Published in final edited form as:
Arch Med Res. 2008 May ; 39(4): 443–451.

Plasma Selenium Measurements in Subjects from Areas with Contrasting Gastric Cancer Risks in Colombia

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Abstract

Background—An inverse association between selenium status and incidence of different neoplasias including gastric cancer has been reported. This pilot study aimed to determine and compare selenium status in two Colombian populations with different gastric cancer risks: a high-risk area in the volcanic region of the Andes Mountains and a low-risk area on the Pacific coast.

Methods—Eighty nine adult males were recruited in the outpatient clinics of two public hospitals (44 and 45 from high- and low-risk areas, respectively) and provided a blood sample. Seventy one (79.8%) participants underwent upper gastrointestinal endoscopy. Plasma selenium was assayed using a fluorometric method, selenoprotein-P by ELISA, and glutathione peroxidase activity by a spectrophometric method. Histological diagnosis and *Helicobacter pylori* infection were evaluated in gastric biopsy samples. Unpaired samples *t*-test and linear regression analyses were used for statistical analyses.

Results—Although none of the subjects in either of the two geographic areas was selenium deficient, the level of plasma selenium was significantly lower in men from the high-risk area compared with those from the low-risk area. Levels of selenoprotein-P and glutathione peroxidase activity were similar between groups after adjustment for confounders. Selenium measurements were not associated with histopathological diagnosis.

Conclusions—The high incidence of gastric cancer in the Andean region of Colombia is unlikely to be explained by selenium deficiency. We cannot exclude, however, that suboptimal selenium levels may exist in the gastric mucosa of subjects in the high-risk area. Therefore, the benefit of selenium supplementation in gastric cancer prevention cannot be dismissed.

Keywords

Selenium; Selenoprotein-P; Glutathione peroxidase; Gastric cancer risk

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Introduction

Cancer of the stomach is the second most common cause of death from cancer and the fourth most common cancer worldwide. Incidence varies greatly among populations and is higher in Asian, Central and South American countries and lower in North America and Western Europe (1,2). In Latin America, high-risk pockets are found in the high altitude Andean regions where volcanoes abound (2). Migration studies reporting dramatic decreases in gastric cancer within one generation in subjects who have moved from areas of high to low incidence suggest that environmental factors may be involved in its etiology (3,4). Selenium (Se) is an essential dietary nutrient for all mammalian species. Two selenoproteins, extracellular glutathione peroxidase (GPx3) and selenoprotein P (Sepp1), apparently exert antioxidant effects (5,6). Although several epidemiological studies have reported that subjects who develop cancer are Se deficient, the evidence is not consistent (7). With respect to gastric cancer, ecological studies conducted in areas of high gastric cancer risk in Asia showed a significant inverse correlation between gastric cancer mortality and Se in drinking water (8) or with plasma Se (9). Four large-scale cohort studies have reported statistically significant inverse associations (10–13). Three case-control studies observed no associations between Se and gastric cancer risk or precancerous lesions (14–16). Regarding randomized intervention trials, two studies found no association between a vitamin/mineral dietary supplement and gastric cancer risk. Given that those trials examined the effect of Se in combination with other micronutrients, inferences regarding the individual effect of Se cannot be drawn (17,18). However, a double-blind, randomized trial showed a reduced risk of gastric cancer in individuals supplemented with a combination of Se, β-carotene, and α-tocopherol (19).

The mechanism behind the putative beneficial effect of Se is believed to be its ability to act as an antioxidant, mainly through prevention of cellular proliferation and through inhibition of cellular damage by free radicals (20). Because many selenoproteins have been shown to have antioxidant activity (21), higher intake of Se may lead to increased expression of selenoproteins; hence, protecting DNA against oxidative damage.

Our previous long-term research work in Colombia has identified in the south of the country (State of Nariño) two areas with contrasting gastric cancer risks: a high-risk area in the volcanic region of the Andes Mountains and a low-risk area on the Pacific coast. This difference in cancer incidence persists, although residents of these areas have a similarly high prevalence of infection with *Helicobacter pylori* (22,23), a major environmental gastric carcinogen (24). Because Andean regions commonly have volcanic soil with low Se content (25,26), we hypothesized that plasma Se levels would be different between these populations, especially in those individuals suffering from any *H. pylori*-associated gastric diseases. This pilot study aimed to measure Se, GPx activity, and Sepp1 levels in plasma from men from the above-mentioned areas and to determine differences between them.

Materials and Methods

Study Population

Eighty nine adult males between 31 and 60 years old with dyspeptic symptoms who attended the gastroenterology outpatient clinics of two public hospitals between August and November of 2006 in the towns of Tuquerres and Tumaco were enrolled in this study and provided informed consent. Of these, 71 individuals underwent diagnostic endoscopy of the upper gastrointestinal tract. All participants were born in the studied areas and had lived in those areas for decades (median 40 years). Exclusion criteria included previous gastrectomy, concomitant major diseases (i.e., cancer, cardiac failure), and intake of H_2-receptor antagonists, proton pump inhibitors, or antimicrobials in the 4 weeks prior to the endoscopic procedure. Forty four of the males were residents of the area of high gastric cancer risk and 45 were from

the low-risk area. The high-risk area of Tuquerres (estimated incidence rate of 150/100,000 in 1976) in the volcanic region of the Andes Mountains is located at 3000 m above sea level. Its inhabitants are of mixed Spanish and Amerindian ancestry and have an agriculture-based economy. In the low-risk area of Tumaco on the Pacific coast (estimated incidence rate of 6/100,000 in similar coastal areas in 1976) (27), the population is of Spanish-African ancestry and the economy is based on fishing. These areas are about 143 miles apart. The proposal for this study was approved by the Ethics Committee of the Universidad del Valle and the two local hospitals.

Histopathology

During endoscopy, at least three gastric mucosa biopsies were obtained from each patient: one from the antrum (greater curvature, within 5 cm of the pylorus), one from the lesser curvature (at the incisura angularis) and one from the corpus (middle anterior wall). Gastric biopsies for histology were fixed in buffered formalin and embedded in paraffin. Four-μm-thick sections were stained with hematoxylin and eosin for histopathological diagnosis and with modified Steiner silver stain (28) for evaluation of *H. pylori* infection.

Histopathological diagnoses were independently assessed by two experienced pathologists (PC and MBP) according to established guidelines (29,30) as follows: normal, non-atrophic gastritis (NAG), multifocal atrophic gastritis without intestinal metaplasia (MAG), intestinal metaplasia (IM), and dysplasia (DYS). Cases with discordant diagnoses were reviewed in a double-headed microscope and a consensus was reached. Pathologists were blinded to the site of residence of the participants and to the Se profile results.

Plasma Selenium Measurements

Blood specimens were obtained from participants by venipuncture. A 5-ml blood sample was obtained and treated with EDTA to prevent coagulation. Plasma was separated by centrifugation within 30 min after the sample was taken and stored in a liquid nitrogen tank. Later, the samples were placed in a −70°C freezer. Samples were labeled in Colombia and shipped frozen in dry ice to Vanderbilt University, Nashville, Tennessee.

Reagents for biochemical analysis obtained from Fisher Scientific (Pittsburgh, PA) were of analytical grade or better. The source of specialty chemicals is listed with each reagent. Se levels in plasma were determined using a fluorometric method as described (31). Briefly, 75 μl of plasma was digested in a mixture of perchloric and nitric acid at 190°C. Samples were reduced by incubation with hydrochloric acid at 130°C for 30 min. Se was then derivatized with 2,3 diaminonaphthalene (Tokyo Kasei Kogyo Co. Ltd., Tokyo, Japan) and the complex was extracted into cyclohexane. Se content was quantitated by measuring the fluorescence of the sample (excitation: 375 nm and emission: 525 nm). A standard curve was constructed using sodium selenite. Glutathione peroxidase (GPx) activity was determined as described previously for human plasma samples (32). Briefly, the rate of NADPH (USB Corp., Cleveland, OH) oxidation was measured using hydrogen peroxide as the oxidizing substrate. Sepp1 levels were determined by ELISA as described (33). Monoclonal antibodies N11 and N22 were a generous gift of Dr. T. Naruse (Kaketsuken, Kumamoto, Japan). Other Se pools, presumably mostly selenomethionine in albumin and other plasma proteins, were estimated as described (33). Briefly, the Se content (in μg/dL) in glutathione peroxidase was calculated to be 1.7 times the ratio of the subject's GPx activity to the reference plasma's GPx activity. Se content (μg/dL) of Sepp1 was calculated to be 0.9 times the ratio of the subject's Sepp1 to the reference plasma's Sepp1. The other Se value was the total plasma Se measured minus the Se calculated to be in GPx and Sepp1. This calculation has been previously described (33). Laboratory personnel were blinded to the site of residence of the participants and to the histopathological diagnosis.

Sociodemographic, Lifestyle and Dietary Factors

Sociodemographic and lifestyle information were collected. Height and weight were also recorded. Body mass index (BMI), defined as weight in kilograms divided by height in meters squared, was categorized according to the classification by the Centers for Disease Control and Prevention (34). As a proxy measure of socioeconomic level, two composite indexes were created: household conditions and availability of household appliances. The household conditions index was developed by combining the following variables: in-house availability of drinking water; availability of sewerage, and type of flooring material. Levels were defined as low, medium or high. Availability of household appliances combined availability of television, videocassette recorder, gas stove, refrigerator, heater, and automobile/motorcycle at the time of interview. Levels were defined as low (≤2 appliances), medium (3–4 appliances), or high (≥5 appliances). Crowding was estimated by the number of persons living in the house divided by the number of rooms in the house (excluding kitchen and bathroom). Diet was derived from a questionnaire asking about the usual average consumption (times per week) of selected food items. For the present analysis, consumption levels were converted into four groups as follows: 0: less often than weekly; 1: 1–3 times per week; 2: 4–5 times per week; and 3: ≥6 times per week. Information on salt consumption (low, moderate, or high), regular use of multivitamin supplements (yes or no), and current cigarette smoking (yes or no), was also collected.

Data were analyzed using the statistical software program Stata 9.0 (Stata Corporation, College Station, TX). Sociodemographic characteristics, histological parameters and diet information were compared by risk area using χ^2 and Student's *t*-tests as appropriate. To detect possible relationships between plasma Se and the other Se status measurements, Pearson correlation coefficients were estimated according to risk area. In order to assess the degree to which various factors explained the differences between areas in Se measurements, linear regression models were constructed that also included known predictors of plasma Se levels such as age, smoking, and BMI. Association among dietary factors and Se measurements was also assessed. Adjustment for confounders was performed by two different approaches. The first models included education, consumption of vitamin supplements and socioeconomic indexes as covariables. The final models included the listed variables plus the dietary variables associated with plasma Se levels.

Results

Characteristics of the study subjects are presented in Table 1. There were no significant differences between risk areas regarding age, *H. pylori* infection, household conditions index, crowding, consumption of multivitamin supplements, and salt intake. As expected, a significantly greater proportion of subjects with more advanced gastric lesions (MAG/IM/DYS) was observed in the high-risk area in comparison to the low-risk area. Residents from the high-risk area had a lower level of education and had fewer household appliances than those from the low-risk area. The proportion of men who smoked was significantly greater in the high-risk area. BMI values >24.9 were more often seen in the low-risk area.

As shown in Table 2, higher consumption of fresh vegetables, fruits, seafood and chicken was observed in subjects from the low-risk area in comparison to those from the high-risk area. Men from the high-risk area tended to report a higher consumption of potatoes and fava beans than men from the low-risk area. Both groups had similar consumption of milk, red meat, tuna, eggs, rice, oatmeal, wheat, beans and lentils (data not shown). In the entire set, consumption of fresh fish and seafood was positively and significantly associated with plasma Se levels (both *p* values for trend <0.001).

Results of Se measurements by risk area are shown in Table 3. Unadjusted mean plasma Se was lower among men from the high-risk area than among those from the low-risk area (~12% difference). A similar trend (40% difference) was observed in the estimated levels of the "other Se" pool. In contrast, mean values of Sepp1 were significantly higher in men from the high-risk area than in men from the low-risk area. Mean GPx levels did not differ significantly between groups.

Comparison of the Se measurements with one another is presented in Table 4. In the high-risk area, moderately positive and significant correlations were found between plasma Se and Sepp1, as well as between plasma Se and the "other Se" pool. In addition, there was a slight degree of correlation between plasma Se and GPx activity. In the low-risk area, comparison of Se measurements revealed that with the exception of the high correlation between Se and the "other Se" pool, plasma Se did not correlate with other markers.

Overall and by risk area, simple linear regression models showed no significant effect of age, smoking status, BMI, consumption of vitamin supplements, education level, crowding, household conditions index and availability of household appliances index on plasma Se. In models adjusted for confounders, the observed differences between risk area and plasma Se, and risk area and the other Se pool remained statistically significant. Adjustment for covariables significantly attenuated the difference between Sepp1 levels and risk area.

Interestingly, BMI was found to significantly predict GPx activity both overall and by risk area. Overweight and obese subjects exhibited significantly lower GPx activity levels than subjects with normal weight. These differences remained statistically significant after adjustment for confounders (Table 5).

Results of Se measurements by risk area according to histological diagnosis are presented in Table 6. The mean values of the evaluated Se status measurements did not differ significantly between subjects with or without precancerous lesions. No variations were observed in the estimates after adjustment for confounders (data not shown). Finally, subjects infected with *H. pylori* exhibited similar Se status as uninfected subjects (data not shown).

Discussion

Gastric cancer is considered a multistep and multifactorial process in which infection with *H. pylori* plays a prominent role. It has been postulated that the infection may exert its proneoplastic role by inducing an oxidative stress that may last several decades. Se has been studied in relation to this neoplasia due to its possible preventive effects on DNA damage. The chemical form of Se and the dose are determinants of its biological activities as an essential nutrient, chemopreventive agent, or toxicant (33,35–37).

A plasma Se level of 8.5 μg/dL or greater has been suggested to indicate a replete Se status (38). This cut-off point may not represent the biological needs of specific tissues under stress due to chronic inflammation and possible deficiencies of other antioxidants. Levels higher than this are due to non-specific incorporation of selenomethionine into proteins. Based on this value, none of the study participants had Se deficiency. However, men from the high-risk area for gastric cancer had a mean plasma Se value that was on average 12% lower than the value in subjects from the low-risk area indicating incorporation of less non-specific Se. Adjustment for socioeconomic conditions, which directly influence diet and food availability, and other confounders did not attenuate the difference. Although deficiency was not documented in our sample, the difference found in circulating Se levels between the populations may be of crucial importance in antioxidant defense during the chronic inflammatory process leading to gastric carcinogenesis. There may be a threshold effect, such that Se levels must reach certain concentrations to protect against carcinogenesis (39,40). Suboptimal Se levels may interact

with other nutritional deficiencies (such as vitamin C deficiency) to increase gastric cancer risk. In addition, it is possible that a subject might develop a tissue-specific Se deficiency, such as within the gastric mucosa, while not being Se deficient overall. As previously reported (41), plasma and gastric tissue Se levels do not show correlation. Higher concentrations of Se in the *H. pylori*-infected gastric mucosa may be a protective response to increased oxidative stress in association with this bacterial infection. However, when the gastric lesion advances to the point of MAG or IM, tissue levels are lower. Successful eradication of *H. pylori* is reported to significantly decrease mucosal Se levels (41).

In addition to plasma Se, we measured Sepp1 and GPx activity. Total plasma Se reflects the sum of two dynamic pools. The selenoprotein pool represents the Se within the Sepp1 and GPx3 (together comprising ~50% of the plasma concentration of Se). The “other Se” pool involves selenomethionine contained in albumin and other plasma proteins. Plasma Se levels increase (as selenomethionine) in response to Se supplementation, even in Se-replete subjects (42). The same is not true for plasma selenoprotein levels. Conversely, in the setting of Se deficiency, the selenomethionine pool shrinks out of proportion to the selenoprotein pool. Thus, measuring plasma selenoproteins in addition to total plasma Se allows more accurate determination of Se nutritional status (42).

In the high-risk area, significant correlations among Se markers were observed. Levels of plasma Se and selenoproteins were not significantly correlated in the low-risk area. Intake of Se in the form of selenomethionine was probably higher in the low-risk area than in the high-risk area.

Gastrointestinal glutathione peroxidase (GPx2), a member of the GPx family, is expressed predominantly in the gastrointestinal tract. GPx2 might provide a barrier against hydroperoxides derived from the diet or from metabolism of ingested xenobiotics (43). In our study, no difference in the activity of GPx was observed between risk areas. This finding contrasts with data from a previous study conducted in Bolivia (44), in which GPx activity was significantly lower in subjects from high altitudes (4000 m above sea level) than in those from low altitudes (300 m above sea level). The authors argued that the aged erythrocytes and/or the low Se intake in subjects from the high-altitude area may account for the observed difference.

Sepp1 distributes Se and controls cell redox status (45). Therefore, Sepp1 is a key factor in Se homeostasis and host oxidant defense. Similar to plasma Se and GPx activity measurements, levels of Sepp1 do not suggest any deficiency. Although the unadjusted comparison showed that Sepp1 levels were significant higher in subjects from the high-risk area (~12% higher) than those from the low-risk area, adjustment by lifestyle and dietary co-variables attenuated the association. Obesity has been postulated to be associated with oxidative stress (46,47). It is likely that once the obesity persists, sources of the antioxidant enzymes become depleted, leading to a low level of GPx activity, as we found in our study. The result of the low activity of antioxidant enzymes is progressive tissue damage, which may eventually lead to a variety of chronic diseases.

Se is found throughout the food supply. Although concentrations in food vary according to the soil content of the region where it is produced, the richest sources of Se are fish, cereal grains, and meats (48,49). In this study, higher consumption of fresh fish and other seafood products in the low-risk area partially explain the plasma Se difference observed between areas. High concentrations of antioxidants such as vitamin C are present in fresh vegetables and fruits, food items that are also more frequently consumed by residents in the low-risk area. Adequate intake of vitamin C is associated with lower gastric cancer risk (50). Therefore, the different dietary

pattern in the two studied populations may contribute to the difference in gastric cancer risk between them.

In agreement with our results, ethnic differences in Se status have been reported in the U.S., and it has been suggested that they might partially explain racial disparities in cancer incidence rates. Based on a subsample from the Third National Health and Nutrition Examination Survey (1988–1994), a recent study reported that Afro-Americans in the U.S. have lower serum Se concentrations relative to Caucasians (39). This difference was not explained by lifestyle factors or Se intake. The different ethnic backgrounds in the two studied populations may raise concerns about genetically modulated pathways of Se metabolism including selenoprotein expression (51). Future studies are needed to investigate the mechanism(s) for racial disparities.

To assess a potential selection bias, we compared Se measurements and other characteristics (such as age, education level, smoking, proxy variables of socioeconomic status) between participants who underwent endoscopy and participants without endoscopy. No significant differences were observed. Despite the small size of the sample, the analysis showed that it was adequate to conclude that there was a difference in plasma Se levels between the residents of the studied areas. Although Se deficiency was not documented in this study, the difference in Se levels between areas may be of public health importance and may partially account for the disparities in gastric cancer incidence. It is likely that suboptimal levels could adversely affect cancer risk. The protective role of the higher Se levels in the chronic multifactorial process leading to gastric neoplasia cannot be dismissed. Further examination of genetic and environmental factors including the role of other nutritional deficiencies may help to explain population differences in gastric cancer incidence. Future research should try to determine if there is a threshold level for Se to protect against gastric cancer development.

Acknowledgments

We acknowledge the contribution of the dedicated research team and the study participants in Colombia. This work was supported in part by Grant PO1CA-028842 of the National Cancer Institute and Grant R01 DK058763 from the National Institute of Diabetes and Digestive and Kidney Diseases.

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Table 1

Sociodemographic characteristics and histological diagnosis by gastric risk area in males from Nariño, Colombia (2006)

Variables	Gastric cancer risk area		Two-sided *p* value
	Low-risk (*n* = 45)	High-risk (*n* = 44)	
Age (years) (mean ± SD)	48.4 (5.9)	49.2 (5.2)	0.487
Histological diagnosis[b] (*n*, %)	*n* = 26	N = 44	
Normal and NAG	16 (61.54)	16 (36.36)	0.041
MAG, IM and DYS	10 (38.46)	28 (63.64)	
H. pylori status (by Steiner), *n* (%)	*n* = 27	*n* = 44	
Uninfected	3 (11.11)	5 (11.36)	1.00[a]
Infected	24 (88.89)	39 (88.64)	
BMI (*n*, %)			
Underweight (<18)	2 (4.44)	0 (0)	0.014[a]
Normal (18.5–24.9)	19 (42.22)	27 (61.36)	
Overweight (25–29.9)	13 (28.89)	15 (34.09)	
Obese (≥30)	11 (24.44)	2 (4.55)	
Higher level of education attained (*n*, %)			
Less than elementary	4 (8.89)	2 (4.55)	<0.001
Elementary	19 (42.22)	36 (81.82)	
Junior/high school/university	22 (48.89)	6 (13.64)	
Household appliances index (*n*, %)			
Low	17 (37.78)	29 (65.91)	0.006
Medium	17 (37.78)	13 (29.55)	
High	11 (24.44)	2 (4.55)	
Household conditions index (*n*, %)			
Low	8 (17.78)	12 (27.27)	0.336
Medium	23 (51.11)	16 (36.36)	
High	14 (31.11)	16 (36.36)	
Crowding (persons per room) (*n*, %)			
≤1.5	28 (62.22)	23 (52.27)	0.579[a]
1.6–3.5	16 (35.56)	19 (43.18)	
≥3.6	1 (2.22)	2 (4.55)	
Current smoker (*n*, %)			
No	35 (77.78)	26 (59.09)	0.058
Yes	10 (22.22)	18 (40.91)	
Multivitamin supplement consumption (*n*, %)			
No	32 (71.11)	37 (84.09)	0.142
Yes	13 (28.89)	7 (15.91)	

SD, standard deviation; NAG, non-atrophic gastritis; MAG, multifocal atrophic gastritis; IM, intestinal metaplasia; DYS, dysplasia; BMI, body mass index.

[a] *p* value from Fisher's exact test.

[b] A case classified as gastritis, NOS (atrophy could not be assessed) was not included in this comparison.

Table 2

Average consumption of selected food items by risk area in males from Nariño, Colombia (2006)

Food items (average consumption in times per week)	Gastric cancer risk area		Two-sided *p* value[a]
	Low risk (*n* = 45)	High-risk (*n* = 44)	
Fresh fish intake (*n*, %)			
Less often than weekly	3 (6.67)	32 (72.73)	<0.001
1–3	17 (37.78)	12 (27.27)	
4–5	5 (11.11)	0 (0.0)	
6–7	20 (44.44)	0 (0.0)	
Seafood intake (*n*, %)			
Less often than weekly	21 (46.67)	43 (97.73)	<0.001
1–3	21 (46.67)	1 (2.27)	
4–5	2 (4.44)	0 (0.0)	
6–7	1 (2.22)	0 (0.0)	
Chicken intake (*n*, %)			
Less often than weekly	5 (11.11)	20 (45.45)	<0.001
1–3	33 (73.33)	22 (50.00)	
4–5	5 (11.11)	0 (0.0)	
6–7	2 (4.44)	2 (4.55)	
Fava bean intake (*n*, %)			
Less often than weekly	41 (91.11)	15 (34.09)	<0.001
1–3	4 (8.89)	27 (61.36)	
4–5	0 (0.0)	2 (4.55)	
6–7	0 (0.0)	0 (0.0)	
Bread intake (*n*, %)			
Less often than weekly	9 (20.00)	1 (2.27)	<0.001
1–3	13 (28.89)	6 (13.64)	
4–5	3 (6.67)	0 (0.0)	
6–7	20 (44.44)	37 (84.09)	
Vegetable intake (excluding tubers) (*n*, %)			
Less often than weekly	11 (24.44)	6 (14.29)	0.008
1–3	22 (48.89)	30 (71.43)	
4–5	2 (4.44)	5 (11.90)	
6–7	10 (22.22)	1 (2.38)	
Potatoes (cooked) intake (*n*, %)			
Less often than weekly	2 (4.44)	0 (0.0)	<0.001
1–3	11 (24.44)	0 (0.0)	
4–5	4 (8.89)	2 (4.55)	
6–7	28 (62.22)	42 (95.45)	
Fruit intake (excluding juices) (*n*, %)			
Less often than weekly	11 (24.44)	8 (20.00)	0.019
1–3	25 (55.56)	25 (62.50)	
4–5	0 (0.0)	5 (12.50)	
6–7	9 (20.00)	2 (5.00)	
Citrus fruit juice intake (*n*, %)			
Less often than weekly	7 (15.56)	29 (65.91)	<0.001
1–3	16 (35.56)	9 (20.45)	
4–5	0 (0.0)	4 (9.09)	
6–7	48 (48.89)	2 (4.55)	
Citrus fruits (*n*, %)			
Less often than weekly	11 (24.44)	22 (50.00)	0.033
1–3	23 (51.11)	16 (36.36)	
4–5	3 (6.67)	4 (9.09)	
6–7	8 (17.78)	2 (4.55)	
Banana intake (*n*, %)			
Less often than weekly	13 (28.89)	19 (43.18)	0.001
1–3	19 (42.22)	25 (56.82)	
4–5	2 (4.44)	0 (0.0)	
6–7	11 (24.44)	0 (0.0)	
Papaya intake (*n*, %)			
Less often than weekly	9 (20.00)	26 (59.09)	<0.001
1–3	29 (64.44)	18 (40.91)	
4–5	7 (15.56)	0 (0.0)	
6–7	0 (0.0)	0 (0.0)	

[a] *p* values from Fisher's exact tests.

Table 3

Mean levels of plasma selenium measurements by risk area in males from Nariño, Colombia (2006)

Plasma levels	*Gastric cancer risk area*		*Unadjusted difference*	*Two-tailed p value*[a]	*Adjusted difference*[b]	*Two-tailed p value*[b]	*Adjusted difference*[c]	
	Low risk n=45	**High risk n=44**						
	Mean(SD)	**Mean(SD)**	*(SE)*		*(SE)*		*(SE)*	
Plasma selenium (ug/dL)	12.1 (1.4)	10.7 (1.2)	−1.4 (0.3)	<0.001	−1.7 (0.3)	<0.001	−1.3 (0.5)	0.006
Sepp1 (ug/ml)	5.2 (1.10)	5.8 (0.92)	0.6 (0.2)	0.009	0.6 (0.3)	0.017	0.4 (0.4)	0.266
GPx activity (nmol/min/ml plasma)	110.5 (17.2)	107.3 (16.9)	−3.2 (3.6)	0.379	−3.2 (4.0)[d]	0.677[d]	−1.0 (6.0)[e]	0.869[e]
Other selenium pool	5.0 (1.8)	3.0 (1.0)	−2.0 (0.3)	<0.001	−2.4 (0.4)	<0.001	−1.7 (0.5)	0.002

Abbreviations: SD, standard deviation; SE, standard error; Sepp1: selenoprotein-P; GPx: extracellular glutathione peroxidase

[a] P-values for difference from t-test.

[b] Differences and p-values from linear regression models adjusted for vitamins, schooling, household appliances index and household conditions index.

[c] Differences and p-values from linear regression models adjusted for vitamins, schooling, household appliances index, household conditions index, and consumption of fresh fish and seafood.

[d] Differences and p-values from linear regression models adjusted for BMI, vitamins, schooling, household appliances index and household conditions index.

[e] Differences and p-values from linear regression models adjusted for BMI, vitamins, schooling, household appliances index, household conditions index, and consumption of fresh fish and seafood.

Table 4

Correlations among plasma selenium measurements by risk area in males from Nariño, Colombia (2006)

Plasma measurements	Gastric cancer risk area			
	Low-risk *n* = 45		High-risk *n* = 44	
	Coefficient	*p* value	Coefficient	*p* value
Selenium vs. Sepp1	0.09	0.5466	0.52	0.0003
Selenium vs. GPx activity	0.12	0.4316	0.37	0.0133
Selenium vs. other selenium pool	0.71	<0.001	0.58	<0.001
GPx activity vs. Sepp1	0.01	0.9656	0.01	0.9590
GPx activity vs. other selenium pool	−0.03	0.8412	0.22	0.1460
Sepp1 vs other selenium pool	−0.63	<0.001	−0.38	0.0114

Sepp1: selenoprotein-P; GPx: extracellular glutathione peroxidase

Table 5

Mean differences of GPx activity according to body mass index by risk area in males from Nariño, Colombia (2006)

Variables	Gastric cancer risk area					
	Low-risk n=43		High risk n=44		Total n=87	
	Difference	P value	Difference	P value	Difference	P value
Unadjusted mean differences						
Normal vs. overweight	−8.8	0.155	−12.8	0.018	−10.7	0.008
Normal vs. obese	−14.6	0.027	−8.5	0.474	−11.6	0.027
p-trent [a] (excluding underweight men)	0.022		0.035		0.005	
Adjusted mean differences						
Normal vs. overweight	−8.0	0.268	−13.2	0.015	−11.3	0.005
Normal vs. obese	−16.7	0.037	−9.4	0.423	−16.7	0.004
p-trend [b] (excluding underweight men)	0.034		0.028		<0.001	

[a] P-values from simple linear regression models

[b] P-values from linear regression models adjusted for age, smoking, schooling, household appliances index and household conditions index.

Table 6

Mean levels of plasma Se measurements according to the presence of gastric precancerous lesions (MAG/IM/DYS) by risk area in males from Nariño, Colombia (2006)

Variables	*Gastric cancer risk area*					
	Low risk n=26[a]			**High risk n=44**		
	Normal/NAG n=16	**MAG/IM/DYS n=10**	**Two-tailed P value**[b]	**Normal/NAG n=16**	**MAG/IM/DYS n=28**	**Two-tailed P value**[b]
	Mean (SD)	**Mean (SD)**		**Mean (SD)**	**Mean (SD)**	
Plasma selenium (ug/dl)	12.1 (1.5)	11.5 (0.8)	0.240	10.6 (0.9)	10.7 (1.3)	0.834
Sepp1 (ug/ml)	5.4 (1.1)	4.7 (1.3)	0.155	5.6 (0.7)	5.9 (1.0)	0.293
GPx activity (nmol/min/ml plasma)	110.3 (15)	111.7 (20)	0.620	104.9 (15)	108.6 (18)	0.490
Other selenium pool	4.8 (1.8)	5.0 (1.6)	0.865	3.1 (0.8)	2.8 (1.)	0.353

Abbreviations: SD: standard deviation; NAG, non-atrophic gastritis; MAG, multifocal atrophic gastritis; IM, intestinal metaplasia; DYS, dysplasia; Sepp1, selenoprotein-P; GPx, extracellular glutathione peroxidase

[a] A case classified as gastritis, NOS (in which atrophy could not be assessed) was not included in this comparison

[b] P-values for difference from t-test.