A preliminary study of mercury exposure and blood pressure in the Brazilian Amazon

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Abstract

Background

Fish is considered protective for coronary heart disease (CHD), but mercury (Hg) intake from fish may counterbalance beneficial effects. Although neurotoxic effects of methylmercury (MeHg) are well established, cardiovascular effects are still debated. The objective of the present study was to evaluate blood pressure in relation to Hg exposure and fish consumption among a non-indigenous fish-eating population in the Brazilian Amazon.

Methods

The study was conducted among 252 persons from six communities along the Tapajós River, a major tributary of the Amazon. Data was obtained for socio-demographic information, fish consumption, height and weight to determine body mass index (BMI), systolic and diastolic blood pressure, and Hg concentration in hair samples.

Results

Results showed that overall, systolic and diastolic blood pressure, were relatively low (mean: 114.2 mmHg ± 15.3 and 74.2 mmHg ± 12.2). Blood pressure was significantly associated with hair total Hg (HHg), age, BMI and gender. No association was observed between fish consumption and blood pressure. Logistic regression analyses showed that the Odds Ratio (OR) for elevated systolic blood pressure (≥130mmHg) with HHg ≥15 μg/g was 2.22 [1.11 - 4.46], taking into account age, BMI, smoking and gender. For those above 50 years of age, the OR for elevated systolic blood pressure with higher HHg was 3.8 (p=0.04), while for diastolic blood pressure, HHg showed a tendency with an OR of 3.68 (=0.06).

Conclusion

The findings of this preliminary study add further support for Hg cardiovascular toxicity. Although fish consumption was not associated with blood pressure, fish is a dietary mainstay and may, in part, explain the overall low blood pressure. More extensive studies on cardiovascular parameters, including R-R variability and the role of fatty acids are currently under way. Intervention strategies should seek to promote fish consumption while reducing Hg exposure by selecting fish species with lower Hg level.

Background

Mercury (Hg), a worldwide pollutant transported by air and water throughout the planet, poses a particular challenge to global health. On the one hand, Hg is recognized as one of the most dangerous environmental contaminants (Watanabe and Satoh 1996). On the other hand, fish, a very nutritious food, is the major vehicle for its transmission to humans in its organic form, methylmercury (MeHg). For populations that rely on fish as their main source of protein, this represents an important dilemma and public health issue (Mahaffey 2004). Hg neurotoxicity has been extensively studied (for review see Clarkson et al. 2003), but recent evidence suggests that fish can be both cardio protective and cardio toxic depending upon their contribution to essential fatty acids and Hg body burden (Guallar et al. 2002; Rissanen et al. 2000; Chan and Egeland 2004; Stern 2005; Pedersen et al. 2005).

Fish is indeed a very healthy food, rich in proteins, poor in saturated fats, and considered protective for coronary heart disease (CHD) (Millen and Quatrimoni 2001; Whelton et al. 2004). Fish oils are rich in omega-3, an essential fatty acid known to reduce CHD risk by decreasing risk for arrhythmias, thrombosis, triglyceride and remnant lipoprotein levels, as well as the growth rate of atherosclerotic plaque, and by improving endothelial function, reducing inflammatory responses and lowering blood pressure (Kris-Etherton et al. 2003a, 2003b; Sinclair 2000; Calder 2004). Populations that traditionally consume large amounts of marine fish, such as Inuit communities, have elevated levels of omega-3, and experience lower rates of mortality from heart disease (Dewailly et al. 2001a, 2002, 2003). Fatty fish, richest in omega-3, are particularly protective against CHD mortality (Oomen et al. 2000). It is generally recommended that people with personal or family history of heart disease or circulatory problems should increase their omega-3 intake in order to reduce their risk to suffer from these problems (Sinclair 2000).

Even though fish is a highly recommended food for cardiovascular functions, Hg intake from fish may counterbalance beneficial effects (Chan and Egeland 2004; Stern 2004). In the Greenland Inuit population, autopsies revealed that MeHg levels in organs are generally high, and blood pressure levels calculated from renovascholopathia of hypertension indicate prevailing levels similar to those in industrialized countries (Mulvad et al. 1996). Hg exposure has been associated with an increased risk of myocardial infarction, as well as death from coronary, cardiovascular disease and any death (Salonen et al. 1995; Guallar et al. 2002). Guallar et al. (2002) observed both the negative effects of Hg exposure and the positive effects of omega-3's in a case-control study involving a group of men with a first diagnosis of myocardial infarction and a reference group of healthy men; risk for myocardial infarction increased with Hg levels in toenails and decreased with blood omega-3 levels (Guallar et al. 2002). However, the United States Health Professionals Follow-up Study did not support an association between Hg and risk for coronary heart disease (Yoshizawa et al. 2002).

Blood pressure, a good indicator of risk for cardiovascular disease, is a parameter relatively easy to measure, even in remote field conditions. Bulliyya et al. (1999) showed that fish consumption was associated with lower mean systolic and diastolic blood pressure among older men and women from coastal fishing villages in India. In contrast, an increased incidence of hypertension and cerebrovascular disease has been reported among aging patients with chronic Minamata disease, from Hg poisoning (Uchino et al. 1995). In animal studies, fish proteins lowered blood pressure in spontaneously hypertensive rats (Aguila et al. 2004; Ait-Yahia et al. 2003, 2004), while in rats who had developed hypertension after sucrose administration, fish oils were able to reverse the alterations on metabolic parameters and blood pressure (Aguilera et al. 2004). However, long term experimental studies suggest that low dose MeHg exposure can lead to irreversible hypertension that remains many months after cessation of exposure (Wakita et al. 1987).

Extensive interdisciplinary studies on the source, transmission and Hg contamination and its effects on populations of the Tapajós River have shown that Hg contamination is very widespread in this region and mainly derived from deforestation and 'slash and burn' agricultural practices (Roulet et al. 1999, 2000, 2001a, 2001b; Farella et al. 2001). When erosion drains soil sediments into the waterways, the inorganic Hg, naturally present in these soils, is transformed into MeHg through bacterial activity and enters the aquatic food chain (Spry et al. 1991; Guimarães et al. 2000a, 2000b). For the traditional populations, living on the banks of the Amazon and its tributaries, fish is the dietary mainstay, with the large majority eating fish daily or several times a week (Lebel et al. 1997; Dolbec et al. 2001; Passos et al. 2003). Hg exposure is higher among those who eat mainly predatory fish and varies seasonally with fish bioavailability (Lebel et al. 1997; Dolbec et al. 2001).

Most communities living along the Tapajós River are not indigenous peoples, but traditional communities with mixed ethnic backgrounds (Murrieta 2001). Their diet consists primarily of fish, with manioc, rice, tomatoes, beans, fruit and some meat

(Passos et al. 2003). Common risk factors for high blood pressure, such as a fatty diet, obesity and a sedentary life style are rare. As part of a global, interdisciplinary project on the sources, transmission and effects of Hg in a riverside Amazonian environment (state of Pará, Brazil), we conducted this preliminary study to examine blood pressure parameters with respect to Hg exposure and fish consumption among traditional communities living along the Tapajós River.

Methods

Population and sampling

The targeted population was from 6 communities (São Luiz do Tapajós, Nova Canaã, Santo Antônio, Mussum, Vista Alegre and Açaituba), living along the Tapajós River, a major tributary of the Amazon River (Figure 1). Since it was not possible to carry out a rigorous random sampling strategy in the conditions of the Amazon, a convenience sample was used and the age and sex distributions were compared to the underlying population, determined through a house-to-house survey. Recruitment into the study was carried out during the house-to-house survey and at village meetings, during which the research project was explained, and villagers were invited to participate on a voluntary basis.

The study was approved by the Federal University of Rio de Janeiro, which has a mandate from the Ethics Review Board of the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) of Brazil, and the University of

Quebec at Montreal and all participants signed an informed consent form, which was read to them.

Socio-demographic information

Two trained interviewers met the participants in their villages. All participants went through an interview of approximately one hour. A questionnaire was used to determine the socio-demographic variables: age, education, work and residence history, smoking and drinking habits, as well as fish consumption and medical history. At the end of the interview, all participants were weighed and measured, and the body mass index (BMI = weight (kg)/ height $(m)^2$) was calculated.

Characterization of fish consumption

A seven-day recall of fish consumption was used. To facilitate the detailing of their fish consumption, a list of the fish species usually consumed in the Tapajós region was prepared (Passos et al. 2001). For each of the past seven days, the participants indicated the number of fish meals and the species consumed at each meal.

Mercury exposure assessment

Hair has been extensively used as a bioindicator for current and retrospective evaluation of Hg (NRC, 2000). This non-invasive method provides samples that can be stored for a long time without deterioration before being analyzed. When hair grows, the intense metabolic activity at the follicle level exposes hair to elements present in the blood, including heavy metals (Katz and Katz 1992).

In the present study, hair strands from the root were cut from the occipital region and stored in plastic bags, with the end root stapled. The first centimetre was analyzed for each sample. Hair mercury concentration (HHg) was determined by cold vapor atomic absorption spectrometry (CVAAS) after digestion with HNO_3, H_2SO_4 and K_2MnO_4 and spinning with hydroxylamine chlorhydrate before reading (Bastos et al., 1998). Hair samples were analyzed in the Laboratório de Traçadores, Centro de Ciências da Saúde, Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Brazil. Precision and accuracy of Hg determination were ensured using internal hair standards, provided by the International Atomic Energy Association.

Blood pressure assessment

Blood pressure was measured in a sitting position, by the same nurse throughout the study. Systolic and diastolic pressure, measured in mmHg, was assessed using a sphygmomanometer (Blood Pressure Monitor Kit, Mark of Fitness, Model MF-20, Stethoscope attached to cuff).

Statistical analyses

Data was entered and analyzed in the StatView (Version 5.0.1) software (SAS Institute). Descriptive analyses were performed to characterize the population. Multivariate analyses were performed to identify the factors that influenced systolic and diastolic blood pressure. Logistic regression analyses, using categorized data, were used to determine the Odds Ratio (OR) for elevated arterial blood pressure.

Results

Relevant data were collected from 259 adults (≥15 years of age) representing 35% of the total adult population. Participants' age and sex distribution were similar to the underlying population (Table 1). The age distribution in the population is typical of that found in developing countries, with about 45 % of the population under 15 years of age (543 people < 15 years from a total population of 1204 persons).

Of the 259 adults who participated in the study, 7 were excluded from the present analyses for reported diagnosed diabetes, a known risk factor for hypertension. The characteristics of the remaining 252 participants are reported in Table 2. Mean age of the study population was 35.2 years (15 to 89 years); 20.2% were over 50. Only 17.5% of the population was overweight, with a BMI above 25 kg/m^2, and 4% were considered obese (BMI > 30 kg/m^2). Although 29.8% of the population smoked, the mean number of cigarettes/day was 8.0 (median=5.0).

Fish consumption

Mean fish consumption was 7.1 meals in the week preceding the interview, an average of 1 fish meal / day (Table 3). The five species most commonly consumed were: Aracu (*Shizodon* sp.), Pescada (*Plagioscion* sp.), Tucunaré (*Cichla* sp.), Caratinga (*Geophagus* sp.) and Pacu (*Mylossoma* sp.). Fish consumption did not vary with any of the socio-demographic variables listed in Table 2.

Mercury exposure

Figure 2 presents the distribution of HHg. Mean HHg was 18.0 µg/g ± 12.52 (0.21µg/g – 77.2µg/g) and 56.0% of the participants had HHg ≥ 15µg/g. No relation was observed between HHg and any of the socio-demographic variables ($p>0.05$). HHg was positively associated with fish consumption ($r^2=0.043$; $p=0.0009$).

Blood pressure

Figure 3 presents the distribution of systolic and diastolic pressures. Mean systolic and diastolic pressures were 114.2 mmHg ± 15.3 and 74.2 mmHg ± 12.2, respectively.

Univariate analyses showed that systolic blood pressure was positively associated with age (r^2=0.12; p<0.0001), higher in men than in women (r^2=0.05; p=0.0007), positively associated with BMI (r^2=0.06; p<0.0001), higher among smokers (r^2=0.03; p=0.005), and positively associated with HHg levels (r^2=0.04; p=0.001). Diastolic blood pressure showed the same relations: age (r^2=0.14; p<0.0001), higher in men than in women (r^2=0.05; p=0.0007), positively associated with BMI (r^2=0.08; p<0.0001), higher among smokers (r^2=0.04; p=0.02), and positively associated with HHg levels (r^2=0.04; p=0.001).

Multivariate analyses showed that all of the previous variables, with the exception of smoking, entered significantly into the regression model for systolic pressure and diastolic pressure. Systolic pressure: adjusted r^2=0.20; p<0.001, with HHg explaining 3% of the total variance (ß=0.19; p=0.008); diastolic pressure: adjusted r^2=0.23; p <0.001, with HHg explaining 2.8% of the total variance (ß=0.15; p<0.01). Fish consumption, measured by the total number of fish meals over the seven days previous to the interview, did not enter to the models (p>0.05). Species-specific analyses with the five most commonly consumed fish (Aracu, Pescada, Tucunaré, Caratinga, Pacu) also showed no influence of fish consumption on systolic and diastolic blood pressures. Village of residence did not influence the results (p>0.05). There was no relation between malaria and Hg exposure.

A total of 53 persons (21.0%) had elevated systolic blood pressure (≥130mm Hg), while 43 (17.1%) had elevated diastolic pressure (≥90 mm Hg). Elevated systolic pressure was higher in those over 50 years (37.3% vs. 16.9%; Fisher's Exact test: $p<0.01$), for those with BMI above 25 kg/m^2 (36.4% vs. 17.8%; $p=0.01$) and for smokers (29.3% vs. 17.5%; $p=0.04$); men had a higher prevalence than women (26.9% vs. 14.4; $p=0.02$), as did those with HHg levels ≥15 µg/g (27.0% vs. 13.5%; $p=0.012$). Neither village of residence nor fish consumption influenced these results. Elevated diastolic pressure was significantly associated with age over 50 years (13.4% vs. 31.4%; $p=0.01$), BMI over 25 (14.8% vs. 30.2%; $p=0.03$) and sex (21.6% in men vs. 11.9% in women; $p=0.04$), while HHg showed a tendency (21.3% when HHg<15µg/g vs. 11.7% when HHg≥15µg/g; $p = 0.07$).

Logistic regression analysis, performed with the independent variables age, sex, BMI, smoking and HHg showed a twofold risk for elevated systolic pressure with HHg ≥15 µg/g (Table 4a); elevated diastolic pressure showed a tendency ($p=0.08$) (Table 4b). Table 5 shows the results, stratified for age. For those under 50 years, sex and BMI entered significantly into the model, but not HHg. For those 50 years and older, only HHg entered significantly into the model with an OR of 3.80 ($p=0.04$) for systolic pressure, while for diastolic pressure, HHg showed a tendency with an OR of 3.68 ($p=0.06$).

Discussion

This preliminary study shows that, in this population where fish is a dietary mainstay, blood pressure is relatively low, with only 8% showing hypertension

(≥140mmHg), there is a significant dose-effect relation between Hg exposure and blood pressure. Even at these relatively low levels of blood pressure, an increase was observed with age, BMI, and men had higher levels as compared to women, confirming that the methods were sensitive enough to detect expected changes. These findings in a population with minimal risk factors for hypertension and with an elevated environmental Hg exposure, offer strong support to a negative effect of Hg on blood pressure parameters.

A positive relation between Hg and blood pressure has been reported in animal studies (Wakita et al. 1987), but human studies have not all observed this relation (Yoshizawa et al. 2002). In a recent study, Pedersen et al. (2005) measured blood Hg and blood pressure among four groups of healthy subjects: 1) Danes living in Denmark consuming European food; 2) Greenlanders living in Denmark consuming European food; 3) Greenlanders living in Greenland consuming European food; 4) Greenlanders living in Greenland consuming mainly traditional Greenlandic food. They reported higher blood Hg in Greenlanders as compared to Danes, which they attributed to their higher fish consumption. Pulse pressure was higher, and diastolic BP lower in Greenlanders than Danes and blood Hg was positively correlated to pulse pressure. Another study showed that in middle-aged Finnish men, Hg accumulation in the body was associated with accelerated progression of carotid atherosclerosis (Salonen et al. 2000). In that study, the strongest predictors of the progression of atherosclerosis were elevated systolic blood pressure, high HHg content, treatment for dyslipidemia, high dietary intake of iron, cigarette smoking and old age. The authors suggest that Hg may be a major environmental risk factor for atherosclerosis in humans, even at subtoxic levels, which have not been previously recognized as harmful.

Several studies have reported associations between prenatal exposure to MeHg and cardiovascular functions, however manifestations vary from one study to another. Although a study on patients with fetal type Minamata disease showed that parasympathetic nervous dysfunction might exist in these patients, they did not show elevated blood pressure (Oka et al. 2003). Sørensen et al. (1999) reported increased systolic and diastolic blood pressures among the Faroese 7 year olds, born from mothers without hypertension, in relation to prenatal MeHg exposure. At 14 years of age, there was no relation with blood pressure, although MeHg exposure was associated with decreased sympathetic and parasympathetic modulation of heart rate variability (Grandjean et al. 2004).

Dórea et al. (2005) reported a trend of lower increase in blood pressure with age among the higher fish consumers, but had no direct measure of fish consumption. Although in the present study, we did not observe a dose-response relation between fish consumption and blood pressure, the relatively low blood pressure observed in the Tapajós riverine villagers may be related to their general diet of fish, coupled to other lifestyle factors. Some fish may have more of a positive effect than others, but this was not apparent in the present study, which relied on the number of fish meals over the past seven days as an indicator of fish eating habits. Cardio-protection has been reported in relation to omega-3 (Dewailly et al. 2001a, 2001b, 2002, 2003) and to fish consumption (Whelton et al. 2004). However, a recent study of freshwater sport's fishers showed no relation between fish consumption, omega-3 levels in blood and/or blood pressure (Godin et al. 2003). Freshwater fish have lower levels of omega-3 fatty acids compared to marine fish (Innis et al 1995; Mahaffey 2004), which might explain the lack of relation between fish consumption and blood pressure in this study and others, but no data on fish omega-3 levels exist for Amazonian fish. Further studies should consider the fatty acid composition of the most consumed fish of the Brazilian Amazon.

Studies have shown that fish cooking methods, such as deep frying and surface frying with oil, changes the lipid and moisture content as well as the fatty acid composition of fish products (Aro et al. 2000; Echarte et al. 2001). Deep-frying Baltic herring (*Clupea harengus membras*) in rapeseed oil changed the fatty acid compositions to that of the frying oil, increased the amounts of monounsaturated fatty acids and omega-6, while decreasing the levels of omega-3 (Aro et al. 2000). Better fatty acid ratios have been observed for roasted salmon compared to fried samples; roasting did not modify the fat content, whereas frying increased the fat content 2-fold (Echarte et al. 2001). In the Tapajós region, fish is mainly fried or boiled, which possibly influences the fatty acid composition.

In the Brazilian Amazon, our research group is working with local populations to identify factors that influence Hg uptake and metabolism in fish and humans in order maximize the nutritional intake from fish and minimize toxic risk. This is an appropriate region to carry out case control studies to further knowledge on the positive and negative effects of fish consumption and Hg exposure on cardiovascular health. More extensive studies on cardiovascular parameters, including R-R variability and the role of fatty acids are currently under way.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

MF is a doctoral student. She participated in the fieldwork, data entry and analysis and writing of the present paper. DM is principal investigator of this study. As such, she participated in the design and the planning, data analysis and writing of the present paper. CJSP is a doctoral student. He co-ordinated the fieldwork and the laboratory analysis for hair mercury levels and participated in the data entry. FL is a professor in the mathematics department of Université du Québec à Montréal. He supervised the statistical analysis. ML is a doctoral student who participated in the preparation and realisation of the fieldwork. JRDG is a co-investigator in the study. He supervised the fieldwork and the laboratory analyses for hair mercury. All authors read and approved the final manuscript.

Abbreviations

BMI – body mass index

CHD – coronary heart disease

Hg – mercury

HHg – hair total mercury

MeHg – methylmercury

OR – Odds Ratio

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Figures

Figure 1 - Map of the study area

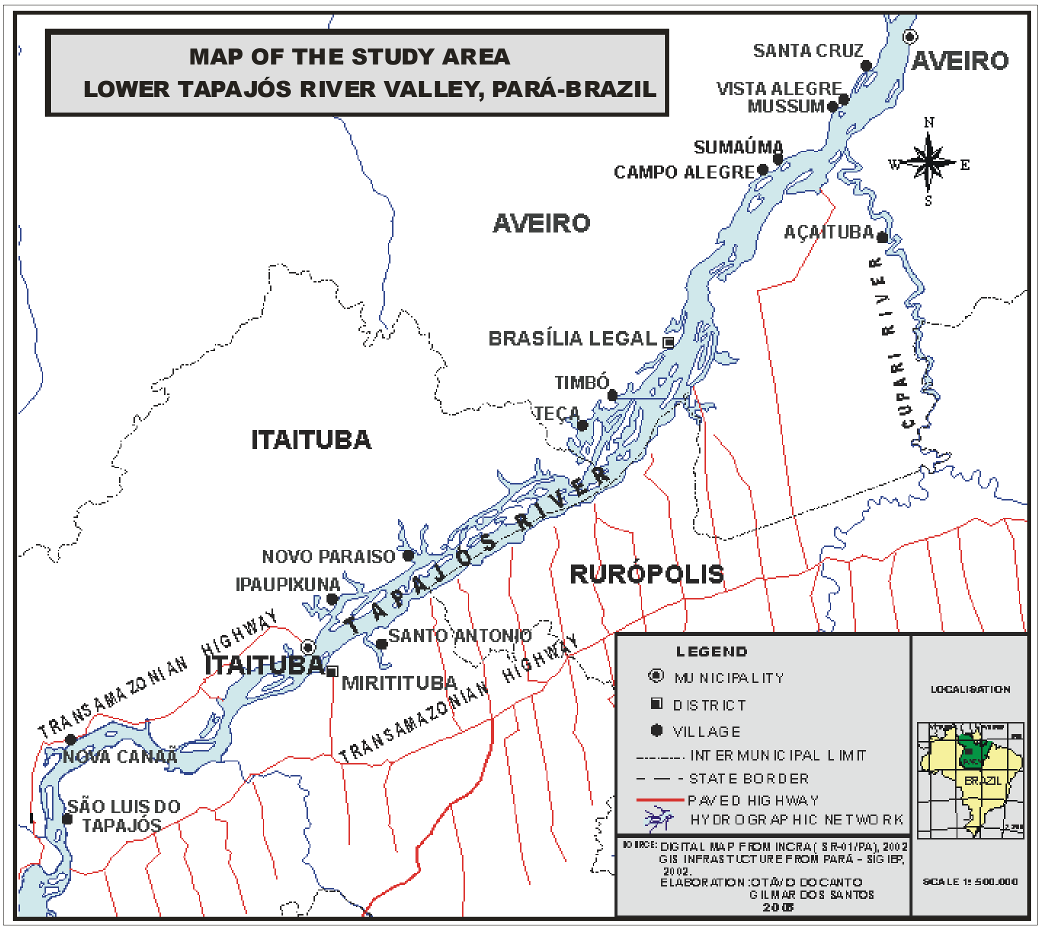


Figure 2 - Distribution of HHg concentrations among the participants

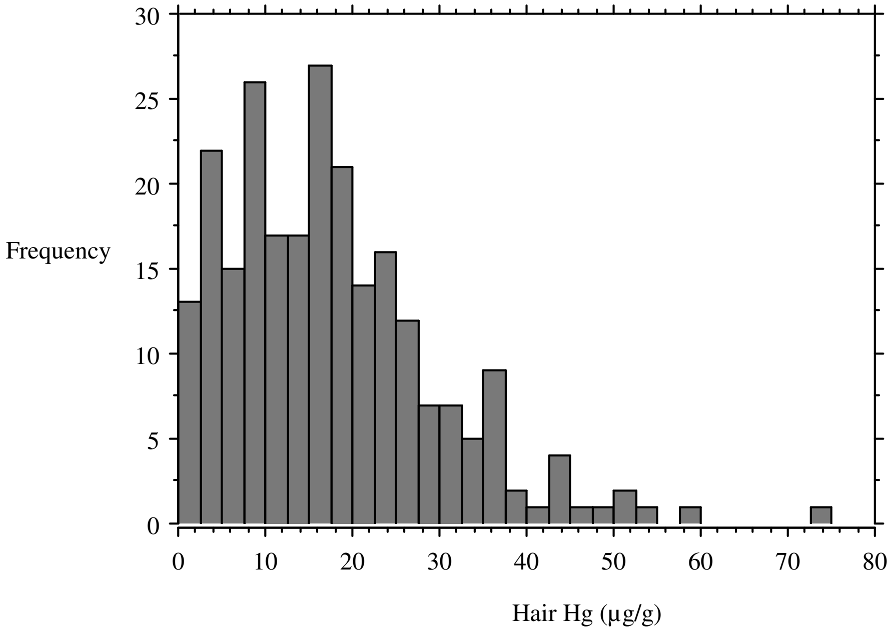
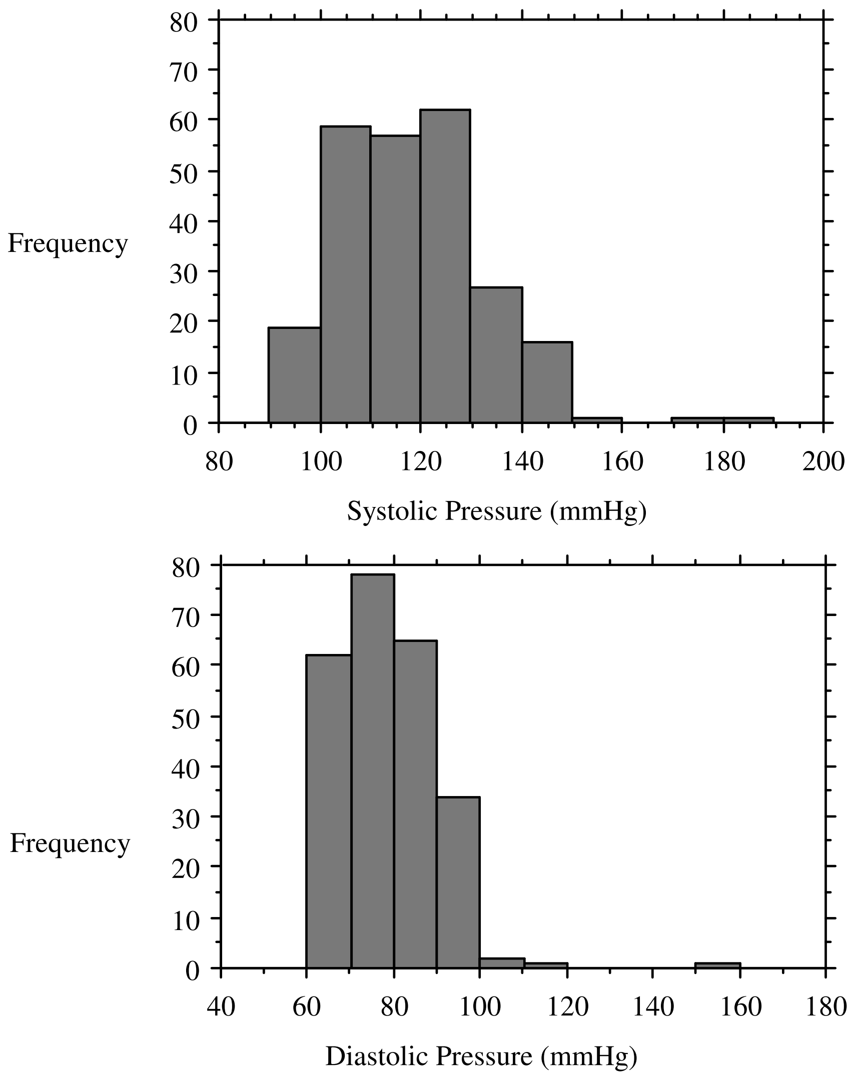


Figure 3 - Distribution of systolic and diastolic blood pressure among the participants (n = 252)



Tables

Table 1 - Age distribution and participation in the study population

Age categories	Total population	# of participants	% participation
15 – 24	217	79	36,4
24 – 34	142	57	40,1
35 – 44	117	56	47,9
45 – 54	84	29	34,5
55 – 64	58	23	39,7
≥ 65	43	15	34,9
Total	661	259	39,2

Table 2 - Demographic characteristics of the study population

	Women				Men			
Characteristics	n	Mean ± SD	Range	%	N	Mean ± SD	Range	%
Age (years)	118	34.4±15.3	15 - 88	100	134	35.9±16.2	15 - 89	100
Education (years)	118	4.1±2.6	0 - 11	100	134	3.3±2.5	0 - 11	100
Alcohol consumption								
Drinks	27			22.9	68			50.7
No longer drinks	15			12.7	25			18.7
Never drank	76			64.4	41			30.6
Smoking habits								
Smokes	25			21.2	50			37.3
No longer smokes	22			18.6	28			20.9
Never smoked	71			60.2	56			41.8
Malaria	56			47.5	95			70.1
Body mass index	118	22.5±4.1	16.4 – 40.2	100	134	22.2±3.0	15.8 – 34.5	100

Table 3 - Frequencies of fish consumption

Fish consumption	Mean number of meals in the last week ± SD
Total fish	7.1 ± 4.8
Piscivorous fish	3.3 ± 3.5
Non-piscivorous fish	3.8 ± 3.4

Table 4 - Odds ratio (OR) and 95% confidence interval for:

a) elevated systolic blood pressure (≥130mmHg)

Variable	OR	p
Hair mercury (≥ 15 µg/g)	2.22 [1.11 - 4.46]	0.02
Age (≥50y)	2.60 [1.26 - 5.36]	<0.01
Sex (men/women)	2.40 [1.19 - 4.86]	0.01
BMI (≥25)	2.70 [1.24 - 5.88]	0.01
Smoking (smokers/non)	1.51 [0.77 - 2.96]	0.23

b) elevated diastolic blood pressure (≥90mmHg)

Variable	OR	p
Hair mercury (≥ 15 µg/g)	1.90 [0.91 – 4.70]	0.09
Age (≥50y)	2.60 [1.22 - 5.53]	0.01
Sex (men/women)	4.34 [1.05 - 4.70]	0.04
BMI (≥25)	2.45 [1.09 - 5.55]	0.03
Smoking (smokers/non)	1.50 [0.73 – 3.06]	0.27

Table 5 - Odds ratio (OR) and 95% confidence interval for:

a) elevated systolic blood pressure (≥130mmHg) for those below 50 years

Variable	OR	p
Hair mercury (≥ 15 µg/g)	1.69 [0.74 – 3.98]	0.22
Sex (men/women)	4.68 [1.94 – 12.74]	<0.01
BMI (≥25)	5.20 [1.99 – 13.99]	<0.01

b) elevated systolic blood pressure (≥130mmHg) for those above 50 years

Variable	OR	p
Hair mercury (≥ 15 µg/g)	3.80 [1.15 – 14.36]	0.04
Sex (men/women)	0.77 [0.24 – 2.50]	0.67
BMI (≥25)	0.62 [0.16 – 2.16]	0.46

c) elevated diastolic blood pressure (≥90mmHg) for those below 50 years

Variable	OR	p
Hair mercury (≥ 15 µg/g)	1.49 [0.62 – 3.77]	0.38
Sex (men/women)	3.36 [1.34 – 9.44]	0.01
BMI (≥25)	3.70 [1.33 – 10.02]	0.01

d) elevated diastolic blood pressure (≥90mmHg) for those above 50 years

Variable	OR	p
Hair mercury (≥ 15 µg/g)	3.68 [1.04 – 15.66]	0.06
Sex (men/women)	1.68 [0.50 – 6.02]	0.41
BMI (≥25)	0.79 [0.20 – 2.89]	0.73