

Smoking and alcohol, both alone and in combination, for risk of gastric cancer: A systematic review

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ABSTRACT

Introduction: Stomach cancer is the fifth most common cancer and the fourth leading cause of cancer deaths worldwide in 2020. Moderately increased risk of stomach cancer has been associated with tobacco smoking and Alcohol drinking. In this systematic review, we summarized the current knowledge on the relation between smoking and alcohol, both alone and in combination, to the risk of gastric cancer.

Method: This study was conducted in 2023 with a structured overview in the Science Directe , PubMed, Web of Science (ISI) databases. We investigated the studies that were published between 2010 and 2023. In the first step, articles were extracted based on their titles and abstracts; the quality of 58 articles was evaluated using the STORBE tool. Inclusion criteria were English language (first step), year of the study and the study type (second step).

Findings: Of these 39 articles, 17 ones were case-control studies, 21 were cohort studies, one was a descriptive study. eleven articles were related to alcohol consumption and risk of gastric cancer, twenty-three articles were related to smoking and risk of gastric cancer, five articles were related smoking and alcohol consumption in combination and risk of gastric cancer. Many studies reported a significant association between alcohol and gastric cancer risk. Also, three studies showed that smoking acts as a risk factor for developing gastric cancer only in certain genotype and not in all people.

Conclusion: Based on the best our knowledge and present studies, consumption of alcohol and smoking are risk factors of gastric cancer. It is better to conduct more studies on this issue in different populations in the future. We also suggest that future studies focus more on the intracellular mechanisms of these associations than on epidemiological outcomes.

Keywords: Alcohol, smoking, Gastric cancer, Stomach neoplasms, Epidemiology

INTRODUCTION:

Gastric cancer has been described early 3000 BC in hieroglyphic inscriptions and papyri manuscripts from antiquarian Egypt [1]. Stomach Neoplasm is generally an adenocarcinoma arising in the stomach, and contains tumors arising at or right below the gastroesophageal junction [2]. According to the International Agency for Research on Cancer (IARC), stomach cancer is the fifth most common cancer and the fourth leading cause of cancer deaths worldwide in 2020. There were 1,089,103 new cases and 768,793 deaths in 2020 worldwide [3]. However, the incidence and mortality rates for gastric cancer have reduced worldwide since the middle of the 20th century, gastric cancer still has great incidence and mortality rates in Eastern Asian countries, where about half of the universal gastric cancer burden was placed [4, 5], and several Asian countries containing South Korea, Latin American countries, and some former Soviet European countries still represent great incidence and mortality rates of gastric cancer [6]. Incidence rates were increased in younger adults (<50 years) [7, 8], especially for non-cardiac tumors in wealthier populations [9, 10]. The creation of gastric cancer is a multifactorial process and some status influence the likelihood of incidence, of them, family history of gastric cancer, Helicobacter pylori infection (a common bacteria that can also cause stomach ulcers), history of an adenomatous gastric polyp larger than 2 centimeters, history of chronic atrophic gastritis, history of pernicious anemia, obesity, alcohol, smoking, red meat and low socioeconomic status are all believed to be important [11] but the significant risk factors of gastric cancer are H. pylori, obesity, smoking, red meat, alcohol, and low socioeconomic condition [12]. Recent studies have confirmed that alcohol drinking can raise the risk of stomach cancer; and the basic mechanism is likely related to the early metabolites, acetaldehyde, that have a local toxic result that raising the risk of stomach cancer [13-15]. Moderately increased risk of stomach cancer has been associated with tobacco smoking [16-20]. Alcohol and smoking, alone and in combination, are associated with increased risks of neoplasm

at various sites [21]. The list of alcohol-associated neoplasms is growing. Even low use of alcohol may increase neoplasm risk, in specific when combined with either tobacco smoking or excess body weight [22, 23]. At higher levels of alcohol intake (from 45 g of alcohol per day) there is a non-linear dose-response association between alcohol use and gastric cancer risk [24]. However, the communication between alcohol drinking and tobacco smoking and risk of gastric neoplasm has been the focus a lot of studies, also results have been contradictory and remain controversial [25]. The purpose of this study is to summarize systematically the current knowledge on the relation between smoking and alcohol, both alone and in combination, to the risk of developing gastric cancer, and to provide more evidence with which to establish effective prevention methods. Therefore, the main question of this study is to identify and investigate the risk factors of smoking and alcohol, both alone and in combination, for gastric cancer.

Materials and Methods:

search strategy and selection of articles

This was a systematic review study; We investigated studies that were published between 2010 and 2022, we focused on articles related to the topic that examined alcohol consumption and smoking on risk of gastric cancer. Articles collected and screened in three stages using the English keywords: (stomach cancer OR gastric cancer OR stomach neoplasms OR gastric neoplasms OR gastric malignancy OR stomach malignancy OR stomach tumor OR gastric tumor) AND (cigarette OR smoking OR tobacco OR alcohol OR ethanol) AND epidemiology AND combined in PubMed, Web of Science, and science direct databases. we used AND and OR operators to increase sensitivity. The reference lists of the included studies were also explored; therefore, all studies were evaluated by two researchers and the search results of all databases were combined using EndNote.

Inclusion criteria

The inclusion criteria in the first stage were English-language articles on the risk factors (alcohol consumption and smoking) associated with gastric cancer of any type

(adenocarcinoma, lymphoma, sarcoma, or carcinoid) and location (cardia or non-cardia), among the general population, regardless of age, sex, race, ethnicity, and geographical region. In the second stage, the inclusion criteria included study type. Randomized clinical trial and Observational (cohort and case-control and descriptive) studies addressing the association between stomach cancer and any of the above factors were included in the review study, irrespective of the nationality, race, sex, and age of participants. In the second stage, the inclusion criteria included access to the full text of the studies then the full texts of potentially relevant studies were retrieved for further evaluation.

Exclusion criteria

authors independently screened the titles and abstracts and excluded ineligible studies. duplicated and unrelated studies were excluded. In the next stage (abstract review), studies that were not relevant to the subject and purpose of the study, very old studies (before 2010) and the reviews were excluded. Supplementary Figure 1 provides the flowchart for the selection of articles.

Data extraction

The data from the relevant studies were extracted using an electronic data collection form included the title of the article, the first author's name, the study year, the study type, the sample size, the study place and the results of the study.

Ethical considerations

This study was a systematic review study in which no human subject or animal was employed. Also, Ethical considerations were considered in the search for articles. Therefore, Open Access articles were used.

Results:

In total, 2,161 studies were identified, including 2000 studies obtained by searching the electronic databases through 2010 to 2023 and 161 articles identified by searching the reference lists of the included studies. In the next step, repeated and unrelated studies (1111) were excluded after the initial screening (title review), and 1050 studies were entered into the secondary screening (abstract review) process. At this stage, two researchers

separately reviewed the abstracts of the articles for improve the accuracy and quality of the study. It became clear that some of these articles were not a valid criterion to assessment the risk factors for gastric cancer, were not related to the study objectives, were very old (before 2010), and were reviews. Therefore, 56 studies were extracted. Two more related articles were extracted after reviewing the references of these articles (n=58). Then, the quality of the remaining 58 articles was reviewed using a STROBE evaluation checklist. At this stage, 19 articles were excluded due to weak quality and methodology; the studies decreased to 39 articles. End Note software was used to extract the results (Figure 1). Of these 39 articles, 17 ones were case-control studies, 21 were cohort studies, one was a descriptive study. eleven articles were related to alcohol consumption and risk of gastric cancer (Table 2), twenty-three articles were related to smoking and risk of gastric cancer (Table 3), five articles were related tobacco and alcohol consumption in combination and risk of gastric cancer (Table 1).

Discussion:

The aim of this study is to summarize systematically the

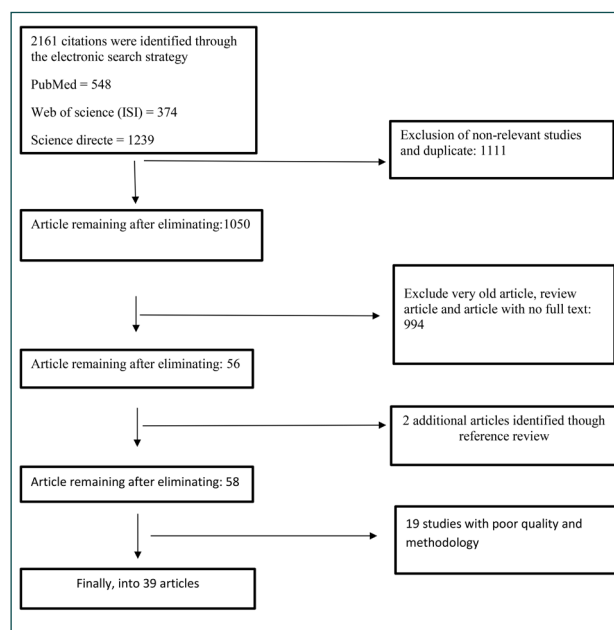


Figure 1. Flowchart of publication selection for the systematic Review

Table 1. The Articles were related smoking and alcohol consumption in combination and risk of gastric cancer.

Study	Author	Year	Title	Country /region of origin	Sample size	Research design	Main results	Ref
1	Yoon Jin Choi et al	2017	The relationship between drinking alcohol and esophageal, gastric or colorectal cancer	Korea	23,323,730 adults	cohort	The synergistically increased cancer risk between excessive amount of alcohol consumption and currently smoking or underweight individuals was observed only in the esophageal cancers.	(26)
2	J Steevens et al.	2010	Alcohol consumption, cigarette smoking and risk of subtypes of oesophageal and gastric cancer: a prospective cohort study	Netherlands	120 852 participants	cohort	A positive interaction was found between alcohol consumption and smoking status regarding oesophageal squamous cell carcinoma (OSCC) risk.	(27)
3	Haibo Zhou et al.	2019	Combined effect between WT1 methylation and Helicobacter pylori infection, smoking, and alcohol consumption on the risk of gastric cancer	China	400 GC cases and 402 controls	a case-control	A significant combination was observed between WT1 methylation and alcohol consumption, and smoking for the risk of gastric cancer. Smoking and alcohol consumption effect on GC risk.	(28)
4	Kristin A. Moy	2010	Alcohol and Tobacco Use in Relation to Gastric Cancer: A Prospective Study of Men in Shanghai, China	Shanghai, China	18,244 middle-aged and older men	cohort	heavy drinkers experienced a statistically significant increase in risk of gastric cancer (HR, 1.46; 95% CI, 1.05-2.04) among all subjects and a statistically nonsignificant 80% increased risk among never smokers.	(29)
5	Dalia Luksiene	2017	The Prognostic Value of Combined Smoking and Alcohol Consumption Habits for the Estimation of Cause-Specific Mortality in Middle-Age and Elderly Population: Results from a Long-Term Cohort Study in Lithuania	Lithuania	6,729 subjects	Cohort	Alcohol and cigarette smoking each have an individual effect on the risk of mortality (from any cause, CVD, cancer, or external causes) but, when combined, they act synergistically	(30)

Table 2. The Articles were related alcohol consumption and risk of gastric cancer.

Study	Author	Year	Title	Country/region of origin	Sample size	Research design	Main results	Ref
1	Yuting Li et al.	2021	Alcohol Consumption and Risk of Gastric Cancer: The Japan Collaborative Cohort Study	Japan	54,682 men and women	Cohort	Alcohol consumption is associated with increased risk of gastric cancer among Japanese men, regardless of anatomical subsite of the cancer. However, no such trend is observed in women.	(31)
2	Everatt et al.	2012	Alcohol consumption and risk of gastric cancer: a cohort study of men in Kaunas, Lithuania, with up to 30 years follow-up	Vilnius/Lithuania	7,150 men	cohort	An association with heavy wine consumption was observed, but the effect of exposure to acetaldehyde on the development of gastric cancer in this cohort was not confirmed.	(32)
3	Mi Hui Kim et al.	2019	Alcohol consumption and gastric cancer risk: a case-control study	Korea	316 cases(208 men, 108 women) and 316 controls	case-control	excessive alcohol consumption rather than the current status or frequency of alcohol consumption contributes to the increased gastric cancer risk, especially in women.	(33)
4	Jung Eun Yoo et al	2021	Association of the Frequency and Quantity of Alcohol Consumption With Gastrointestinal Cancer	Korea	11,737,467 participants	Case-control	Lee et al and Yoo et al. indicated frequent drinking may be more important risk factor for GC incidence than the amount of alcohol consumed per time.	(34)
5	Cheol Min Shin et al	2011	Association between alcohol intake and risk for gastric cancer with regard to ALDH2 genotype in the Korean population	Korea	445 patients with gastric cancer and 370 control	case-control	ALDH2 polymorphism are find to modify the susceptibility to the development of gastric cancer associate with alcohol intake, especially in case of ALDH2 *1/*2 genotype.	(35)

6	Eric J Duell et al	2011	Alcohol consumption and gastric cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort consumption and gastric cancer risk in the European Prospective	Europe	444 cases of first primary gastric adenocarcinoma	cohort	Heavy (but not light or moderate) consumption of alcohol at baseline (mainly from beer) is associated with intestinal type noncardia GC risk in men.	(36)
7	Akihisa Hidaka et al	2015	Genetic polymorphisms of ADH1B, ADH1C and ALDH2, alcohol consumption, and the risk of gastric cancer: the Japan Public Health Center-based prospective study	Japan	68 722 men and 71 698 women	cohort	No association between alcohol consumption, ADH1B(rs1229984), ADH1C(rs698) and ALDH2(rs671) polymorphisms and gastric cancer risk.	(37)
8	Shin Ah Kim et al	2019	Prediagnostic Smoking and Alcohol Drinking and Gastric Cancer Survival: A Korean Prospective Cohort Study	Korea	The participants were 508 GC patients	Cohort	Alcohol drinking are weakly associated with GC survival.	(38)
9	Hwi-Won Lee et al	2022	Frequent low dose alcohol intake increases gastric cancer risk: the Health Examinees-Gem (HEXA-G) study	Korea	128,218 participants	cohort	Frequent intake of alcohol, even in low quantities per session, increases GC risk.	(39)
10	Seung-Hyun Ma et al	2015	Impact of alcohol drinking on gastric cancer development according to Helicobacter pylori infection status	Korea	949 participants from the 18 863	cohort	Heavy and binge alcohol consumption is an important risk factor related to an increasing incidence of gastric cancer in a population not infected by H. pylori	(40)
11	Sarah Yang et al	2017	Effects of alcohol consumption, ALDH2 rs671 polymorphism, and Helicobacter pylori infection on the gastric cancer risk in a Korean population	Korea	450 cases and 1,050 controls	case-control	Increased GC risks were evident for rs671 A allele carriers and H. pylori-infected individuals, but no dose-response association with alcohol consumption was observed.	(41)

Table 3. The Articles were related smoking and risk of gastric cancer.

Study	Author	Year	Title	Country /region of origin	Sample size	Research design	Main results	Ref
1	Hang Thi Minh Lai et al	2016	Waterpipe Tobacco Smoking and Gastric Cancer Risk among Vietnamese Men	Vietnam	454 patients with gastric cancer and 628 control	case-control	The present findings revealed that WPT smoking was positively associated with GC risk in Vietnamese men.	(42)
2	Padmavathy Amma Jayalckshmi et al	2015	Gastric cancer risk in relation to tobacco use and alcohol drinking	India	65553 men	cohort	Among a male cohort in South India, gastric cancer risk increased with the number and duration of bidi smoking.	(43)
3	Hung Xuan Le et al	2022	A prospective cohort study on the association between waterpipe tobacco smoking and gastric cancer mortality in Northern Vietnam	Vietnam	25,619 participants	cohort	Waterpipe tobacco smoking would significantly increase the risk of gastric cancer mortality in the Vietnamese population	(44)
4	Mridul Malakar et al	2014	p53 codon 72 polymorphism interactions with dietary and tobacco related habits and risk of stomach cancer in Mizoram, India	India	105 patients and 210 normal controls	case-control	this study revealed that p53 codon 72 polymorphism and dietary and tobacco habit interactions influence stomach cancer development	(45)
5	Mridul Malakar et al	2012	Genetic polymorphism of glutathione S-transferases M1 and T1, tobacco habits and risk of stomach cancer in Mizoram, India	Mizoram, India	102 histologically confirmed stomach cancer cases and 204 matched healthy population controls	case-control	tobacco smoking, especially meiziol is the important risk factor for stomach cancer.	(46)
6	Khanpaseuth Sengngam et al	2022	Interaction of Helicobacter pylori Infection with Waterpipe Tobacco Smoking in the Development of Stomach Cancer in Vietnamese Men	Vietnam	80 stomach cancer cases and 146 controls	case-control	Compared to participants who were negative with both H. pylori infection and tobacco smoking individuals exposed to both these factors showed significantly greater odds of stomach cancer.	(47)

7	Sadigheh Razavi et al	2021	Development and psychometric testing of a Gastric Cancer Behavioral Risk Assessment Inventory (GC-BRAI)	Iran	175 GC patients and 350 matched non-GC patients as a control group	case-control	The identified components were specific nutritional behaviors and smoked foods, and tobacco smoking/alcohol consumption, which all indicated a significant association with high-risk of GC.	(48)
8	Xiaowen Liu et al	2016	Prognostic significance of cancer family history for patients with gastric cancer	China	1805 gastric cancer patients	cohort	Positive family history of cancer correlated with younger age, more frequent alcohol and tobacco use, worse differentiation, smaller tumor size, and more frequent tumor location in the lower 1/3 of the stomach.	(49)
9	Arun Kumar Barad et al	2014	Gastric cancer-a clinicopathological study in a tertiary care centre of North-eastern India	India	158 patients of primary gastric cancer	cohort	use of tobacco is associated with high occurrence of gastric cancer in this part of the India.	(50)
10	Ali Nemati et al	2012	Case-control study of dietary pattern and other risk factors for gastric cancer	Iran	42 people with gastric cancer and 86 healthy people	case-control	No significant relationship was observed between tobacco smoking and alcohol consumption with gastric cancer.	(51)
11	L M Canseco-Ávila et al	2019	Gastric cancer epidemiology in tertiary healthcare in Chiapas	Chiapas	84 cases of gastric cancer	A descriptive, a mb- ispective, longitudinal	consumption of alcohol and tobacco played an important role in the development of gastric cancer.	(52)
12	Kristin A Moy et al	2010	Mexico	Mexico	18,244 men	cohort	These results suggest that cigarette smoking and alcohol consumption may exert independent effects on the development of gastric cancer in this high-risk population.	(25)

13	Satoshi Abiko et al	2023	Alcohol and tobacco use in relation to gastric cancer	China	77 patients who underwent endoscopic resection (ER) for GC	cohort	Continued cigarette smoking, at a high level, may be an important risk factor for the development of metachronous GC.	(53)
14	Longyue Wang et al	2022	Effects of activation of an alcohol metabolic gene, cigarette smoking, and alcohol intake on the incidence of metachronous gastric cancer in patients who underwent endoscopic resection for gastric cancer: A multicenter retrospective pilot study	Japan	483 case 968 control	case - control	current smokers with AG or GG genotype have the highest GC risk, compared to never-smokers with AA genotype, OR (95% CI) = 2.43 (1.64-3.28).	(54)
15	Julia Butt et al	2019		China	1,446 non-cardia gastric cancer cases and 1,796 controls	case - control	current smoking is associated with an increased gastric cancer risk, however, only among individuals that are simultaneously sero-positive for the leading causal factor for gastric cancer, H. pylori.	(55)
16	Xiao-Qin Wang et al	2011	Interaction Between Vascular Endothelial Growth Factor Gene Polymorphism and Smoking on Gastric Cancer Risk in Chinese Han Population	China, Japan, and Korea	257 cases and 514 frequency-matched controls	case-control	smoking and CagA positive H. pylori infection was found to be important risk factors in non-cardiac gastric cancer. When both of these risk factors were present, the risk of non-cardiac gastric cancer was synergistically higher. smoking may somehow influence the carcinogenic processes associated with CagA positive H. pylori infection.	(56)

17	Sung Keun Park et al	2022	Smoking, Helicobacter pylori serology, and gastric cancer risk in prospective studies from China, Japan, and Korea	China	97,700 Korean men	cohort	In all categories of smoking status, current smoking was associated with the highest risk of gastric cancer. Heavy smoking was associated with an increased risk of gastric cancer, even in former smokers.	(57)
18	Wu-Hsien Kuo et al	2014	Interactions between CagA and smoking in gastric cancer	Korea	358 cases 358 controls	case-control	AG and GG genotype at IL10 A-1082G, together with smoking, synergistically contribute to individual susceptibility for gastric cancer in Taiwan.	(58)
19	Asahi Hishida et al	2010		Taiwan	576 cases and 1,599 controls	case-control	smoking behavior contributed to the increased risk of gastric carcinogenesis from gastric atrophy, but had little influence on H. pylori infection or gastric atrophy development.	(59)
20	Z Q Zha et al	2020	The risk of gastric cancer according to changes in smoking status among Korean men	Japan	736 patients	cohort	After adjusting for gender, alcohol consumption, body mass index and household registration type, the risk of early stomach cancer in people who quit smoking was lower than that in smokers. Also Smoking is one of the risk factors for the earlier onset of stomach cancer in Anhui.	(60)
21	Mi Ah Han et al	2013		China / Anhui	238 patients	cohort	Cigarette-smoking history at the time of diagnosis, but not drinking history, is associated with cancer recurrence and poor survival after surgery in male patients with stage III-IV gastric cancer.	(61)

22	Abraham M Y Nomura et al	2012	Effects of interleukin-10 polymorphisms and smoking on the risk of gastric cancer in Taiwan	Korea	215,000 men and women	cohort	this study shows an association of current cigarette smoking with gastric cancer in both sexes	(62)
23	Chen Jing et al	2012	Smoking behavior and risk of helicobacter pylori infection, gastric atrophy and gastric cancer in Japanese	Hawaii and Los Angeles	410 gastric cancer cases and 410 cancer-free controls.	Case - control	GSTM1 and GSTT1 null genotypes are associated with increased risk of gastric cancer, and smoking modifies the association.	(63)

current knowledge on the relation between smoking and alcohol, both alone and in combination, to the risk of developing gastric cancer, and to provide more evidence with which to establish effective prevention methods. Despite differences in findings, the included articles showed consistent finding from the impact of alcohol consumption and smoking on risk of gastric cancer. In this systematic review from the impact of alcohol consumption and smoking on risk of gastric cancer, three domains of existing research were identified related to gastric cancer. Firstly, area of research was identified related to alcohol consumption and risk of gastric cancer. Secondly, area of research was identified related to smoking and risk of gastric cancer. Thirdly, area of research was identified related to Risk with combined alcohol consumption and smoking.

Risk of gastric cancer associated with Alcohol consumption

The effect of alcohol consumption on the development of gastric cancer is different among the established studies and there are no similar results. Many studies reported a significant association between alcohol and gastric cancer risk. Several studies surveyed effect of light to heavy alcohol consumption on risk of gastric cancer incidence. Based on the results, one of the important factors mentioned in more studies was heavy alcohol consumption (in comparison with light consumption) which was referred to in three studies. As observed by

mi hui Kim et al. excessive consumption of alcohol rather than frequency of alcohol consumption contributes to the increased risk of gastric cancer. In the other word, high alcohol consumption (≥ 20 g/day for women or ≥ 40 g/day for men) had a significantly association with GC, but alcohol consumption status and frequency were not associated with gastric cancer risk [33]. Duell et al. showed consumption of Heavy alcohol (≥ 60 g/d) was positively associated with GC risk to comparison on lower consumption amounts (< 60 g/d) [36]. Also, a study of cohort in Korea showed that heavy and binge alcohol consumption is an important risk factor related to an increasing incidence of gastric cancer [40]. Despite of these studies, frequent drinking is another risk factor reported in 2 studies. Lee et al and Yoo et al. indicated frequent drinking may be more important risk factor for GC incidence than the amount of alcohol consumed per time [34, 39]. We observed many studies indicated consumption of alcohol is not associated with gastric cancer or has weak association between alcohol and incidence gastric cancer [32, 37, 38, 41]. Genetic field which refers to the characteristics of a person at the genome level is one of the causes of human cancers. The main components of the genetic field are mutations and polymorphisms that affect by altering the expression amount or by changing the function of proteins. A study showed that alcohol consumption acts as a risk factor for developing gastric cancer only in certain genotype and not in

all people. Shin et al. reported in their study that ALDH2 polymorphisms leads to the susceptibility to the development of gastric cancer associated with alcohol intake, especially in case of ALDH2 *1/*2 genotype [35]. gender factor can also play a role in the biology of gastric cancer. most studies report that alcohol consumption is associated with a higher risk of stomach cancer in men than in women. Results of a study conducted by Yuting Li et al. showed that male gender was positively associated with gastric cancer regardless of anatomical subsite of the cancer [31]. Duell et al. concluded that men were more likely to be exposed to gastric cancer compared to women [36]. But a study showed that drinking heavy alcohol causes stomach cancer in women [33].

Risk of gastric cancer associated with smoking

In this review, 23 studies pointed to the role of smoking in the risk of gastric cancer. In this section also three studies showed that smoking acts as a risk factor for developing gastric cancer only in certain genotype and not in all people. Results of a study conducted by Wang et al. showed that current smokers with AG or GG genotype have the highest GC risk, compared to never-smokers with AA genotype [54]. Kuo et al. concluded that AG and GG genotype at IL10 A-1082G, together with smoking, synergistically contribute to individual susceptibility for gastric cancer [58]. Also, jing et al. indicated GSTM1 and GSTT1 null genotypes are associated with increased risk of gastric cancer, and smoking modifies the association [63]. On the other, in this systematic review, two studies showed that smoking increases the risk of stomach cancer in people with *Helicobacter pylori* infection. In this regard, Butt et al. pointed to current smoking is associated with an increased gastric cancer risk, however, only among individuals that are simultaneously sero-positive for the leading causal factor for gastric cancer, *H. pylori* [55]. Also, Wang et al. indicated smoking and CagA positive *H. pylori* infection was found to be important risk factors in non-cardiac gastric cancer. When both of these risk factors were present, the risk of non-cardiac gastric cancer was synergistically higher [56]. Despite of these studies, we observed a study indicated smoking is not associated with gastric cancer.

Risk associated with combined alcohol consumption and smoking

The results of some studies indicated smoking and alcohol consumption in combination have important effect on occurrence of gastric cancer. In China, the study was conducted by Haibo Zhou et al. a significant combination was observed between WT1 methylation and alcohol consumption, and smoking for the risk of gastric cancer [28]. Also, Moy et al. indicated heavy drinkers experienced a statistically significant increase in risk of gastric cancer among all subjects and a statistically nonsignificant 80% increased risk among never smokers [29]. Luksiene et al. concluded that alcohol and cigarette smoking each have an individual effect on the risk of mortality (from any cause, CVD, cancer, or external causes) but, when combined, they act synergistically [30]. Despite of these studies, we observed two study indicated the synergistically increased cancer risk between excessive amounts of alcohol consumption and currently smoking was observed only in the esophageal cancers [26, 27].

Conclusion:

Gastric cancer is one of multifactorial cancers, and many factors can play a role in its incidence. In the present review a number of studies investigated the relationship between alcohol consumption and smoking with the genotype of people, but it is better to conduct more studies on this issue in different populations in the future. We also suggest that future studies focus more on the intracellular mechanisms of these associations than on epidemiological outcomes. Ultimately, despite many gaps that exist regarding the causes and risks of gastric cancer, studies with appropriate design are required to address some of the risk factors that may interfere with gastric cancer.

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