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The role of diet and other environmental factors in the causation of gastric cancer in Iran—A population based study

Farhad Pourfarzi^{1*}, Anna Whelan², John Kaldor² and Reza Malekzadeh³

¹*Division of Community Medicine, Ardabil University of Medical Science, Ardabil, Iran*

²*School of Public Health and Community Medicine, University of New South Wales, Sydney, Australia*

³*Digestive Disease Research Center, Shariati Hospital, Tehran University of Medical Science, Tehran, Iran*

Despite a declining trend in the incidence of gastric cancer (GC), it is still a major global public health concern of the 21st century. The rates of GC reported from Ardabil Province, Iran, are among the highest in the world. To investigate risk factors for GC in Ardabil, we undertook a population-based case-control study. The study aimed to recruit all Ardabil residents newly diagnosed with GC in the time period of 2004–2005, and 2 controls per case. Participants were interviewed using a structured questionnaire. Ten milliliters of blood was collected for blood grouping and investigating the presence of IgG antibodies against *Helicobacter pylori*. During the study period, 217 people with GC and 394 controls were recruited. In multivariate analysis, diet and *Helicobacter pylori* infection (OR = 2.41; 95% CI: 1.35–4.32) were found to be the factors that were most strongly related to GC. High intake of Allium vegetables (OR = 0.35) and fruit, especially citrus fruit (OR = 0.31) and consumption of fresh fish (OR = 0.37) were significantly protective. On the other hand, consumption of red meat (OR = 3.40) and dairy products (OR = 2.28) were positively associated with the risk of GC. People who had a preference for higher salt intake (OR = 3.10) and drinking strong and hot tea (OR = 2.64 and 2.85, respectively) were at higher risk. In conclusion, *Helicobacter pylori* infection as measured by serum IgG as well as the consumption of red meat and dairy products increases the risk of GC in Ardabil, while the intake of fresh fruit and fresh fish decrease the risk.

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Key words: gastric cancer; *Helicobacter pylori*; lifestyle; occupation; diet

Despite declining incidence and mortality, gastric cancer remains among the most common forms of malignant disease worldwide. With a million new cases and 750,000 deaths estimated to occur annually, gastric cancer is the fourth most frequently occurring malignancy after lung and breast cancer¹ and the second cause of cancer-related mortality in the world.

There is considerable variation in the incidence (ASR) among different geographic regions of the world, with ~100-fold difference between the highest and lowest rates. The highest incidence has been reported from some eastern Asian countries such as Korea, Japan and China, while the rate is very low in some African countries (Cameroon, Mozambique) with an ASR incidence of less than 1 per 100,000 people.²

In Iran, it is the most frequently diagnosed form of cancer but there is wide intra-country variation. Ardabil province in the North West has been reported to have the highest incidence rate in the country with age standardized incidence rates of 49.1 and 25.4 per 100,000 in men and women, respectively.³ These rates are ~7 times the rate reported from the Southern Iran⁴ and twice the national rate.⁵ A major proportion (36%) of GC in Ardabil is the gastric cardia cancer and the incidence of this type of GC in Ardabil region (North-West of Iran) is the highest recorded anywhere in the world.⁶ GC constituted approximately one-third of all cancer related deaths each year in Ardabil,⁷ compared to 20% for the entire country,⁸ and the 5 year survival is less than 5%.⁹

A number of published studies have investigated the causes of gastric cancer.^{10–14} Family history has been shown to be associated with its occurrence, suggesting a genetic basis^{15–21} but some classic immigrant studies^{22,23} showed that the incidence of the disease could change quickly across generation, implicating environ-

mental factors, and analytical studies have shown strong links with diet,^{10,11} *H. pylori* infection^{24–29} and smoking.^{30–32} Despite importance of gastric cancer in Iran, no risk factor study has ever been conducted there. We undertook a case-control study to elucidate potential cause in the part of Iran that has the highest incidence.

Material and methods

Definition and selection of cases

Cases were identified via the Ardabil Cancer Registry, which was established in 1999 and receives case reports from all doctors and pathology services making a cancer diagnosis apart from non-melanoma skin cancer in Ardabil. Cases were eligible if they were in people who had been Ardabil residents for at least 5 years before diagnosis, were aged more than 18 years, had not had previous gastric surgery and had a positive histopathologic report of gastric carcinoma. In addition to the cases routinely reported to the Cancer Registry, active surveillance for gastric cancer was conducted by the cancer registry through all hospitals and clinics, particularly those of 3 gastroenterologists, to maximise completeness of case ascertainment. All reported cases were classified according to the International Classification of Disease for Oncology (ICD-O: 16.0–16.9).

Definition and selection of controls

Two controls were sought for each case, frequency matched to the case group by 5-year age groups and gender. Controls had to satisfy the same residency and age criteria as cases and were randomly selected from the community using a computer-based sampling frame that had been created for the annual household survey by the health department. This database was used to select random households, which were then visited by health professionals seeking eligible individuals. If such a person was not available or did not satisfy the inclusion criteria, the immediate neighbor to the right hand side was visited. The interviews took place mostly in subjects' home.

A structured questionnaire administered to cases and controls sought information on demographic characteristics, socioeconomic status, smoking history, beverage consumption, medical history, occupation and eating habits. Each subject's main job was defined using the International Standard Industrial Classification (ISIC) grouping scheme which is compatible to the classification which had been used in the Iranian National Census.³³ For the purposes of analysis, jobs were categorised into 5 groups; agriculture, manufacturing, construction, wholesale and retail trade and other professional activities, made up of financial services, real estate, public administration, education and private households with employed persons. In the dietary section all odds ratios were com-

*Correspondence to: Division of Community Medicine, Faculty of Medicine, Ardabil University of Medical Sciences, P.O. Box: 56135-665, Ardabil, Iran. Fax: +98-451-5510057. E-mail: f.pourfarzi@arums.ac.ir

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