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# Childhood and Adulthood Risk Factors of Gastric Cancer: A Hospital-Based Case-Control Study in Iran

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ABSTRACT

**Background:** Gastric cancer (GC) is the most common cancer among Iranian men. This study aimed to investigate the association between early and late lifestyle risk factors and GC among the Iranian population.

**Method:** A hospital-based case-control study recruited GC patients from the Cancer Institute in 2010-2012. Controls were healthy visitors to be frequency-matched based on sex, age, and residential place, and were recruited from the non-oncology wards. We collected exposure to various established risk factors before the diagnosis in patients and prior to the interview in controls. Additionally, we obtained information on socioeconomic factors during childhood. Logistic regression models were employed to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for various potential risk factors.

**Results:** The study included a total of 210 GC patients and 210 controls. The average age of cases was 59.9 years, and controls were 56.7 years. Participants with a family history of GC had a 4-fold higher risk of GC than those without a family history (OR=4.1, 95% CI: 1.7, 9.6). We observed an inverse association between GC with education (P-value for trend =0.003). Individuals reported coffee consumption had a lower risk of GC (OR=0.5, 95% CI: 0.3, 0.8) as compared to non-coffee users. The study found that individuals with high intake of fruit (OR=0.6, 95% CI: 0.3, 1.3) and medium (OR=0.5, 95% CI: 0.3, 1.0) and high (OR=0.3, 95% CI: 0.1, 0.6) intake of vegetables had lower odds of GC, while higher consumption of red meat (OR=5.3, 95% CI: 2.8, 10.2) had higher odds of GC. Analysis of factors related to the childhood period showed that lack of access to tap water increased odds of GC compared to access to tap water (OR: 2.9, 95% CI: 1.3, 6.7). We did not observe any significant associations between h. pylori infection, opium use, waterpipe smoking, cigarette smoking, alcohol consumption, BMI, and other early life risk factors, and the risk of GC.

**Conclusion:** The occurrence of GC is influenced by several factors, including family history of GC, dietary habits, and socioeconomic status (SES) during both childhood and adulthood.

**Keywords: Gastric Cancer; Risk Factors; Iran**

## INTRODUCTION:

Despite the declining trends in the incidence rates of gastric cancer (GC) in high-income countries such as the United States, Western Europe, and Japan, it remains a significant global concern. In 2020 alone, there were over one million new cases of GC reported, with 769,000 resulting in death, making it the fifth most common cancer in terms of incidence and fourth in terms of mortality worldwide [1]. The prognosis of GC is poor, with a 5-year survival rate for advanced stage hardly exceeding 20% [2]. Therefore, implementing an effective prevention program that includes primary prevention and early detection is a top priority.

The age-standardized incidence rate (ASR) of GC is particularly high in Iranian men (ASR=19 per 100,000) and women (ASR=8.8 per 100,000). Notably, ASRs vary among Iranian women, ranging from 20.3 per 100,000 in Ardabil province to 4.6 per 100,000 in Hormozgan province [3,4]. Unfortunately, GC patients in Iran, similar to global trends, face a poor prognosis, with a 5-year net survival rate below 20% for both genders [5]. Clinical studies consistently show that the majority of Iranian patients are diagnosed at advanced stages, resulting in unfavorable prognoses [6].

Helicobacter pylori (H. pylori) infection is the main risk factor for GC, affecting approximately 90% of individuals residing in high-risk areas of Iran [7]. Other risk factors for GC include genetic susceptibility and a positive family history of GC [8], cigarette smoking, alcohol consumption, and unhealthy dietary habits, such as excessive salt intake, low consumption of fruits and vegetables, high consumption of processed food, and red meat [9]. Additionally, the use of opium and waterpipe smoking, prevalent in Iran and other Middle Eastern countries has been associated with an increased risk of GC [10–12]. Lower socioeconomic status (SES) has also been associated with a higher risk of GC and poorer survival outcomes [13,14]. The association between low SES and GC is likely driven by factors such as high transmission and colonization of H. pylori infection [15], lower consumption of fruits and vegetables, higher smoking rates, and unhealthy diets among low SES groups [13]. Furthermore, studies have shown that living in low SES conditions during childhood is associated with a higher prevalence of H. pylori infection and, therefore, a higher risk of GC [16–18]. Immigrant populations who relocate from high-risk areas to low-risk areas retain their risk in the first generation, but the risk converges to that of the host country's population from the second generation [19]. This highlights the importance of long-standing effects and a life course assessment of GC risk factors.

While previous epidemiological studies have confirmed the association between established risk factors and GC, these studies were mainly conducted in the high incidence areas located in the northern and northwestern parts of Iran, such as Golestan, Mazandaran, and Ardabil provinces [9,20]. We conducted a hospital-based case-control study at the Cancer Institute of Iran to address the GC risk factors among the population who are at medium risk for GC [3]. In this study, we also explored the potential role of risk factors during childhood on GC risk.

## Methods:

We conducted a hospital-based case-control study. The cases were patients who had a histologically confirmed diagnosis of GC (ICDO3-C16) and were referred to the Cancer Institute of Iran between 2010 and 2012. To avoid survivor bias, we only included cases that had been diagnosed within one year prior to the date of the interview.

The control group comprised healthy visitors and caregivers of non-cancer patients at Imam Khomeini General Hospital Complex, a referral hospital. Controls were frequency matched the GC patients by sex, age (in five-year age bands), and residential place, specifically living in Tehran or coming from other provinces. We conducted interviews with the control group every six months after case enrollment. The study proposal was reviewed and approved by the Ethics Committee of Tehran University of Medical Sciences (Code: 87-02-51-7345), and each participant provided written informed consent.

We developed a structured questionnaire based on a thorough evaluation of the literature. After a pilot phase, the questions were validated and finalized by our research group. Trained interviewers utilized the questionnaires designed for this study and gathered data on age, sex, ethnicity, family history of GC, alcohol drinking, coffee consumption, tobacco use (i.e., cigarettes and water pipe), opium use, socioeconomic status (SES) before the cancer diagnosis in cancer patients and prior to interview among controls. We also collected information about using tap water, and access to a refrigerator during childhood as well as data on the father's job as proxies for SES and early life exposure to risk factors. Trained nutritionists interviewed participants and using the Farsi version of the dietary history questionnaire (DHQ) to collect information about the dietary habits of both cases and controls. We asked patients to recall dietary habits before the appearance of any sign of cancer. A detailed report on the validation of DHQ has been published elsewhere [21]. The DHQ consisted of 146 questions related to the past 12 months' consumption of food and Iranian mixed dishes [22] Furthermore, we collected 10 ml of venous blood to assess H. pylori infection. Serum samples were evaluated for IgG antibodies using available ELISA kits. Experienced technicians, blinded to the study design and participants, monitored the status of the samples and performed the serologic assays. Seropositivity was defined as the presence of H. pylori antibodies, indicating a previous infection during the individual's lifetime. The seropositivity cut points were defined as > 0.87 for positive, < 0.64 for negative, and between 0.64 and 0.87 for borderline seropositivity.

### Statistical Analysis

We defined education in four categories, including illiterate (reference group), elementary (1-6 years), secondary (6-11 years), and college. Drinking coffee, alcohol consumption, tobacco and opium use were classified as never use (reference group) and ever use during participants' lifetime. Family history of GC and seropositivity to H. pylori were categorized as negative (reference group) and positive. Body mass index (BMI) and dietary factors (intakes of fruit, vegetables, red meat, and processed meat) were grouped based on tertiles. In addition, we used access to tap water (yes/no), and using a refrigerator (yes/ no) during childhood, and fathers' occupation as proxies of early life exposure and SES. To avoid data deletion due to missing values in the regression model, we identified the individuals with a missing value as an unknown category.

We applied unconditional logistic regression to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) to assess the association between GC and potential risk factors. Variables with a p-value less than 0.20 in the univariate analysis were included in the multivariable model. We also employed the log-likelihood ratio test to evaluate the robustness of the model and exclude variables that did not improve the model's fitness using the likelihood ratio test [23] the area under the curve (AUC) for all models was 0.83, which is considered the best performance. The final model comprised age, sex, residential place, education, opium use, drinking coffee, family history of GC, and BMI ten years ago, and fruits, vegetables, and red meat intake. Additionally, we investigated the association between dietary factors, such as fruits, vegetables, red meat, and processed meat, in a separate model. Furthermore, to evaluate the role of early life socioeconomic indicators, including access to tap water, using a refrigerator during childhood, and the father's occupation as proxies of SES. We performed statistical analyses using STATA version 17 (StataCorp, College Station, TX).

## Results:

We included 210 GC patients and 210 controls, who were frequency-matched by age, sex, and residential place. The response rate of the patients was 95%, while the control group response rate was 70%. The average age of patients was higher than the controls (with a mean age of 59.9 (±11.7) vs. 56.7 (±10.2) years, with a higher percentage of males (76.2%) in both groups. They were also more likely to be residents of Tehran Province (63.8% in cases vs. 45.7% in controls. Patients had a lower average intake of fruit (294.9 g/day vs. 405.0 g/day) and vegetables (140.9 vs. 230.1), but higher consumption of red meat (28.9 g/day vs. 22.9) compared to controls (Table 1).

The results of a multivariate analysis showed that individuals who had a positive family history of GC had a significantly higher risk of developing GC compared to those with no family history of GC (OR=4.1, 95% CI: 1.7, 9.6). However, individuals with an elementary (OR=0.4, 95% CI: 0.2, 0.8), secondary level (OR=0.3, 95% CI: 0.2, 0.6), and college education (OR=0.2, 95% CI: 0.1, 0.6) had lower odds of GC compared to illiterate individuals (p-value for trend 0.003). The study also found that drinking coffee showed 50% lower odds of GC compared to those who didn't drink coffee (OR=0.5, 95% CI: 0.3, 0.8). However, we did not find any significant associations between the risk of GC and other lifestyle risk factors, including alcohol drinking, cigarette smoking, opium use, body mass index (BMI), and H. pylori seropositivity. Since the inclusion of these variables didn't improve the fitness of our model so we dropped them from the model (Table 2). The results showed that individuals who had high intake (third tertile) of fruits (OR=0.6, 95% CI: 0.3,1.3) and a medium (second tertile) (OR=0.5, 95% CI: 0.3, 1.0) and high (third tertile) (OR=0.3, 95% CI: 0.1, 0.6) intake of vegetables showed a lower odds of GC compared to those who had a lower intake (p-value for trend= 0.001). On the other hand, higher consumption of red meat was associated with higher odds of GC (OR=2.3, 95% CI: 1.2, 4.4) for the second tertile and (OR=5.3, 05%

**Table 1.** Characteristics of gastric cancer (GC) patients and controls recruited in the hospital-based case-control study at the Cancer Institute of Iran, 2010-2012.

| Variables | GC patients N=210 | Controls N=210 |
|---|---|---|
| **Sex** | | |
| **Female, N (%)** | 50(23.8) | 50 (23.8) |
| **Male, N (%)** | 160 (76.2) | 160 (76.2) |
| **Current place of residence*** | | |
| **Tehran Provinces N (%)** | 134 (63.8) | 96 (45.7) |
| **Other Province, N (%)** | 76 (36.2) | 112 (53.3) |
| **Unknown** | 0 (0.0) | 2 (1.0) |
| **Age, Mean (±SD)** | 59.9 (±11.7) | 56.7 (±10.2) |
| **Fruit intake (grams/day), Mean (±SD)** | 294.9 (±210.0) | 405.0 (±262.9) |
| **Vegetable intake (grams/day), Mean (±SD)** | 140.9 (±108.1) | 230.1 (±164. 0) |
| **Red meat intake (grams/day), Mean (±SD)** | 28.9 (±25.2) | 22.9 (±22.2) |
| **Processed meat intake (grams/day), Mean (±SD)** | 6.5 (±18. 3) | 8.0 (±19.9) |

CI: 2.8, 10.2) (p-value for trend= 0.000). Consumption of processed meat was less than 10 grams per day and showed no association with GC and was dropped from the model. From the childhood factors, lack of access to tap water during childhood was significantly associated with about 3-fold higher odds of GC (OR=2.9, 95% CI: 1 3, 6.7) compared to those who had access to tap water. While the crude model showed a non-significant inverse association between the use of a refrigerator and the odds of GC (OR=0.7, 95% CI: 0.4, 1.2), this association disappeared in the adjusted model.

## Discussion:

In this study, a positive family history of GC, lack of access to tap water during childhood, low education level, coffee consumption, lower consumption of fruits and vegetables, and higher intake of red meat were significantly associated with a higher risk of GC. However, we observed no significant associations between H. pylori seropositivity, BMI, waterpipe smoking, cigarette smoking, drinking alcohol, and opium use and risk of GC.

Our study showed a strong association between a family history of GC and the risk of GC. This finding is in line with previous studies that focused on the role of the family history of GC and the risk of GC. Shin et al. showed a 3-fold increase in the risk of GC in patients with a positive family history of GC in South Korea [24]. In addition, a case-control study in the United States reported a strong association between the family history of any gastrointestinal cancer with both cardia and non-cardia GC [25]. This association is linked to either shared exposure to environmental factors or genetic susceptibility within families.

Even though we did not find a significant association between tobacco use and risk of GC, it has been estimated that smoking is responsible for approximately 18% of GC cases and 21% of GC-related deaths [26]. According to the results of a meta-analysis of cohort studies and pooled analyses of case-control studies, individuals with a history of cigarette smoking have a higher risk of GC, regardless of sex [27,28]. Moreover, the evidence from multiple studies, including large cohort studies and meta-analyses, indicates that opium use is associated with a significantly increased risk of gastric cancer [29,30]. However, we found no significant association between GC and waterpipe smoking, which is a common mode of tobacco use in the Eastern Mediterranean Region. This finding contradicts previous studies [31], which could be due to insufficient power in our study or residual confounding by cigarette and opium consumption. We found that those who drink coffee and have high intakes of fruits and vegetables had a lower risk of GC. Coffee drinking has been considered a cancer-protecting factor in several studies due to its high concentration of antioxidants.

**Table 2.** Odds ratios (ORs) and 95% confidence interval (CIs) of different socioeconomic and lifestyle factors and risk of gastric cancer based on a hospital-based case-control study in the Cancer Institute of Iran in 2010-2012

| Variable | N. Cases (%) N=210 | N. Controls (%) N=210 | OR (95% CI) | |
|---|---|---|---|---|
| | | | Crude | Adjusted[2] |
| **Family history of GC** | | | | |
| No | 174 (82.9) | 197 (93.8) | References | References |
| Yes | 36 (17.1) | 13 (6.2) | 3.5 (1.7, 6.9) | 4.1 (1.7, 9.6) |
| **Education** | | | | |
| Illiterate | 96 (45.7) | 38 (18.1) | References | References |
| Elementary (1-6 years) | 29 (13.8) | 27 (12.9) | 0.4 (0.2, 0.9) | 0.4 (0.2, 0.8) |
| Secondary (6-11 years) | 70 (33.3) | 107 (51.0) | 0.3 (0.2, 0.5) | 0.3 (0.2, 0.6) |
| College degree | 12 (5.7) | 27 (12.9) | 0.2 (0.1, 0.4) | 0.2 (0.1, 0.6) |
| Unknown | 3 (1.4) | 11 (5.2) | - | - |
| P-value for trend | - | - | 0.000 | 0.003 |
| **Body Mass Index** | | | | |
| <18.5 | 9 (4.3) | 8 (3.8) | 1.0 (0.4, 3.0) | 0.7 (0.2, 2.3) |
| 18.5-24.9 | 75 (35.7) | 75 (35.7) | References | References |
| 25-29.9 | 73 (34.8) | 53 (25.2) | 1.3 (0.8, 2.2) | 1.4 (0.8, 2.5) |
| >=30 | 39 (18.6) | 34 (19.2) | 1.1 (0.6, 1.9) | 1.9 (0.9, 3.9) |
| Unknown | 14 (6.7) | 40 (19.1) | - | - |
| P-value for trend | | | 0.9 | 0.1 |
| **Alcohol Drinking** | | | | |
| Never | 168 (80.0) | 171 (81.4) | References | References |
| Ever | 34 (16.2) | 35 (16.7) | 1.3 (0.8, 2.3) | - |
| Unknown | 8 (3.8) | 4 (1.9) | - | - |
| **Cigarette Smoking** | | | | |
| Never | 120 (57.1) | 122 (58.1) | References | References |
| Ever | 86 (41.0) | 78 (37.1) | 1.3 (0.9, 2.1) | - |
| Unknown | 4 (1.9) | 10 (4.8) | - | - |
| Waterpipe smoking | | | | |
| Never | 198 (94.3) | 202 (96.2) | References | References |
| Ever | 12 (5.7) | 12 (5.7) | 1.4 (0.5, 3.7) | - |
| **Opium Use** | | | | |
| Never | 157 (74.8) | 180 (85.7) | References | References |
| Ever | 32 (15.2) | 24 (11.4) | 1.9 (1.0, 3.5) | 1.3 (0.6, 2.7) |
| Unknown | 21 (10.0) | 6 (2.9) | - | - |
| **Coffee Drinking** | | | | |
| Never | 172 (81.9) | 126 (60.0) | References | References |
| Ever | 35 (16.7) | 84 (40.0) | 0.4 (0.2, 0.6) | 0.5 (0.3, 0.8) |
| Unknown | 3 (1.4) | 3 (1.4) | | |
| **Helicobacter pylori serostatus** | | | | |
| Negative | 56 (26.7) | 44 (21.0) | References | References |
| Positive | 100 (47.6) | 108 (51.4) | 0.7 (0.4, 1.1) | - |
| Unknown | 54 (25.7) | 58 (27.6) | - | - |

The multivariate model included residential place (Tehran/others), age categories (five categories), sex (male/female), education (four groups), family history of GC (yes/no), opium use (yes/no), coffee use(yes/no), BMI (four groups); tertiles of fruits, vegetables and red meat intakes.

However, the association between coffee intake and the risk of cancers, including GC, is controversial [32]. Both carcinogenic and anticancer effects have been assigned to caffeine in experimental studies [33,34]. However, a recent systematic review showed a null association and suggested that the observed association between coffee intake and GC is confounded by other factors, including dietary habits and smoking [32]. Usually, coffee drinkers tend to smoke more and follow irregular sleeping patterns [35]. In addition, coffee consumers are commonly in the high SES and tend to eat more red meat and processed food [36]. Although the inverse association between coffee consumption and GC risk was significant after adjusting for several confounders, including smoking, dietary habits, and SES, we cannot completely exclude the role of residual confounding. The results need to be replicated in other studies.

Our results on an inverse association between the intake of fruits and vegetables and the risk of GC support several studies conducted in other countries [37,38]. Citrus fruits have a higher concentration of antioxidants like carotenoids and vitamin C, which can protect against oxidative damage and H. pylori infection, thereby reducing the risk of GC [39,40]. On the other hand, non-citrus fruits like apples and berries are also rich in flavonoids that have similar activity to that of citrus fruits, making them protective factors for GC [41,42]. Additionally, fruits and vegetables are rich in fiber, which can act as a scavenger of nitrates, preventing the formation of carcinogenic N-nitroso compounds and other cancer-preventive agents [43]. Therefore, the findings on the protective effect of fruits and vegetables are consistent and plausible and should be highlighted in the cancer prevention campaign and implementation of public health policies.

A meta-analysis of 12 cohorts and 30 case-control studies has shown a significant association between red meat and the risk of GC [44]. Similarly, a pooled analysis of 22 studies in the StoP consortium revealed a significantly higher risk of GC among those who had a high intake of red and processed meat compared to low users [45]. Red and processed meat contains a high concentration of carcinogenic compounds such as heme iron and N-nitroso compounds[46,47]. Furthermore, processing by smoking and grilling of meats leads to the formation of more polycyclic aromatic hydrocarbons, heterocyclic amines, and other carcinogens that can contribute to the risk of GC [48,49]. Although processed meat was reported to be a risk factor for GC in previous studies, we could not show such an association because the intake of processed meat was lower than 10 grams per day in both the cases and controls.

Previous reports have suggested an inverse association between GC risk and higher SES, and our observations support this association [50,51]. We found a significantly inverse association between education level and risk of GC development. Although the use of refrigerators during childhood showed an inverse association in the crude model, we did not observe this association in the adjusted model. The lack of access to tap water was strongly associated with risk of GC. The result was in line with the bounded number of studies that have investigated this association, including a case-control study from Golestan province in the northeastern part of Iran[52]. Similar results were also reported in other countries, such as Germany [53]. Italy, and Turkey[54]. It was hypothesized that the carcinogenic process of GC starts during the childhood and teenage periods. Previous studies showed that the acquisition of H. pylori infection occurs at the age of 10 or younger. This infection usually persists during the entire life [55]. Only 28% of the control group reported access to the tap water during childhood, suggesting that 40-50 years ago, most people relied on water from wells, springs, and rivers. These sources may have contained high levels of nitrosamines and, as a proxy for poor sanitation, may increase the chance of H. pylori infection, a known risk factor for GC. Although we found no reports on the coverage of access to tap water in the past, according to the World Bank, almost 100% of the Iranian population had access to tap water and electricity in 2020, indicating that the SES of Iranian population has improved and the incidence rate of GC will decrease in the future. [56].

In the United States, GC was once the leading cause of cancer death in 1930, but with improvements in SES over time, its incidence rate has significantly decreased and now ranks 14$^{th}$ [57]. Similar trends have been observed in other Western countries. In 2017, more than 122 million GC cases occurred worldwide, and about 865,000 patients died due to this cancer, contributing to 191 million. Globally, there were over 356,000 new GC diagnoses and approximately 96,000 deaths between 1990 and 2017, but the ASR of GC has decreased by 38.2% during the same period [58]. This reduction has been linked to a decline in H. pylori infection prevalence, improvements in food storage and hygiene, and tobacco control efforts [59]. Since access to clean water and the SES of the Iranian population have been improved [60]We expect to observe a low risk of GC in the future. However, there would be a disparity in the risk of cancer, and the population with a low SES will still be at a higher risk of GC among the Iranian population. Disparities within countries have been reported in multiple studies. For instance, Alaskan native people had a higher incidence rate, poorer survival, and were diagnosed at a younger age compared to non-Hispanic populations [61]. It was also shown a 6-fold difference in the mortality of GC in different provinces of Iran [4]. These findings indicate that improving the SES or implementing targeted cancer prevention measures among low SES groups can reduce the incidence of GC and other SES-related outcomes.

There was no significant association between GC and H. pylori, alcohol consumption, waterpipe smoking, opium consumption, and cigarette smoking in the present study. The association between H. pylori infection and GC has been shown in a large number of epidemiological and clinical studies, and H. pylori is considered a causal factor for GC [9,16]. Although the association between H. pylori and GC risk is established, similar to this study, several studies failed to find an association, which may be attributed to the time of sampling and method of H. pylori seropositivity assessment. Because anti H. pylori IgG may reduce during the gastric atrophy before the cancer development and tumor growth in the stomach [14], Cohort studies or measuring Cag A antibody, which remains in the serum even after tumor development and shows the past exposure is needed to verify the role of H. pylori in the occurrence of GC.

The lack of association between GC and alcohol in this study could be due to the low prevalence of alcohol use in Iran, where alcohol consumption is illegal, and relatively few of the Iranian population are regular users, in particular among old age people who were recruited in this study [21]. In addition, alcohol consumption is a risk factor for cardiac cancer, which is less common than non-cardiac cancer in Iran. This finding was consistent with observations from a large-scale prospective cohort study in the Netherlands [53]. Although there are some inconsistencies about the causative role of alcohol in the pathogenesis of GC among different epidemiological studies, this role is merely suggested for heavy amounts (≥60 g/d) or frequent daily usage (>4 drinks/d) of alcohol [54].

A limitation of this study is its hospital-based design, which is inferior to the population-based approach and may lead to bias due to the selection of hospital controls. Because there is no regular referral system for cancer patients, they are referred to the hospital from everywhere, including different parts of Tehran province and other provinces [22]. We decreased the risk of bias by matching the cases and controls by age, sex, and referral pattern. To avoid bias and overmatching due to the selection of friends and relatives, we selected the friends [55, 56] and relatives of patients who were admitted for non-cancer-related diseases. We matched the cases and controls based on age, sex, and residential place, and the final data showed that the cases were properly matched with the controls. Another limitation of this study was that we did not have sufficient power to study the risk factors by sex and GC sub-sites (Cardia /Non-cardia). Larger studies are needed to perform the above sub-analyses.

In conclusion, the risk of GC in Iran is significantly influenced by various factors, including dietary and lifestyle habits, as well as SES during both childhood and adulthood. Furthermore, individuals with a history of GC display a higher susceptibility to this form of cancer in Iran. While it is anticipated that an improvement in SES conditions will lead to a reduction in the incidence of GC, the disparity in risk may persist among low SES groups and regions in Iran. Further research, with a larger sample size, is needed to replicate these results and to investigate the risk factors associated with cardia and non-cardia GC.

**Table 3.** Odds ratios (ORs) and 95% confidence interval (CIs) of dietary factors for gastric cancer based on a hospital-based case-control study in the Cancer Institute of Iran in 2010-2012

| Variable | N. Cases (%) N=210 | N. Controls (%) N=210 | OR (95% CI) | |
|---|---|---|---|---|
| | | | Crude | Adjusted* |
| **Fruits (gr/day)** | | | | |
| First tertile | 89 (42.4) | 51 (24.3) | Reference | Reference |
| Second tertile | 76 (36.2) | 82 (39.0) | 0.5 (0.3, 0.8) | 1.2 (0.6, 2.3) |
| Third tertile | 45 (21.4) | 77 (36.7) | 0.4 (0.2, 0.6) | 0.6 (0.3, 1.3) |
| P-value for trend | - | - | 0.000 | 0.2 |
| **Vegetables (gr/day)** | | | | |
| First tertile | 93 (44.3) | 47 (22.4) | Reference | Reference |
| Second tertile | 80 (38.1) | 69 (32.9) | 0.6 (0.4, 1.0) | 0.5 (0.3, 1.0) |
| Third tertile | 37 (17.6) | 94 (44.8) | 0.2 (0.1, 0.4) | 0.3 (0.1, 0.6) |
| P-value for trend | - | - | 0.000 | 0.001 |
| **Red meat (gr/day)** | | | | |
| First tertile | 54 (25.7) | 86 (41.0) | Reference | Reference |
| Second tertile | 71 (33.8) | 69 (32.9) | 1.8 (1.1. 3.0) | 2.3 (1.2, 4.4) |
| Third tertile | 85 (40.5) | 55 (26.2) | 2.8 (1.7, 4.7) | 5.3 (2.8, 10.2) |
| P-value for trend | - | - | 0.000 | 0.000 |
| **Processed meat(gr/day)** | | | | |
| **First tertile** | **107 (51.0)** | **95 (42.2)** | **Reference** | **Reference** |
| Second tertile | 42 (20.0) | 37 (17.6) | 1.1 (0.6, 1.8) | - |
| Third tertile | 61 (29.0) | 78 (37.1) | 0.8 (0.5, 1.4) | - |
| P-value for trend | - | - | 0.5 | - |

The multivariate model included dietary factors and residential place (Tehran/others), age categories (5 categories), sex(male/female), residential place (Tehran/Others), education (4 categories), BMI (four groups), family history of GC (yes/no), opium use (yes/no), coffee use (yes/no), tertiles of fruits, vegetables and red meat intakes.

**Table 4.** Odds ratios (OR) and 95% confidence intervals (CIs) of childhood lifestyle factors and risk of gastric cancer based on a hospital-based case-control study in the Cancer Institute of Iran in 2010-2012

| Variable | N. Cases (%) N=210 | N. Controls (%) N=210 | OR (95% CI) | |
|---|---|---|---|---|
| | | | Crude | Adjusted* |
| **Refrigerator use during childhood** | | | | |
| No | 160 (76.2) | 133 (63.3) | Reference | Reference |
| Yes | 47 (22.4) | 67 (31.9) | 0.7 (0.4, 1.2) | 1.8 (0.9, 3.9) |
| Unknown | 3 (1.4) | 10 (4.8) | - | - |
| **Access to tap water during childhood** | | | | |
| Yes | 21 (10.0) | 59 (28.1) | Reference | Reference |
| No | 180 (85.7) | 141 (67.1) | 3.5 (1.9, 6.3) | 2.9 (1.3, 6.7) |
| Unknown | 9 (4.3) | 10 (4.8) | - | - |
| **Father job** | | | | |
| Clerk | 32 (15.2) | 55 (15.2) | Reference | Reference |
| Self-employed | 18 (8.6) | 23 (11.0) | 1.3 (0.6, 2.8) | 2.1 (0.8, 4.6) |
| Labor | 29 (13.8) | 33 (15.7) | 1.3 (0.7, 2.7) | 1.9 (1.0, 4.5) |
| Farmer | 131 (62.4) | 99 (47.1) | 2.0 (1.1, 3.4) | 1.7 (0.9, 3ö3) |

*The multivariate model included residential place (Tehran/others), age (five categories), sex (male/female), education (four groups), family history of GC (yes/no), refrigerator use during childhood (yes/no), father job (four groups), access to tap water during childhood (yes, no), ever cigarette smoking (yes/no), opium use (yes/no), coffee use (yes/no), BMI (four groups), tertiles of fruits, vegetables and red meat intakes.

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