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Original article

Sodium intake and *Helicobacter pylori* infection in the early stages of life

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ABSTRACT

Introduction: *Helicobacter pylori* infection is mainly acquired during childhood and is associated with an increased risk of developing gastric cancer. High amounts of sodium intake can lead to the onset of pre-malignant lesions contributing to the process of carcinogenesis, and potentiate the effect of *H. pylori* infection. This study aimed to evaluate the exposure to sodium in children until 4 years of age and to quantify its association with *H. pylori* infection.
Methods: This study includes 503 children from the cohort Generation XXI, recruited after childbirth and re-evaluated at 6 months and at 4 years of age. Information about socio-demographic characteristics, food intake after birth and status of *H. pylori* infection (assessed by serum ELISA) was collected. Scores of sodium exposure were calculated using the consumption of milk and other food items (evaluated at 6 months), and food items with the highest contribution to sodium intake and sodium intake (evaluated at 4 years). Logistic regression models were used to compute adjusted odds ratio (OR) and respective 95% confidence intervals (CI).
Results: We found that 28.2% of children were infected with *H. pylori* at 4 years of age, with a daily sodium intake that exceeded World Health Organization recommendations in 26%. No statistically significant association between sodium intake and *H. pylori* infection was observed, with the exception of the 2nd quarter in the score concerning consumption of "other food items" in the assessment at 6 months of age (OR = 2.41; 95%CI: 1.29–4.50).
Conclusion: No association between sodium intake and *H. pylori* infection was found; however, to the best of our knowledge, the present epidemiologic study is the first to test the influence of sodium intake in *H. pylori* infection in children.

Introduction

Gastric cancer is the third most common cause of cancer deaths worldwide.[1] In Portugal, gastric cancer mortality has been decreasing since the 1970s, though with large regional differences.[2] The high prevalence of *Helicobacter pylori*, a major risk factor for gastric cancer, at young ages is associated with a higher mortality due to this type of cancer compared with cases for whom the infection was acquired later in life.[3]

Although dietary sodium intake is independently associated with an increased gastric cancer risk,[4] a significant positive interaction may exist between this factor and *H. pylori* infection contributing to the risk of gastric cancer.[5] The biological plausibility for such a synergism has been demonstrated in animal studies.[6,7] Excessive sodium intake may increase *H. pylori* colonization and exacerbate gastritis, enhancing the carcinogenic process,[6] and a dose-response relationship was even demonstrated in experimental models.[7] However, no epidemiologic study has tested the influence of sodium intake in *H. pylori* infection. Demonstrating the existence of a causal relationship between sodium intake and *H. pylori* infection would allow for the identification of potential targets for intervention strategies for the prevention of infection by *H. pylori*, resulting in a decrease in the future burden of gastric cancer.

This study aimed to evaluate the exposure to sodium in children until 4 years of age, through data collected since birth, and to quantify its association with *H. pylori* infection in the early stages of life.

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Methods

Study participants and data collection

The present study was carried out within the cohort Generation XXI (G21). The cohort comprises 8647 children, born between April 2005 and August 2006 in the Porto Metropolitan Region.[8,9] Recruitment was conducted at five public maternity units, responsible for 95% of the deliveries in the region in that moment, and 91.4% of the eligible mothers accepted to participate.

All phases of the study complied with the Ethical Principles for Medical Research Involving Human Subjects expressed in the Declaration of Helsinki. The study was approved by the University of Porto Medical School/S. João Hospital Centre Ethics Committee and by the Portuguese Authority of Data Protection. Written informed consent was obtained from all participants.

Recruitment

Participants were face-to-face interviewed by trained interviewers between 24 and 72 h after delivery. Data were collected using structured questionnaires on maternal socio-demographics, obstetric and gynaecologic history, planning and occurrence of the current pregnancy, prenatal care, lifestyle before and during the pregnancy. Pregnancy complications, delivery and newborn-related data were retrieved from the medical records by the same interviewers using standard forms. They also performed more detailed measurements of the newborns as well as of their parents (*i.e.*, weight, height and head circumference) using standardized methods. Whenever possible, venous blood samples were collected from the parents, as well as an umbilical cord sample of the children. Serum samples were stored at −80 °C until analysis.

Re-evaluation at 6 months of age

Trained interviewers collected information about each child through a standardized questionnaire, including socio-demographic and clinical data, and food consumption. Besides information on breastfeeding practices, the consumption of other types of milk was also registered. Additionally, data on the consumption of other food items was collected, namely, water, tea, tisanes, barley, juices, yogurts, fruit, cereal and gluten free cereal, bread, cookies, eggs, vegetable soup, potatoes, meat, fish, salt and sugar, as well as the age at which these food items started to be consumed by the child.

Re-evaluation at 4 years of age

Between April 2009 and August 2011, a follow-up evaluation of the entire cohort was performed. Most children were evaluated in a face-to-face interview, a physical examination was also performed and a blood sample was collected from the children and their mothers, whenever possible. Parents answered a structured questionnaire to gather data on socio-demographic characteristics, physical activity, dietary habits, sleep features and healthcare use. Information on the main caregiver for the child since birth was also collected. Furthermore, a food frequency questionnaire was applied, and the parents were asked to fill a 3-day food diary at home (two week days and one day of the weekend). Conversion of food items into nutrients was performed using the database Food Processor Plus software (1997; ESHA Research, Salem, Oregon, USA), which has been adapted to traditional Portuguese food and dishes presented in the Portuguese table of food composition.[10]

Children whose parents had provided a blood sample at the baseline evaluation were eligible for this study. Mothers from the children included in this study ($n = 503$) were older and more educated than the total number of mothers recruited in G21.

Scores of exposure to sodium

To estimate the amount of sodium intake at 6 months of age through milk, data regarding the sodium content per 100 ml of product for each specific milk consumed by the child since birth, as reported by the parents, was retrieved. The different types of milk, its commercial designation and the age at which the child started and ended, if applicable, its consumption were also taken into account. The mean sodium content of the milks reported to be consumed by the children was estimated to be 20 mg/100 ml. This value was used as a reference to calculate exposure to sodium through milk consumption. For each milk, we also computed the time of exposure by subtracting the end date to the start date of consumption. For children consuming more than one type of milk since birth, the different parcels were summed to build a single score.

Exposure to sodium through milk consumption at 6 months of age (mean sodium intake in months)

$$\sum \left(\frac{\text{Sodium content in milk}(\text{mg}/100\,\text{ml})}{\text{Mean sodium content of milks}(20\,\text{mg}/100\,\text{ml})} \right) \times \text{exposure time interval}\,(\text{months})$$

Regarding the other food items consumed at 6 months of age, information concerning their sodium content was retrieved from the Portuguese table of food composition,[11] considering the mean sodium content in each food item per 100 g of product. To build the score of exposure to sodium for each food item, the time of exposure to that specific food item (difference between end date and start date of consumption reported by the parents) in months was multiplied by the value obtained for the mean sodium content per 100 g.

Exposure to sodium through consumption of other food items at 6 months of age (mean sodium intake in months)

$$\text{Mean sodium content of food item} \left(\frac{\text{mg}}{100\,\text{g}} \right) \times \text{exposure time interval}\,(\text{months})$$

Daily sodium intake was evaluated through 3-day food diaries at 4 years of age. These diaries allowed for the identification of food items with the highest contribution to sodium intake, such as: vegetable soup; dairy products; meat, fish and eggs; cereal and potatoes; cookies and biscuits; savory snacks; ham, bacon and sausages; fruits and vegetables; cakes and sweets.[12] These food items were also part of the food frequency questionnaire applied at 4 years of age, and we evaluated the frequency of consumption for each one. To build the score of sodium exposure for the food items with the highest contribution to sodium intake, the number of times that the food item was consumed per week was multiplied by the mean sodium content of that specific item.

Exposure to sodium through consumption of food items with the highest contribution to sodium intake at 4 years of age (mean sodium intake per week)

$$\text{Frequency of weekly consumption} \times \text{mean sodium content of food item}\,(\text{mg}/100\,\text{g})$$