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RESEARCH ARTICLE

# Modeling of Influential Predictors of Gastric Cancer Incidence Rates in Golestan Province, North Iran

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## Abstract

**Golestan province has a reputation for relatively high incidence rates of gastric cancer in Iran. Along with dietary, lifestyle and environmental influential factors, soil selenium and high levels of pesticide used may exert influence in this region. The present study was designed for modeling the influential predictors on incidence of gastric cancer in Golestan. All registered cases of gastric cancer from March 2009 to March 2010 (49 females and 107 males) were investigated. Data were gathered by both check list and researcher made questionnaire (demographic, clinical and lifestyle characteristics) and analysed using logistic regression. Mean (±SD) age at diagnosis was 62.9±13.8 years. CIR and ASR of gastric cancer showed 9.16 and 13.9 per 100,000 people, respectively. Based on univariate logistic regression, a history of smoking (OR= 2.076), unwashed hands after defecation (OR= 2.612), history of cancer in relatives (OR= 2.473), history of gastric cancer in first-degree relatives (OR= 2.278), numbers of gastric cancers in first-degree relatives (OR= 2.078), history of X-ray and dye exposure (OR= 2.395), history of CT scan encounter (OR= 2.915), improper food habits (OR= 3.320), specific eating behavior (OR= 0.740), consumption of probable high risk foods (OR= 2.942), charred flesh (OR= 1.945), and animal fat (OR= 2.716) were confirmed as a risk factors. Changes in lifestyle may be expected to increase gastric cancer incidence dramatically in the near future. Therefore, appropriate educational interventions should be designed and implemented by competent authorities**

**Keywords:** Incidence rate - predictors - logistic regression gastric cancer - Golestan , Iran

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## Introduction

Gastric cancer is the second leading causes of death in worldwide (GLOBOCAN 2008), The highest mortality rate is 28.1 and 13.0 per 100,000 in men and women, respectively (Stomach Cancer Incidence and Mortality Worldwide in 2008, 2011). The lowest mortality rate has been reported 2.8 per 100,000 in men and 1.5 per 100,000 in northern American (Stomach Cancer Incidence and Mortality Worldwide in 2008, 2011). Gastric cancer is the most common cancer in men and the third cancer in women in Iran. Golestan province has the highest incidence rate of gastric cancer in Iran (Mousavi et al., 2009 ; Malekzadeh et al., 2009). This cancer was presented over time but it increased after development of urbanization, may be as a result of changing dietary pattern, lifestyle and medical technology. technology, promoting health knowledge, improvement of hygiene, better food storage and effective elimination of helicobacter pylori have decreased the trend of gastric cancer incidence in the recent decades (Sonnenberg, 2010), in contrary, dietary, socioeconomic- and environmental factors like nitrite and nitrate, Ionizing radiation, smoking and alcohol consumption have increased gastric cancer occurrences (Kelley and Duggan, 2003; Compare et al., 2010; Saghier et al., 2013). the cancer still is the main cause of cancer death in the world (Dikshit et al., 2011).

Although some inheritance factors might be unchangeable but some dietary, lifestyle and environmental factors are modifiable. The modifiable factors have both stimulating and preventing effects on occurrence of gastric cancer. While some factors such as smoking, alcohol, food and diet, predisposing gastrointestinal disease, environmental factors increase the occurrence of the cancer (Anand et al., 2008), other factors such as consumption of vegetables, fresh fruits (Giordano and Cito, 2012) and physical activity may prevent the occurrence of the cancer (Wen and Song, 2010; Leitzmann et al., 2009). It was known that lifestyle factors play an important role on cancer occurrences. it was obvious that poor dietary pattern, alcohol, smoking, lack of activity, unhealthy behaviors can increase potential gastric cancer occurrences (Thomas and Davies, 2007), which responsible for maintaining the burden of gastric cancer (Lee and Derakhshan, 2013), so assessment of these factors is necessary. Golestan province in the northern

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of Iran was reputed for high risk region of gastric cancer. In different geographical areas of the region, variation of gastric cancer frequency was possibly due to various potential environmental risk factors (Malekzadeh et al., 2009).

Along with dietary, lifestyle and environmental influential factors, soil selenium level (Semnani et al., 2010), high levels of pesticide used and exposure in Golestan province may have impact on high cancer incidence in this region (Heidari, 2003; Mohebbi et al., 2012). Regarding difference in gastric cancer incidence rate and its related factors in various populations, this study was designed for modeling the influential predictors on gastric cancer incidence in Golestan.

## Materials and Methods

Cases of gastric cancer are retrieved from academic and private diagnostic centers, public and professional clinics, all hospitals and health centers in the Golestan province from March 2009 to March 2010 (49 females and 107 males). one control from family of the cases and another control from the neighbors of cases were selected for each cases (two controls for each case). Cases and controls were matched (caliper matching) for age, gender and ethnicity. All data were collected by trained personnel through interview with patients and control groups at their homes. Data was collected by using both checklist and researcher made questionnaire which contained demographic, clinical information and lifestyle characteristics (personal hygiene, diet and physical activity). Validity of the questionnaire was confirmed by expert group (Gastroenterologist, Oncologist, Dietitian, Biochemist, Epidemiologist, Biostatistician and experts in the field of Social Welfare, Public Health and Health Education) and based on pilot study, reliability was assessed by Cronbach's Alpha (0.89) and Kuder-Richardson (0.82).

Logistic regression model was used to find Oddes Ratio between cases and controls. All variables were intruded in univariate model. Those variables lower than 0.1 significant levels, selected for multiple logistic regression model.

Before study, participants have been asked to fill in the consent form.

## Results

*Cancer incidence*

Mean (±SD) age at diagnosis in gastric cancer patients were 62.85±13.76 years. Crude incidence rate (CIR) and age-standardized incidence rate (ASR) of gastric cancer

**Table 1. Mean (±SD) Age, Incidence Rate, ASR and Relative Risk of the Patient**

| | | Frequency | Age (Mean±SD) | Incidence Rate (Per 100.000) | ASR | Relative Risk (95% Confidence interval) | P value |
|---|---|---|---|---|---|---|---|
| Gender | Female | 49 | 60.73±15.99 | 5.8 | 8.6 | 1 | - |
| | Male | 107 | 63.82± 12.57 | 12.47 | 19.35 | 2.15 (1.53-3.02) | 0 |
| Residence | Rural | 72 | 62.04±13.85 | 8.43 | 14.74 | 1 | - |
| | Urban | 84 | 63.55±13.73 | 9.89 | 13.14 | 1.17 (0.86-1.61) | 0.32 |
| | Overall | 156 | 62.85±13.76 | 9.16 | 13.93 | - | - |

**Table 2. Modeling of the Influential Predictors on Gastric Cancer Incidence using the Univariate Logistic Regression Model**

| Lifestyle characteristics | | Crude Odds Ratio (95% CI) | p value |
|---|---|---|---|
| High-risk behaviors | History of smoking | 2.076 (1.146-3.759) | 0.016 |
| | Alcohol | 1.937 (0.476-7.893) | 0.356 |
| | Nass | 0.951 (0.280-3.227) | 0.936 |
| Unhealthy behaviors | Unwashed hands after defecation | 2.612 (1.433-4.761) | 0.002 |
| | Unwashed hands after working with toxic materials | 1.509 (0.864-2.633) | 0.148 |
| | Unwashed hands before meal times | 1.456 (0.926-2.288) | 0.104 |
| | Unwashed hands after daily work | 1.341 (0.831-2.165) | 0.23 |
| Familial History | History of cancer in relatives | 2.473 (1.478-4.138) | 0.001 |
| | History of gastric cancer in first-degree relatives | 2.278 (1.134-4.579) | 0.021 |
| | Number of gastric cancer in first-degree relatives | 2.078 (1.108-3.896) | 0.023 |
| | Other cancers (except for gastrointestinal cancer) in first-degree relatives | 2.177 (0.870-5.447) | 0.096 |
| Environmental factor | History of X-ray dye exposure | 2.395 (1.456-3.940) | 0.001 |
| | History of CT scan encounter | 2.915 (1.699-5.001) | 0 |
| | Both | 4.243 (2.266-7.943) | 0 |
| Food and Nutritional Culture | Improper food habits | 3.320 (1.304-8.451) | 0.012 |
| | Specific eating behaviors | 0.740 (0.555-0.988) | 0.041 |
| | Probable high risk foods | 2.942 (1.013-1.802) | 0.001 |
| | Dietary pattern Relatively poor | 2.092 (1.198-3.654) | 0.009 |
| | Poor | 3.165 (1.257-7.965) | 0.014 |
| | Charred flesh | 1.945 (1.158-3.268) | 0.012 |
| | Consumption of animal fat | 2.716 (1.298-5.684) | 0.008 |
| Predisposing factors | Achalasia | 20.122 (6.751-59.971) | 0 |
| | Helicobacter pylori | 5.310 (1.087-25.950) | 0.039 |
| | Polyp | 3.200 (0.813-12.598) | 0.096 |
| | Gastric ulcer | 3.920 (2.047-7.509) | 0 |
| | Other chronic digestive diseases | 1.304 (0.583-2.914) | 0.518 |
| Physical activity | Low mobility and lack of appropriate activities | 1.865 (0.978 - 3.559) | 0.059 |

**Table 3. Modeling of the Influential Predictors on Gastric Cancer Incidence using the Multivariate Logistic Regression Model**

| Lifestyle characteristics | | Adjusted Odds Ratio (95% CI) | P-Value |
|---|---|---|---|
| High-risk behaviors | History of smoking | 2.076 (1.146-3.759) | 0.016 |
| Unhealthy behaviors | Unwashed hands after defecation | 2.612 (1.433-4.761) | 0.002 |
| Familial History | | | |
| History of gastric cancer in first-degree relatives | | 2.464 (1.215-4.994) | 0.012 |
| Other cancers (except for gastrointestinal cancer) in first-degree relatives | | 2.349 (0.925-5.965) | 0.072 |
| Other cancers (except for gastrointestinal cancer) in second-degree relatives | | 4.386 (1.146-16.797) | 0.031 |
| Environmental factor | History of X-ray dye exposure | 1.561 (0.853-2.858) | 0.148 |
| | History of CT scan encounter | 2.322 (1.212-4.447) | 0.011 |
| Food and Nutritional Culture | Charred flesh | 1.651 (0.994-2.888) | 0.079 |
| | Irregular lunch-time | 3.962 (0.961-16.329) | 0.057 |
| Predisposing factors | Achalasia | 76.970 (28.357-208.921) | 0 |
| | Helicobacter pylori | 18.584 (1.633-211.520) | 0.019 |
| | Gastric ulcer | 2.711 (1.154-6.366) | 0.022 |
| Physical activity | Low mobility and lack of appropriate activities | 4.787 (1.349-16.995) | 0.015 |

showed 9.16 and 13.93 per 100,000 people, respectively. Relative risk of gastric cancer in rural population comparing with urban inhabitants was 1.173, and male to female ratio was 2.151 (Table 1).

*Influential predictors on cancer incidence*

All influential factors on gastric cancer were identified and based on univariate logistic regression model were confirmed as risk factors of cancer incidence. In sub category of high-risk behaviors, unhealthy behaviors, familial History, environmental factors, food and nutritional culture, predisposing factors and physical activity were seen statistically association with gastric cancer incidence (Table 2).

Statistical significant risk factors were entered into the multiple conditional logistic regression models. Sub categories of high-risk behaviors [history of smoking (OR=2.076)], unhealthy behaviors [unwashed hands after defecation (OR=2.612)], familial history [history of gastric cancer in first-degree relatives (OR=2.464), other cancers in second-degree relatives (OR=4.386)], environmental factors [history of CT scan encounter (OR=2.322)], predisposing factors [achalasia (OR= 76.970), Helicobacter pylori (OR=18.584), gastric ulcer (OR=2.711)] and physical activity [low mobility and lack of appropriate activities (OR=4.787)] remains in the final model (Table 3).

## Discussion

The crude incidence rate and ASR, for men were 12.47 and 19.35, for women 5.80 and 8.60, in total 9.16 and 13.93 per 100,000 people in this region, respectively, that has been declined compared with previous years (Semnani et al., 2010), but was higher than average in Iran (Mousavi et al., 2009) and lower than average in the world, less developed areas, eastern Asia and central and eastern Europe (Jemal et al., 2011).

Previous studies in Golestan and Iran showed, declining incidence of gastric cancer during recent years. High incidence of gastric cancer reported in previous studies might be influenced by diet culture (regimen ), personal hygiene, lack of essential substructure Facilities for healthy lifestyle (like access to tap water and electricity) in crowded rural areas and little knowledge of peoples about these predictors.

Mean (±SD) age of gastric cancer patients was 62.85±13.76 years which was lower than Tehran (68.5 ±12.9) (Aghaei et al., 2013), USA (70) (American cancer society, 2013) and Japan (65.07±11.54) (Yu et al., 2010), and higher than South West Nigeria (53.5) (Komolafe et al., 2008) and China (57.20±11.15) (Yu et al., 2010).

In subcategory of high-risk behaviors, history of smoking was identified as a risk factor for gastric cancer which is consistent with other studies (Trédaniel et al., 1997; gonz´alez et al., 2003; Moy, 2010). Alcohol consumption had not statistically significant association with gastric cancer. Different findings were found in other studies: one cohort study results showed wine and vodka consumption was not associated with gastric cancer risk (Everatt et al., 2011), another study mentioned light drinking had a protective effect on gastric cancer compared to nondrinking and heavy drinking (kim et al., 2002), though some studies reported alcohol consumption as significant risk factors (Moy et al., 2010; Duell et al, 2011; Jarl et al., 2013). Our study population reported low frequency and quantity of alcohol consumption. It seems that the collected data by interviewing may not be very accurate that is because of alcohol consumption forbidden law in Iran. Maybe the number of positive reports of alcohol consumption is underestimation of real situation. This subject is seen in both case and control groups.

In sub category of unhealthy behaviors influential predictors, inappropriate hand washing after defecation was identified as a risk factor for gastric cancer. We could not find any study which mentioned or surveyed this subject. It seems that individual performance in field of personal health behaviors was not in acceptable level which may be due to insufficient and unpractical health education program.

In addition inappropriate hand washing after working with toxic materials, before meal times and after daily work was not confirmed as a risk in regression model. An appropriate hand washing was considered as an important personal hygiene especially after defecation. Some people think that washing hands with water only,

is corrected and eat foods with apparently clean hands. In last decades of Iranian culture, eating with hands was very commonplace. We notice that in some cases purity of washing water was on doubt. Although hand washing with water is good but it is insufficient for elimination of pollutant microorganism after defecation or toxic materials. By attention to frequent time of defecation and improper hands washing technique, we can expect emerge of disease related to pollutant microorganism such as gastritis, gastric ulcer or gastrointestinal cancer related to H.pylori infection (Lim et al., 2013).

In sub category of family history, gastric cancer history in first-degree relatives was confirmed as a risk factor that is consistent with other studies (Zanghieri et al., 1990; La Vecchia et al., 1992; Foschi et al., 2008; Shin et al., 2010).

Another study showed that there are environmental factors to reinforce the aggregation of gastric cancer in families (Shinmura et al., 1999). Also, other cancers (except for gastrointestinal cancer) in first and second-degree relatives, was identified as a risk factor which was consistent with other studies (Gong et al., 2012) but is in contrast with Safaee findings (Safaee et al., 2011).

In sub category of environmental factors, findings revealed history of CT scan encounter as a risk factor for gastric cancer which was consistent with one study (Dong et al., 2012). we found few studies in gastric cancer and CT scan exposure and some studies magnified the impact of diagnostic X- ray and increasing risk of cancer occurrence (De González and Darby, 2004;Linet et al., 2012). It seems that in the last decades, using of modern technology for detecting diseases was acceptable, but there was no attention to side effects of these medical detecting technologies such as CT scan and now-a-days in Iran we observe high usage of this diagnostic X-rays for simple diseases without thinking about future consequences.

In food and nutritional culture subcategory, our findings revealed improper food habits had impact on gastric cancer incidence (Shimada, 1986; Yi et al., 1998; Pakseresht et al., 2011; Yassıbaş et al., 2012).

Along with other studies, results showed that specific eating behaviors (effective food chewing, eating slowly (speed of eating)), were identified as a preventive factor (Gao et al., 1999; Sierpinska et al., 2007; Sun et al., 2013).

Some factors not only by physical aspects but also by psychological effects had synergic effects on cancer occurrence. Effective food chewing is important factor in life span; so ineffective chewing and too fast velocity of eating especially when are associated with stress and horrible situations, possibly have negative impact on gastric function.

Probable high risk foods (salted fish, kipper, salted meat, kaleh pache (head and hoof soup)) was confirmed as a risk factor for gastric cancer incidence which is consistent with some studies (Rao et al., 2002; Kim et al., 2002; De Stefani et al., 2004; Strumylaitė et al., 2006). Although frequency, portion size and type of these foods were very important for interpreting of risk factors role, but many studies showed the potential side effects of permanent usage of this kind of foods.

Alike with some of studies, results showed that poor dietary pattern was associated with increased risk of gastric cancer (Chen et al., 2002; Campbell et al., 2008). one study reported positive association between gastric cancer risk and "the animal products" dietary patterns (Bertuccio et al., 2009). another study reported that the risk of gastric cancer was higher with dietary pattern II (low consumption of fruit, salads, vegetables, dairy products, fish and meat) compared with dietary pattern I (high consumption of fruits and dairy products, and low consumption of alcoholic beverages (Bastos et al., 2010). Poor dietary pattern include selection of animal product, consumption of high dense calorie foods, traditional style of cooking foods in line with unhealthy dietary habits maybe has a synergic effect with heredity and environmental factors for gastric cancer occurrences.

Irregular lunch-time -has also impact on cancer incidence which is consistent with other studies (Yi et al., 1998; Gao et al., 1999; Cai et al., 2003; Wu et al., 2013). but in Sun`s study there was no significant relationship between irregular lunch-time and risk of gastric cardia cancer (Sun et al., 2013). It seems that irregular meal time leads to gastritis or gastro duodenal ulcers (Lim et al., 2013), if these predisposing factors presented for long time with no treatments, we could expect gastric cancer occurrence.

Consumption of animal fat was confirmed as a risk factor but in findings of Jędrychowski (Jędrychowski et al., 2001) and Konstansa (Konstansa et al., 2009), there was no significant relationship between animal fat and risk of gastric cancer .

In addition, consumption of oil was confirmed as a preventive factor for cancer occurrence. Various reports were seen in other studies, one of them mentioned that frequent use of the same cooking oil has impact on cancer incidence (Ngoan et al., 2002) and Wang mentioned that the consumption of oils was not clearly associated with risk (Wang et al., 2012). When we talk about consumption of animal fat or cooking oil, it is difficult to determine unique cut off point for measuring the number of reheating oil as a risk factor.

Based on results of this study, the number of using of reheated cooking oil (frequent reheating of cooking oil) was statistically associated with cancer incidence. we could not found any article which directly explain about it but Hakamia` s study reported on impact of reuse of cooking oil on esophageal cancer (Hakamia et al., 2013).

Negotiation about the impact of reheated cooking oil associated with gastric cancer was difficult and needed to strong documentation for interpreting it. Maybe frequent use of reheating oil can lead to chemical changes on oil components which can act as cancerogenic agents such as acrolein, PAH (Polycyclic Aromatic Hydrocarbones) and HCA (Heterocyclic Amines) (Stevens and Maier, 2008; Mastrangelo et al., 1996; Purcaro et al., 2006).

Excessive use of salt has impacted on cancer incidence which is consistent with D'Elia study (D'Elia et al., 2012) but in Van den Brandt study have not significant association between use of salt and gastric cancer occurrence (Van den Brandt et al., 2003). Interpreting wide range of reports can be due to various definition of salt consumption in relation to gastric cancer. Also measurement of this item was different in various studies, some of them surveyed

overall dietary salt intake, others table salt, salted fish, salted meat and we evaluated table salt.

Consistent with sun study, result of this study showed that the use of leftover food for breakfast had impact on gastric cancer occurrences (Sun et al., 2013) and in one study this item was associated with esophageal cancer (Phukan et al., 2001).

Charred flesh identified as a risk factor for gastric cancer. Other studies reported that charred flesh contains mutagen substances which increase risk of gastric cancer (Sugimura et al., 2000; Kim et al., 2002; Farouk Aly, 2012).

In sub category of predisposing factors, achalasia was identified as a risk factor for gastric cancer but in some studies achalasia was reported as a risk factor for esophageal cancer (Eckardt, 2010; Zendehdel et al., 2011).

Helicobacter pylori were confirmed as a risk factor too. Some studies showed the association between Helicobacter pylori and gastric cancer (Cancer Collaborative Group, 2001; Polk and Peek, 2010; Dikshit et al., 2011).

Although Helicobacter pylori was well controlled in last decade but it is still one the main causes of gastric cancer.

Gastric ulcer was another risk factor for gastric cancer that identified in this study. H. pylori infection is considered as a main factor for gastric ulcer, duodenal ulcer, and gastric cancer, therefore when combination of gastric or duodenal ulcer and H. pylori infection was seen, we can expect gastric cancer occurrences in later time (Kelley and Duggan, 2003), in another study, among hospitalized patients for gastric ulcers, the risk of gastric cancer was almost twice the expected rate (hansson et al., 1996).

In subcategory of physical activity, low mobility and lack of appropriate activities were identified as risk factor for gastric cancer which is consistent with Sjo¨dahl and Michael studies (Sjodahl et al., 2008; Michael, 2009).

A study reported physical activity is associated with reduced risk of prostate cancer, upper digestive and gastric cancer (Wannamethee et al., 2001). However, in some studies there was no relationship between physical activity and gastric cancer (Vigen et al., 2006). There were many reports for the effect of activity on gastric cancer but these various reports may be due to various definitions about activity, level of activity and qualification of activity in wide range of studies around the world.

In conclusion, Changing incidence rate in certain area, can express changes in the facilitating or predisposing factors which are changeable nature such as environmental and lifestyle factors. Because in this region, there was not performed any comprehensive study which considered all these factors especially joint effect of these, so this study was done to determine the incidence rate and influential predictors on it by statistically models. Results showed; inappropriate personal hygiene, probable high risk foods such as fats, salt, consumption of left over foods, eating in bad psychological situation, etc can impact on cancer incidence as influential predictors. Therefore, in these cases, appropriate educational interventions should be designed and implemented by competent authorities. Changes in lifestyle (low mobility, stress, use of conserved foods and lack of regular time for eating) in two decades can increase gastric cancer incidence dramatically in the near future. Therefore, by considering the large number of variables, development of classification tree model will be useful in future studies which in future work will be done by the authors.

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