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Significance of Chronic Atrophic Gastritis in First-Degree Relatives of Patients With Gastric Cancer

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Gastric cancer is the fourth most common cancer worldwide with approximately 934,000 new cases in 2002. Also, an estimated over 700,000 annual death make it the second most common cause of death from cancer (1). In Iran, gastric cancer is the first and third most common cause of cancer in males and females, respectively and its overall incidence is above the world average (2). Although the worldwide incidence of the gastric cancer has decreased rapidly over the recent few decades, its incidence in Iran does not show any decrease in the same time period (2-4). Ardabil in northwest of Iran is one of the areas with highest incidence of the gastric cancer, with ASR of 49.1 and 25.4 for males and females, respectively (5).

Chronic atrophic gastritis (CAG), as an intermediate step of carcinogenesis cascade of gastric cancer has showed a strong relationship with gastric adenocarcinoma, particularly intestinal subtype (6). Chronic atrophic gastritis is defined as the loss of appropriate mucosal glandular tissue and/or the loss of appropriate mucosal glandular tissue for the biopsy site according to the updated classification and grading of gastritis; the updated Sydney system. There is a high prevalence of CAG in; i.e. Japan with histologic detection rate of 53%, Estonia, in up to 64% of studied population, Finland, between 27% and 44%, and in Columbia with 45% in comparable age groups (7-10). On the other side, lower prevalence of CAG (21%) in Tehran, which is an intermediate risk area for gastric cancer, is not an unexpected finding (11). Results of investigations using histologic methods for diagnosis of CAG in low-risk populations revealed the similar lower prevalence of this precancerous change (e.g. 28% in Sweden and 22% in Australia) (12, 13).

Helicobacter pylori infection induces superficial non-atrophic gastritis which progresses to CAG with loss of acid secretion and then to dysplasia and cancer. A variety of bacterial, host and environmental factors are known to contribute to the progress through these different precancerous stages (14). Traditionally, relationship between CAG and gastric cancer has been defined for noncardia cancer, but recent studies showed that even adenocarcinomas located at the cardia region may demonstrate a relationship with CAG, particularly those with the least relationship with gastroesophageal reflux disease (15, 16). In fact, simplifying the relationship between *H. pylori*, CAG and gastric cancer may result in the ignorance of other intermediate risk factors. Diversity in exposure to dietary factors can partly explain different rates of transition of inflammatory lesions to precancerous and finally to cancer in gastric carcinogenesis (17). It has been shown that a diet high in salt and low in fresh fruit may promote the progression of early mucosal changes to CAG (18-20). Polymorphism of pro inflammatory gene also has been suggested to be responsible for different response to *H. pylori* infection and progression to CAG and gastric cancer in some populations (21, 22). Presence of different antigenic strains of *H. pylori* also is another source of variation of progression rate of inflammatory step to precancerous lesions in different regions (23).

Family history of gastric cancer increases the risk of its development in the other family members and this association is clearer in the first-degree relatives (24). This will include both intestinal and diffuse histological subtypes with different carcinogenic pathways. The increased risk in the former group has been linked to *H. pylori* induced inflammation and subsequent CAG (25) and the latter group shows strong genetic predisposition (26).

Despite the large number of studies indicating a strong relationship between the CAG and gastric cancer, most of these studies have been performed in populations with different risk of noncardia cancer and current knowledge regarding this relationship in the first-degree relatives of gastric cancer is lacking. Moreover, almost all of

these studies have focused on the relationship in populations who are at risk for noncardia cancer and role of CAG in development of gastric cancer in the first-relatives of patients in high-risk area for cardia cancer is unclear. We should note that in further investigations, awareness of histological subtype of cancer in index cases, data on dietary and life style factors and finally determinants of host and *H. pylori* genetic variations may lead to more clear understanding of pathogenesis of familial tendency to gastric cancer.

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Authors' Contributions

Raika Jamali designed and wrote the manuscript.

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