Folic acid, alone or combined with vitamin B-12, is an effective way of reducing tHcy levels, in addition to being a safe and inexpensive therapy.[13] Large trials are in progress to determine whether this therapy can reduce the risk for cardiovascular disease.[2]

In the past, Indians were considered as having low risk for cardiovascular diseases; but with the process of Westernization, there was an increase in the frequency of risk factors and in the development of cardiovascular diseases, as reported among the American Indians.[14] Studying the Parkatêjê Indians is important because they have suffered rapid and intensive changes in their lifestyle in the last years, with significant modifications in their traditional pattern of nutrition and physical activity.[15]

The objectives of this study were: 1) to determine the tHcy, folic acid and vitamin B-12 concentrations and the prevalence of mutation C677T in this Brazilian Indian group; and 2) to verify the relationship of the tHcy levels with other cardiovascular risk factors. Based on the findings, preventive interventions can be planned.

Materials and Methods

The Federal University of São Paulo Ethics Committee and the Tribal Council of the Parkatêjê Indians approved the protocol of this study.

Parkatêjê Indians belong to the Jê group and inhabit the Mãe Maria Reservation. The reservation is located 40 km away from the city of Marabá in the southeastern part of the state of Pará, in the Amazon Region of Brazil (Figure 1).

A total of 90 Indians were included (90.0% of the Indian population aged ≥20 years, without admixture). Thirty-four (37.8%) of the study participants were women while 56 (62.2%) were men. None of the women was pregnant. In this tribe the numbers of men exces-

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Fig 1. Map of Brazil with the location of Parkatêjê Indians

sively predominate; and, there are some cases of polyandry.

Information about alcohol use, smoking and medical history were obtained through an individual interview. The participants were not taking any medication that could interfere with the laboratory analysis, with the exception of one woman with diabetes who was taking insulin. Alcohol consumption is considered disreputable in this tribe and no participant was identified as a chronic consumer of alcohol. Only one man was identified as having discontinued the use of alcohol, doing so about about 10 years ago.

Blood pressure and anthropometric measurements were taken twice and the mean value was used. Blood pressure was measured in the sitting position using a calibrated aneroid sphygmomanometer. Participant's weight and height were measured using a calibrated electronic balance and a vertical anthropometric measurement, respectively. Waist and hip circumferences were measured at the level of the umbilicus and the trochanter, respectively, using a non-elastic metallic tape.

After the participants had fasted overnight, venous blood samples were drawn for extracting DNA and for laboratory analyses (total cholesterol, high-density lipoprotein [HDL] cholesterol, triglycerides, tHcy, folic acid, vitamin B-12, and creatinine). Low-density lipoprotein (LDL) cholesterol was estimated by utilizing the Friedewald formula.[16] Part of whole blood was collected into plain serum separator tubes and kept at 4°C for a period no longer than 60 minutes before centrifugation at 2200 × g for 10 minutes at room temperature. Serum was separated and stored at −20°C until it was analyzed.

Total cholesterol, HDL-cholesterol, and triglycerides were determined by enzymatic methods[17–19] utilizing a commercial kit for the equipment, a BM/Hitachi 917 (Boehringer Mannhein, Germany). Total homocysteine (tHcy) was measured by high-performance liquid chromatography (HPLC).[20] Vitamin B-12 was determined by a competitive immunoassay by chemiluminescence[21] using a commercial kit (Chiron/Diagnostics Corporation, East Walpole, Mass, in ACS: 180 instrument). Folic acid was measured by a competitive immunoassay by chemiluminescence[22] using a commercial kit (Immulite/Diagnostic Products Corporation, Los Angeles, Calif). Serum creatinine was determined by modified Jaffé reaction.[23]

Genomic DNA was obtained from peripheral blood samples from 86 Indians by a standard method.[24] C667T mutation in the MTHFR gene was determined by polymerase chain reaction and Hinf I restriction enzyme digestion according to Goyette et al and Frosst et al.[4,25]

Hyperhomocysteinemia was defined as tHcy concentration ≥14 μmol/L, because an increased risk for cardiovascular disease has been observed above this value.[26] The normal reference ranges of vitamin B-12, folic acid and creatinine concentrations established in our laboratory were 190 to 900 ng/L, 3–17 ng/ml and until 1.4 mg/dl, respectively. Hypertension was defined as systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg and/or using anti-hypertensive drugs.[27] Dyslipidemia was defined as total cholesterol or triglycerides levels ≥200 mg/dl, or HDL-cholesterol <35 mg/dl or LDL-cholesterol ≥130 mg/dl according to the Brazilian Consensus on Dyslipidemias.[28]

Sigma Stat Statistical Software 1.03 for Windows was used for statistical analysis. Results are expressed as mean and standard deviation (SD). *P* value <.05 was considered statistically significant. The skewed distribution of tHcy concentrations was corrected by natural logarithmic (ln) transformation. Student's *t* test was used to compare clinical and laboratory variables between men and women and to compare serum vitamin B-12, creatinine, and folic acid levels between the group with and without hyperhomocysteinemia. Pearson's correlation coefficient was used to test the correlation between clinical and laboratory variables of the studied group. Correlation coefficients adjusted for age and sex are presented with 95% confidence interval (95% CI).[29] One way analysis of variance was used to test the differences in the mean values of tHcy, vitamin B-12, and folic acid among the 3 groups of MTHFR genotypes. Multiple comparison procedures (Student-Newman-Keuls method) were used to isolate the group, or groups, that differ from the others. Multiple linear regression was used to measure the effect of the clinical and laboratory variable on the dependent variable ln tHcy. The statistical significance of differences between frequencies was calculated by the

Table 1. Clinical and laboratory characteristics of Brazilian Parkatêjê Indians by sex

Variables	Women			Men			P‡
	Mean	SD	Range	Mean	SD	Range	
Age (years)	41.7	13.9	23.0–78.0	40.9	15.3	21.0–78.0	.808
BMI (kg/m²)	27.9	3.8	19.0–35.6	25.8	2.6	21.2–34.1	.003*
Waist-to-hip ratio	0.98	0.06	0.89–1.10	0.92	0.05	0.85–1.08	<.001*
Systolic BP (mm Hg)	107.0	14.0	90.0–148.0	111.0	12.0	90.0–152.0	.140
Diastolic BP (mm Hg)	70.0	8.0	60.0–90.0	73.0	7.0	60.0–90.0	.031*
Total C (mg/dl)	165.7	28.7	113.0–226.0	159.6	38.3	101.0–319.0	.430
LDL C (mg/dl)	92.8	25.7	39.0–149.0	89.7	33.4	48.0–238.0	.649
HDL C (mg/dl)	41.5	7.0	26.0–61.0	38.3	8.1	23.0–71.0	.057
Triglycerides (mg/dl)	157.4	83.1	71.0–403.0	158.0	79.5	59.0–453.0	.973
tHcy† (μmol/L)	11.2	3.4	5.0–20.6	14.8	8.8	8.2–72.5	.001*
Vitamin B-12 (ng/L)	468.8	118.0	240.0–760.0	522.1	315.1	240.0–1900.0	.347
Folic acid (ng/ml)	4.1	1.3	2.0–7.2	3.1	1.2	1.4–7.8	<.001*
Creatinine (mg/dl)	1.0	0.1	0.8–1.2	1.1	0.1	0.8–1.4	<.001*

BMI: body mass index; BP: blood pressure; C: cholesterol; tHcy: total homocysteine.
* Statistically significant.
† Student's *t* test performed with natural logarithmic transformation.
‡ *P* value of Student's *t* test.

chi-square or by Fisher's exact tests. Genotype frequencies were compared with those expected according to the Hardy-Weinberg distribution ($p^2 + 2pq + q^2=1$).

RESULTS

Table 1 shows the clinical and laboratory characteristics of the subjects by sex. Body mass index (BMI) and waist-to-hip ratio (WHR) were higher in women than in men. Body mass index (BMI) ≥25 kg/m² and WHR ≥0.9 were found in 61 (67.8%) and 65 (72.2%) individuals, respectively. Diastolic blood pressure (DBP) levels were higher in men than in women. Stage 1 hypertension (SBP ≥140 and <160 mm Hg or DBP ≥90 and <100 mm Hg, according to JNC-6 criteria)[27] was found in 4 (4.4%) individuals. Lipid concentrations were similar in both sexes. Total cholesterol or LDL-cholesterol or triglycerides above the desirable values or HDL-cholesterol below these values were found in 40 (44.4%) individuals; of this total, 14 were women and 26 were men.

Total homocysteine (tHcy) concentrations were higher among men. Hyperhomocysteinemia was found in 24 (26.7%) individuals, 5 women and 19 men. Vitamin B-12 concentrations were similar in both sexes and no case of deficiency of this vitamin was found. Folic acid levels were higher among women. Thirty nine (43.3%) cases of folic acid deficiency were identified, 5 in women and 34 in men. Creatinine levels were higher among men and all participants presented normal values.

The woman described earlier as having diabetes was 60 years old and had tHcy and folic acid values equal to 9.3 μmol/L and 4.3 ng/ml, respectively.

Table 2 shows the distribution of tHcy serum concentrations by sex.

Stratifying the individuals into 2 groups, one with and the other without hyperhomocysteinemia, there was no difference observed between the groups either in relation to vitamin B-12 concentrations (490.4 ± 371.4 and 506.2 ± 207.7 ng/L, *P*=.800) or creatinine levels (1.1 ± 0.1 and 1.1 ± 0.1 mg/dl, *P*=.227). Folic acid concentrations were lower in the group with hyperhomocysteinemia (2.9 ± 0.8 and 3.7 ± 1.4 ng/ml, *P*=.006).

Twenty-three current smokers (25.6%), 5 women and 18 men, were among the group. Four men were ex-smokers while 63 individuals (29 women and 34 men) indicated they had never smoked. Natural logarithmic (ln) tHcy values were similar among the current smokers and non-smokers (classified as both ex-smokers and those who had never smoked) (2.54 ± 0.29 and 2.51 ± 0.37, *P*=.727).

Table 2. Serum total homocysteine (tHcy) concentrations of Brazilian Parkatêjê Indians by sex

tHcy μmol/L	Women		Men		Total	
	N	%	*N*	%	*N*	%
<8	6	17.7	—	—	6	6.7
8–13.9	23	67.6	37	66.0	60	66.7
14–19.9	4	11.8	14	25.0	18	20.0
20–25.9	1	2.9	3	5.4	4	4.4
>25.9	—	—	2	3.6	2	2.2
Total	34	100.0	56	100.0	90	100.0

Table 3. Prevalence of dyslipidemia, body mass index (BMI) ≥25 kg/m², waist-to-hip ratio (WHR) ≥0.9 and smoking in groups with serum total homocysteine concentrations (tHcy) ≥14 μmol/L and <14 μmol/L

	tHcy ≥14 μmol/L (*N*=24)	tHcy <14 μmol/L (*N*=66)	*P*†
Dyslipidemia	50% (*N*=12)	42.4% (*N*=28)	.522
BMI ≥25 kg/m²	70.8% (*N*=17)	66.7% (*N*=44)	.708
WHR ≥0.9	79.2% (*N*=19)	69.7% (*N*=46)	.375
Smoking	33.3% (*N*=8)	22.7% (*N*=15)	.308

† *P* value of chi-square test.

Prevalence of dyslipidemia, BMI ≥25 kg/m², WHR ≥0.9, and smoking were similar among Indians with or without hyperhomocysteinemia (Table 3).

Natural logarithmic (ln) tHcy presented significant positive correlations, after adjustment for age and sex, with SBP (r=0.22; 95% CI: 0.02–0.42) and DBP (r=0.21; 95% CI: 0.01–0.41) and with serum triglycerides concentrations (r=0.39; 95% CI: 0.21–0.58). A significant negative correlation was present after adjustment for age and sex between ln tHcy and folic acid concentrations (r=−0.40; 95% CI: −0.61–−0.20).

Natural logarithmic (ln) tHcy correlated positively with creatinine levels (r=0.36, P<.001), but not after adjustment for age and sex. Natural logarithmic (ln) tHcy did not correlate with vitamin B-12, BMI, WHR, total-, LDL-, and HDL-cholesterol.

The following variables did not correlate with age: ln tHcy, vitamin B-12, creatinine, SBP, DBP, BMI, and serum lipids. Folic acid (r=0.26; 95% CI: 0.07–0.46) and WHR (r=0.42; 95% CI: 0.37–0.47) were positively correlated with age, controlling by sex.

The frequency of the mutated allele (677T) was 40.7% (95% CI: 33.4%–48.0%).

Genotype frequencies were in agreement with those expected values according to the Hardy Weinberg equilibrium (χ^2=1.02; P>.05).

The prevalence of homozygous (TT genotype) and heterozygous (CT genotype) for the mutated allele 677T in the MTHFR gene were 14.0% (95% CI: 6.7%–21.3%), of whom 3 were women and 9 were men, and 53.5% (95% CI: 43.0%–64.0%), 23 women and 23 men, respectively.

No distinct distribution of the frequency of TT and CC (homozygous for normal allele 677C) genotypes by sex was observed. The frequency of CT genotype was higher among women (Table 4).

Table 5 shows the genotype and 677T-allele distribution in the groups with and without hyperhomocysteinemia. The frequencies of TT genotype and 677T-allele were higher among the group with hyperhomocysteinemia.

Table 4. Genotype distribution by sex

Genotype	Women (*N*=33)	Men (*N*=53)	*P*
TT	9.1% (*N*=3)	17.0% (*N*=9)	.357‡
CT	69.7% (*N*=23)	43.4% (*N*=23)	.017*†
CC	21.2% (*N*=7)	39.6% (*N*=21)	.076†

CC: homozygous for normal allele 677C; CT: heterozygous; TT: homozygous for mutated allele 677T.
* Statistically significant.
† *P* value of chi-square test.
‡ *P* value of Fisher's exact test.

Table 6 shows the mean values of tHcy, folic acid, and vitamin B12 concentrations among the MTHFR genotypes. The group TT presented higher tHcy levels than the groups CC and CT. Folic acid and vitamin B12 levels were similar among these groups.

Associations of ln tHcy with sex, age, folic acid, vitamin B-12, presence of homozygosity for the C677T mutation of the MTHFR gene, serum triglycerides, SBP, and DBP were tested by multiple linear regression analysis. The model containing the variables of sex, folic acid, and presence of homozygosity for the C677T mutation and triglycerides concentrations explained 50.0% of the variation of the ln tHcy (Table 7).

DISCUSSION

Reported reference ranges for tHcy contain large variations. The most reported normal range in adults is 5–15 μmol/L, with a mean concentration of about 10 μmol/L.[30] In this study, hyperhomocysteinemia was defined as tHcy concentration ≥14 μmol/L, because an increased risk of cardiovascular disease above this value has been observed.[26]

Hyperhomocysteinemia was found in 26.7% of Parkatêjê Indians. No information is available regarding the tHcy levels among other Brazilian Indian groups. A similar rate of 24.0% was reported among urban indigenous Australians with tHcy ≥15 μmol/L, measured by HPLC using fluorimetry by the method of Dudman.[31,32] The prevalence of hyperhomocysteinemia in different studies varies and depends on the method used to measure the tHcy, as well as the choices of the cut-off points to define high tHcy.

Among Parkatêjê Indians, tHcy concentrations were noted to be higher in men than in women, comparable to other studies.[8,9] Similar to previous re-

Table 5. Genotype and 677T-allele distribution in groups with serum total homocysteine concentrations (tHcy) ≥14 μmol/L and <14 μmol/L

	tHcy ≥14 μmol/L (*N*=22) (alleles *N*=44)	tHcy <14 μmol/L (*N*=64) (alleles *N*=128)	*P*
677T-allele	59.1% (*N*=26)	34.4% (*N*=44)	.004*†
TT	36.4% (*N*=8)	6.3% (*N*=4)	.001*‡
CT	45.5% (*N*=10)	56.3% (*N*=36)	.381
CC	18.2% (*N*=4)	37.5% (*N*=24)	.095

CC: homozygous for normal allele 677C; CT: heterozygous; TT: homozygous for mutated allele 677T.
* Statistically significant.
† *P* value of chi-square test.
‡ *P* value of Fisher's exact test.

ports, tHcy concentrations showed a positive correlation with blood pressure levels[8,33] and serum triglycerides concentrations.[10] No correlation was observed between tHcy levels and age, a finding that contradicts most of the published reports.[8,9] The mean age was 41.2 ± 14.7 years (range: 21–78 years) and 50.0% of the individuals ranged in age from 21 to 39 years.

Renal function is a determinant of tHcy levels in the general population.[12] This study found no case of abnormal creatinine value. Homocysteine (tHcy) had a positive correlation with creatinine, but not after adjusting for age and sex. Creatinine levels were similar in the group with and without hyperhomocysteinemia; hence, this factor does not appear to be responsible for tHcy levels, given the variation of tHcy levels in this tribe.

Smoking is a cardiovascular risk factor and is associated with high tHcy levels.[8] This study found the presence of smokers in this tribe, similar to those observed among other Indian communities,[34] but tHcy levels were similar among the smokers and non-smokers.

Alcohol intake has been associated with raised tHcy levels,[11] but this practice is not common for members in this tribe.

Vitamin B-12 concentrations were normal in the population being studied; and, there were no differences between the group with and without hyperhomocysteinemia. No correlation between vitamin B-12 and tHcy emerged, in contrast to other reports that have identified a negative correlation between these variables.[7,26,35]

High prevalence of folic acid deficiency (43.3%) was observed in this Indian group, mainly among men. In addition, an unexpected weak positive correlation was observed between folic acid and age. Dietary folic acid intake has been found to be low in studies of other indigenous communities, such as the Indians from Venezuela who showed an extremely high prevalence of folic acid deficiency (91.0%).[36] However, folic acid concentrations were lower in the group with hyperhomocysteinemia and presented a negative correlation with tHcy levels, similar to previous studies with Caucasians and indigenous Australians.[32,35]

Table 6. Mean values (mean ± SD) of homocysteine, folic acid, and vitamin B12 concentrations among the MTHFR genotypes

Variable	CC (*N*=28)	CT (*N*=46)	TT (*N*=12)	*P*†
Homocysteine‡ (μmol/L)	11.4 ± 3.0	12.2 ± 2.8	22.2 ± 16.9**	<.001*
Vitamin B-12 (ng/L)	501.8 ± 172.6	522.6 ± 325.6	449.2 ± 152.9	.692
Folic acid (ng/ml)	3.8 ± 1.5	3.5 ± 1.3	3.0 ± 0.8	.178

CC: homozygous for normal allele 677C; CT: heterozygous; TT: homozygous for mutated allele 677T.
* Statistically significant; ** Statistically significant compared to CC and CT groups.
† *P* value of one way analysis of variance.
‡ One way analysis of variance performed with natural logarithmic transformation.

The prevalence of some components of the cardiovascular risk profile, such as dyslipidemia, excess weight and smoking was similarly observed between the Indians with and without hyperhomocysteinemia. Yet, despite this demonstrated association between tHcy levels and other cardiovascular risk factor,[8] hyperhomocysteinemia remains an independent risk factor for cardiovascular disease.[1,2]

The population frequency of the C677T homozygosity shows great variability in different ethnic groups and different geographic regions. The frequency ranges from 1.0% or less among African Blacks to 20.0% or more among Italians.[6] Among the Brazilian population, the frequency of C677T homozygosity was 10.0%, 1.45%, and 1.2% for persons of Caucasian and African descent and for Parakanã Indians, respectively.[37] Among 5 Brazilian Amazon tribes (Wayampi, Wayana-Apalai, Kayapo, Arara, and Yanomami) mutant homozygous manifested at 7.8%, and an inter-tribal heterogeneity was observed.[38] A report regarding another Brazilian Indian tribe, whose tribe was not identified in the paper, reflected a rate of 21.0% of C677T homozygosity.[6,39] This study found an intermediate frequency of 14.0% for TT genotype. The heterogeneity observed among different Brazilian Indian groups is probably caused by isolation of these populations and genetic drift.[38]

The TT group showed higher tHcy levels than the other genotype groups; and, the Indians with hyperhomocysteinemia presented higher frequencies of the mutated allele 677T and TT genotype than the Indians with normal tHcy concentrations. This data shows the important link between the genetic back-

Table 7. Multiple linear regression model (R^2: 50.0%) for ln homocysteine as the dependent variable in women and men combined (*N*=90)

Independent Variables	β	SE (β)	*P* value
Constant	2.341	0.318	.000*
Sex (coded as 0–women, 1–men)	0.146	0.066	.029*
Age (years)	0.001	0.002	.580
Folic acid (ng/ml)	−0.087	0.025	.001*
Vitamin B-12 (ng/L)	0.000	0.000	.690
C677T homozygosity (coded as 0–no, 1–yes)	0.336	0.087	.000*
Triglycerides (mg/dl)	0.001	0.000	.001*
Systolic blood pressure (mm Hg)	0.002	0.004	.636
Diastolic blood pressure (mm Hg)	−0.002	0.006	.757

* Statistically significant.

A high prevalence of folic acid deficiency and 14.0% of homozygous for the mutated allele 677T was noted, and may explain, at least in part, the hyperhomocysteinemia.

ground and the tHcy levels in this Indian group, similar to the scientific literature.[2,4,5]

Parkatêjê Indians have suffered a rapid and intensive process of cultural changes in the last 20 years. The Indians changed their nutritional pattern, leaving their traditional diet, rich in proteins (hunted meats primarily), staple and vegetable fibers, and have adopted eating patterns heavily dependent on industrialized foods. Decreasing their traditional hunting and agricultural activities, they have begun to use motorized vehicles for traveling, becoming themselves more sedentary and more obese.[15]

Obesity and central adiposity are risk factors for cardiovascular disease and for diabetes. Results from Pima Indians have shown that those who gain weight most rapidly are most likely to develop type 2 diabetes.[40] Although the duration of obesity is considered important in determining the risk of obesity-associated conditions, little information is available to quantify this relationship, even from prospective studies.

The BMI is widely used as a reference measure for body mass, with values forming a continuum from underweight to obese. Arguments have been made supporting variations in BMI classification. Some arguments suggest that criterion used to classify obesity should differ among distinct ethnic groups; and, a lower threshold for obesity has been proposed for Asian populations. Among the Parkatêjê, BMI ≥25 kg/m^2 was found in 67.8% of the participants. This rate is higher than the prevalence of 34.0% observed in the urban adult population of the North Region of Brazil, where this tribe is located,[41] and higher than those observed in other Brazilian Indian groups.[42–44] Waist-to-hip ratio (WHR) ≥0.9 was found in 72.2% of the subjects and showed an increase with age. This suggests a pattern of central obesity, like those observed among North American Indians.[34]

Hypertension was found in 4.4% of the participants. This rate is lower than those observed among North American Indians,[45] but higher than the reported ones for other Brazilian Indian groups.[42–44] The age-related rise of blood pressure is a feature of Western populations[27]; and, this phenomenon was not found among the Parkatêjê. This finding is similar to those observed in other Brazilian Indian groups whose members preserve most of their traditional lifestyle,[42] but different from what is reported from acculturated Brazilian tribes and from American Indians.[45,46]

Dyslipidemia was found in 44.4% of the subjects; and, this rate is higher than those observed in other Brazilian Indians.[44,47,48]

The high prevalence of overweight and dyslipidemia among the Parkatêjê may be explained, at least in part, by the rapid and intensive changes in their nutritional pattern and by the lowering of the level of their physical activities.

In conclusion, we found several individuals with hyperhomocysteinemia in the studied population, without evidence of vitamin B-12 deficiency. A high prevalence of folic acid deficiency and 14.0% of homozygous for the mutated allele 677T was noted, and may explain, at least in part, the hyperhomocysteinemia. High rates of dyslipidemia, overweight, and smoking were detected. However, most of the cardiovascular risk factors found in this group are potentially reversible; and, the effect of homozygosity for the mutated allele 677T rising homocysteine levels can be reduced with the correction of folic acid status.[5] The fact that the strongest environmental risk factors are potentially modifiable, points to the need for lifestyle intervention, with the incorporation of a healthy diet and increased physical activity. Promotion of healthy lifestyles, while respecting local culture, poses an enormous challenge; yet, these steps are essential for optimizing health for all members of this Indian group.

The authors of this study would like to point out that the conclusions of this study are limited to this specific indigenous group. Researchers interested in studying metabolic characteristics in other Indian groups should take into consideration the homocysteine levels.

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