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ORIGINAL ARTICLE

Prospective Study

Gastric cancer risk in relation to tobacco use and alcohol drinking in Kerala, India - Karunagappally cohort study

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Abstract

AIM: To assess the risk of gastric cancer (GC) in relation to tobacco use and alcohol drinking in the Karunagappally cohort in Kerala, South India.

METHODS: This study examined the association of tobacco use and alcohol drinking with GC incidence among 65553 men aged 30-84 in the Karunagappally cohort. During the period from 1990-2009, 116 GC cases in the cohort were identified as incident cancers. These cases were identified from the population-based cancer registry. Information regarding risk factors such as socioeconomic factors and tobacco and alcohol habits of cohort members were collected from the database of the baseline survey conducted during 1990-1997. The relative risks (RRs) and the corresponding 95% confidence intervals (95%CIs) for

tobacco use were obtained from Poisson regression analysis of grouped survival data, considering age, follow-up period, occupation and education.

RESULTS: Bidi smoking was associated with GC risk (P = 0.042). The RR comparing current versus never smokers was 1.6 (95%CI: 1.0-2.5). GC risk was associated with the number of bidis smoked daily (P = 0.012) and with the duration of bidi smoking (P = 0.036). Those who started bidi smoking at younger ages were at an elevated GC risk; the RRs for those starting bidi smoking under the age of 18 and ages 18-22 were 2.0 (95%CI: 1.0-3.9) and 1.8 (95%CI: 1.1-2.9), respectively, when their risks were compared with lifetime non-smokers of bidis. Bidi smoking increased the risk of GC among never cigarette smokers more evidently (RR = 2.2; 95%CI: 1.3-4.0). GC risk increased with the cumulative amount of bidi smoking, which was calculated as the number of bidis smoked per day x years of smoking (bidi-year; P = 0.017). Cigarette smoking, tobacco chewing or alcohol drinking was not significantly associated with GC risk.

CONCLUSION: Among a male cohort in South India, gastric cancer risk increased with the number and duration of bidi smoking.

Key words: Bidi smoking; Alcohol drinking; Gastric cancer; The Karunagappally cohort; Kerala; India

Core tip: In South Asia, bidi smoking is a popular form of tobacco smoking. A bidi is 0.15-0.25 g of sun-dried tobacco flakes hand-wrapped in a temburni leaf. Bidi smoking has been shown to cause various cancers, such as cancers of the lung and oral cavity, by several epidemiological studies including the Karunagappally cohort study, one of the most important cohort studies in South Asia. However, only a few studies have examined the relation between bidi smoking and gastric cancer (GC) risk. Our results indicated that GC risk increased with the number and duration of bidi smoking. To our knowledge, the present study is the first cohort study to show an association between bidi smoking and GC risk.

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INTRODUCTION

Tobacco is used in different forms all around the world. The most common form of tobacco use worldwide is cigarette smoking, which is known to cause various cancers including gastric cancer (GC)[1]. In southern India, the most popularly smoked tobacco is bidi, which is made of sun dried flaked tobacco rolled into a conical shape in a dried rectangular piece of temburni leaf (*Diospyros melanoxylon*) with a thread securing the roll. As bidis are hand-rolled, the length and amount can vary; however, the difference is not large, and on average, a bidi in Karunagappally taluk, our study area, contains 0.15-0.25 g of tobacco leaves[1,2]. Tobacco-specific nitrosamine levels in the main stream smoke of bidis were reported to be as high as were those in cigarettes[3]. Bidi smoking has been found to be related to cancers of the oral cavity, lung, head and neck[4-10]. However, only a few studies have examined the relation between GC risk and bidi smoking, and their results are inconsistent[11-13].

Tobacco chewing is another common tobacco-related habit in many Asian countries, particularly in India. The chewing practices vary in different regions, and the most common combination used for chewing is areca nut, betel leaf, slaked lime and tobacco[14]. In the study area, tobacco chewing is always betel quid chewing. The International Agency for Research on Cancer (IARC) classified areca nut as a human carcinogen (Group 1) in 2004[14]. GC has been associated with the habit of chewing; an increase in GC was noted in the case of chewers with a habit of chewing tobacco alone[15]. However, the association that was noted in studies was inconsistent, warranting more in-depth studies[11,12,15,16].

Alcohol consumption is also known to cause various cancers, including cancers of the upper digestive tract and the liver[17]. Regarding the relation between alcohol drinking and GC risk, the IARC concluded in 2007 that the evidence is inconsistent[18]. A recent meta-analysis reported an increase in GC risk in alcohol drinkers, with a higher risk for heavy alcohol drinkers ($\geqslant$ 4 drinks per day) compared to non-drinkers[19]. In India, only a few studies have investigated the relation between alcohol drinking and GC risk[11,12,16].

Alcohol consumption is a common habit all over the world; however, commonly consumed beverages vary from country to country. In South India, the most popular alcoholic beverages are toddy and arrack. Toddy is prepared locally from the sap of coconut flowers or palm trees. This liquid is collected and allowed to ferment. This beverage has an alcohol content of approximately 5%-10%[20]. This preparation method is almost identical everywhere, including in Karunagappally. Arrack is a distilled beverage made from paddy, wheat, or palm sap, depending on the local availability. Jaggery, sugar or sugarcane is added to either one or a combination of these and boiled with water. This mixture is allowed to ferment, after which it is distilled. In Karunagappally taluk, arrack is made primarily from palm sap. This beverage contains approximately 25%-45% alcohol. With no legal control, some of the beverages were found

to have alcohol concentrations as high as 56%. In a study specifying the type of alcohol consumed, arrack drinkers and foreign liquor drinkers showed a significant association with an increased GC risk[11]. In that study, foreign liquors normally had 40% alcohol content.

The present cohort study investigated the association of tobacco use, alcohol drinking and socioeconomic status with GC in Karunagappally, Kerala, India.

MATERIALS AND METHODS

Base line survey

The area of the present study is Karunagappally taluk, which is an administrative unit consisting of 12 panchayats, in the coastal area of Kollam district in Kerala, South India, as described in our previous studies[8-10,21]. Based on the 1991 census, Karunagappally taluk, with an area of 192 km^2, had a total population of 385103 (193954 females and 191149 males). In the late 1980s, a cohort of all residents of Karunagappally was established with the objective of examining the risk of different cancer in association with natural radiation exposure, lifestyle and many other factors[8-10,21]. During the period from January 1st, 1990 to December 31st, 1997, every resident of Karunagappally taluk was surveyed for sociodemographic and other lifestyle-related factors as a part of the investigation. The face-to-face interview survey was conducted with the help of trained field investigators for each resident using a 6-page, standardized questionnaire. The questionnaire was constructed with specific questions to elicit factors such as household socioeconomic status, religion, education, income, and occupation along with lifestyle factors such as smoking and drinking habits, and dietary practices.

The questions pertaining to tobacco chewing, smoking and alcohol drinking included habits practices, and whether the person had a history of the habits in the past or was currently habituated. For the subjects with those habits, a detailed enquiry was made regarding the types of materials consumed, such as (1) pan, pan + tobacco, or tobacco alone in the case of tobacco chewing; (2) bidis or cigarettes in the case of smoking; and (3) and toddy, arrack or foreign liquors in the case of drinking. In addition, information was collected regarding the frequencies of smoking and tobacco chewing per day, the amount alcoholic beverages consumed in milliliters or liters per day, and the ages at starting and stopping those habits.

Study population

During the household survey, personal information on 359614 subjects from 71674 households (corresponding to 93% of the population and 94% of households in Karunagappally according to the 1991 census) were collected. There were 69943 men between the ages of 30-84 at the time of the interview. We excluded subjects younger than 30 because cancer incidence is low in this age group and the smoking effects will be apparent only decades after starting smoking. Subjects older than 84 were also excluded as the elderly tend not to seek medical attention for cancer, which can lower the completeness of case ascertainment and the diagnosis accuracy. The local Rare Earth factory workers were also excluded because of the possible occupational exposures (n = 1428). Additionally, subjects who were deceased or diagnosed with cancer before the base-line survey were excluded from the analysis (n = 136). Furthermore, we excluded subjects who died within 3 years after the interview because their health status might have affected their lifestyle. As a result, the statistical analysis was conducted on the remaining 65553 subjects[10].

Cancer case ascertainment

The present study analyzed cancer incidence among the Karunagappally cohort, during the 1990-2009 period. The regional cancer registry in Karunagappally taluk, which was initiated January 1st, 1990, registered the cancer cases[10,22]. Because this rural area does not have any center dedicated to cancer diagnosis or treatment, it was necessary to use an active registration method. We visited all health and medical facilities, in or outside the taluk, where cancer patients are attended to[23-26]. The registry reports are included in the IARC Cancer Incidence in Five Continents vol. Ⅶ-Ⅹ[23-26].

We obtained the death reports from the death registers of the Vital Statistics Division of each panchayat. To obtain supplemental information for determining the underlying cause of death, the cancer registry office started house visits of the deceased in 1997. The Death Certificate Only proportion was 13% during the 1991–1992 period[23], 10% and 11% for men and women, respectively, during the 1993–1997 period[24] and reduced to 4% and 5% for men and women, respectively, during the 1998–2002 period[25]. The mortality to incidence ratio (M:I %) for all cancers among men was 56% during the 2002-2003 period[25] and 53.8% during the 2006-2010 period[23] and was similar to those in other major cancer registries in this country[27].

To assess the extent of migration among cohort members, periodical door-to-door surveys of all the households in the 12 panchayats were conducted during the years 2001-2003 and 2008. The findings of those surveys were linked to incident cases through name, age, address, house number and so forth. These surveys showed that migration was negligible.

Statistical analysis

Statistical analysis was performed using the EPICURE program (DATAB; AMFIT)[28]. Poisson regression

Table 1 Sociodemographic features of study subjects (men) and their associations with gastric cancer

	n	Person-years	Gastric cancer cases	RR	95%CI	*P* value
Total	65553	900721				
Religion						> 0.5[2]
Hindu	47689	658303	88	1.0	Reference	
Muslim	11841	160475	19	0.9	0.5-1.5	
Christian	6023	81942	9	0.8	0.4-1.6	
Family income[3]						0.191[1]
< 500	4367	66066	10	1.1	0.6-2.2	
501-1200	19460	281461	41	1.0		
1201-2500	24794	332258	37	0.7	0.5-1.1	
2501-3500	10839	141566	14	0.6	0.3-1.0	
3500+	6093	79370	14	1.0	0.5-1.8	
Education						0.164[1]
Illiterate	4143	52337	7	0.5	0.2-1.1	
Primary school	16917	221434	49	1.0	Reference	
Middle school	17310	238947	30	0.7	0.5-1.2	
High school	20775	298699	25	0.7	0.4-1.1	
College	5703	79877	4	0.4	0.1-1.1	
Unknown	705	9427	1	0.5	0.1-3.9	
Occupation						0.008[2]
Farmers and fishermen	21683	302651	51	1.0	Reference	
Skilled workers	12445	169094	21	0.8	0.5-1.3	
White collars	13672	183094	28	0.8	0.5-1.2	
Others	17753	245882	16	0.4	0.2-0.7	

[1]The *P* for trend; [2]The *P* for heterogeneity; [3]Monthly family income in Indian National Rupee (INR). One INR is approximately 0.016 US dollars. In the analysis examining the relation between socioeconomic status and gastric cancer risk, a relative risk was obtained from the following model: $H = H_s \exp(B_i X_i)$, where the background hazard, H_s, was stratified by attained age and calendar time, and X_i denotes categorical variables of the sociodemographic factors shown in the table.

analysis of grouped data was conducted to estimate relative risks (RRs) and 95%CIs using the survival data cross-classified by 5-year categories of attained age (30-84 years), calendar year (1990-1997, 1998-2003, and 2004-2009), and other variables[29].

To examine the relation between GC risk and bidi smoking, the RRs of former smokers (denoted by X_2) and current smokers (denoted by X_3) were estimated using the following model: H_0 (calendar year, attained age, occupation, and education) exp ($\beta_2 X_2 + \beta_3 X_3$), where H_0 denotes the baseline, or background, GC incidence rate (*e.g.*, incidence rate in never smokers). The attained age of each cohort member was calculated at the mid-point of one-year intervals during the follow-up period using the DATAB procedure (EPICURE). The AMFIT procedure of the EPICURE program gave Maximum Likelihood Estimates of β_2 and β_3, after adjusting for calendar year, attained age, occupation, and education. These estimates are the log RRs for the indicator variables X_2 and X_3, respectively, with the reference category X_1[10]. We used similar models for the analysis of all other variables.

The entry date into the cohort was defined as the interview date, from January 1st, 1990 to December 31st, 1997. A cohort member was considered censored when diagnosed with a cancer other than GC or when died of any other cause. Thus, the end of follow-up was defined as the diagnosis date for cancer cases, the date of death for the deceased, the migration date, the date of attaining the age of 85 or the end of the study period (December 31st, 2009).

RESULTS

The present study examined 65553 men aged 30-84 years old. By the end of 2009, 116 cases of GC (ICD9: 151) were identified. Table 1 summarizes the analysis results regarding the association of GC risk with socioeconomic status. No significant association between GC risk and religion, family income or education was found. In contrast, statistically significant heterogeneity in GC risk was found among occupational groups (*P* = 0.008).

Table 2 summarizes the risk analysis results with respect to tobacco use and alcohol drinking. Bidi smoking was significantly associated with GC risk (RR = 1.6; 95%CI: 1.0-2.5; *P* = 0.042). Bidi smoking increased the risk of GC among never cigarette smokers (RR = 2.2; 95%CI: 1.3-4.0) more evidently. The number of only bidi smokers was 7592, and the number of bidi smokers who also smoked cigarettes was 17740. By restricting our further analyses to only bidi smokers, we would have omitted more than two-thirds of the subjects. Therefore, we decided to include all bidi smokers in the further analyses (Table 3), regardless of whether they were cigarette smokers. Former cigarette smokers showed a 40% increase in GC risk (RR = 1.4; 95%CI: 0.8-2.4), which was not statistically significant. Tobacco chewing was not related to GC risk. Current alcohol drinkers had a 30% increase in GC risk compared to never alcohol drinkers (RR = 1.3; 95%CI: 0.9-2.0); however, this association was not statistically significant either.

Table 2 Gastric cancer risk in relation to tobacco use and alcohol drinking among men

	n	Person-years	Gastric cancer cases	RR	95%CI	*P* value[1]
Total	65553	900721				
Bidi smoking						0.042
Never	31277	441290	35	1.0	Reference	
Former	5830	70584	15	1.3	0.7-2.5	
Current	25403	347383	62	1.6	1.0-2.5	
Unknown	3043	41464	4	1.0	0.4-3.0	
Cigarette smoking						0.265
Never	29205	398841	57	1.0	Reference	
Former	5603	71488	18	1.4	0.8-2.4	
Current	27835	390298	39	0.8	0.5-1.2	
Unknown	2910	40093	2	0.4	0.1-1.7	
Tobacco chewing						> 0.5
Never	42190	582656	73	1.0	Reference	
Former	4383	54094	9	0.8	0.4-1.6	
Current	18568	258317	34	0.9	0.6-1.4	
Unknown	412	5653	0			
Alcohol drinking						0.175
Never	33296	454553	51	1.0	Reference	
Former	7857	98248	16	0.9	0.5-1.7	
Current	24399	347905	49	1.3	0.9-2.0	
Unknown	1	14	0			

[1]The *P* for trend (those in unknown categories were excluded). The model used for statistical analysis to obtain the RRs associated with tobacco and alcohol use was as follows: $H = H_s \exp(B_i X_i)$, where the background hazard, Hs, was stratified by attained age, calendar time, occupation and education, and X_i denotes categorical variables related to tobacco and alcohol use. Similar models were used in the analysis that produced the results presented in Tables 3-5.

Table 3 Gastric cancer risk in relation to bidi smoking among men

	Person-years	Gastric cancer cases	RR	95%CI	*P* value[1]
Bidis smoked per day					0.012
Never	441290	35	1.0	Reference	
Former	70584	15	1.3	0.7-2.5	
1-4	40768	4	1.0	0.4-2.8	
5-14	131494	20	1.4	0.8-2.5	
15-24	105359	23	1.9	1.1-3.4	
⩾ 25	67303	15	1.7	0.9-3.2	
Unknown	43924	4	1.0	0.3-2.8	
Duration of bidi smoking					0.036
Never	441290	35	1.0	Reference	
1-14	141330	10	1.3	0.6-2.8	
15-29	123435	14	1.1	0.6-2.1	
30-44	84545	30	2.0	1.2-3.5	
⩾ 45	68393	23	1.6	0.9-3.0	
Unknown	41728	4	1.0	0.4-3.0	
Age at start of bidi smoking					0.161
< 18	64800	14	2.0	1.0-3.9	
18-22	172714	32	1.8	1.1-2.9	
⩾ 23	109709	16	1.3	0.7-2.5	
Never	441290	35	1.0	Reference	
Unknown	41624	4	0.0		
Years since quitting bidi smoking					0.424
Current smokers	347383	62	1.0	Reference	
< 5	28435	6	0.9	0.4-2.0	
5-9	18058	5	1.1	0.5-2.9	
⩾ 10	23055	4	0.6	0.2-1.7	
Never	441290	35	0.6	0.4-1.0	
Unknown	42500	4	0.6	0.2-1.7	

[1]The *P* for trend (those in unknown category were excluded).

As shown in Table 3, where the results of more detailed analysis regarding bidi smoking are summarized, GC risk increased with the number of bidis smoked daily ($P = 0.012$) and with the duration of bidi smoking ($P = 0.036$). Those individuals who started bidi smoking at 22 years old or younger had an elevated GC risk. The cumulative amount of bidi smoking was calculated as the product of the number

Table 4 Gastric cancer risk in relation to cigarette smoking among men

	Person-years	Gastric cancer cases	RR	95%CI	*P* value[1]
Cigarettes smoked per day					0.212
Never	398841	57	1.0	Reference	
Former	71488	18	1.4	0.8-2.3	
≤ 14	357740	36	0.8	0.5-1.2	
≥ 15	43325	3	0.6	0.2-2.1	
Unknown	29327	2	0.6	0.1-2.5	
Duration of cigarette smoking					> 0.5
Never	398841	57	1.0	Reference	
1-14	212691	12	0.9	0.5-1.8	
15-29	134583	14	0.8	0.4-1.5	
30-44	72749	18	1.0	0.6-1.7	
≥ 45	41727	13	0.9	0.5-1.8	
Unknown	40129	2	0.4	0.1-1.7	
Age at start of cigarette smoking					> 0.5
< 18	53786	6	0.8	0.3-1.9	
18-22	193597	20	0.8	0.5-1.4	
≥ 23	143035	13	0.7	0.4-1.3	
Never	398841	57	1.0	Reference	
Unknown	39974	2	0.0		
Years since quitting cigarette smoking					0.109
Current smoker	390298	39	1.0	Reference	
< 5	27180	7	2.0	0.9-4.3	
5-9	18804	6	2.4	1.0-5.6	
≥ 10	24089	5	1.4	0.5-3.5	
Never	398841	57	1.3	0.9-2.0	
Unknown	41508	2	0.5	0.1-2.0	

[1]The *P* for trend (those in unknown categories were excluded).

of bidis smoked per day and the number of years of smoking (bidi-year). GC risk increased with bidi-year (P = 0.017). The RRs for those individuals with 400-799 and 800+ bidi-years were 1.7 (95%CI: 1.0-2.9) and 1.8 (95%CI: 1.0-33), respectively.

As summarized in Table 4, further analysis regarding the effect of cigarette smoking and GC risk showed that the increase in GC risk in former smokers was more evident among those who had quit smoking during the 10 years before the survey. The increase in risk was statistically significant for the group who had quit smoking 5-9 years before the survey (RR = 2.4; 95%CI: 1.0-5.6). The cumulative amount of cigarette smoking, which was calculated as the product of the number of cigarettes smoked daily and the number of years of smoking, was not associated with GC risk.

Further analysis regarding tobacco chewing showed no significant association between GC risk and the amount or duration of the habit (data not shown).

As shown in Table 5, GC risk was not associated with the amount or duration of alcohol drinking. We observed elevated RRs for all types of alcoholic beverages, with the highest RR observed for toddy (RR = 2.3; 95%CI: 0.7-7.3), followed by arrack (RR = 1.7; 95%CI: 0.9-3.3); however, none of the results were statistically significant.

Regarding drinking, we did not have sufficient information to calculate the accurate amount of alcohol consumed per day for each of a wide variety of alcohol types. Therefore, we limited the analyses regarding the amount of alcohol consumption to only arrack drinkers because arrack is the most common liquor (with high alcohol content) among our study population. No association between arrack drinking and GC risk was found in our study population. The RRs for former (n = 862) and current (n = 4139) arrack drinkers versus never alcohol drinkers were 1.5 (95%CI: 0.5-4.9) and 1.7 (95%CI: 0.9-3.2), respectively. In the analysis of daily arrack consumption, the RRs for daily consumption of less than 70 mL per day and 70 mL or more per day were 1.3 (95%CI: 0.3-5.3) and 1.6 (95%CI: 0.8-3.5), respectively. Although GC risk increased with the amount of daily arrack consumption, P for the trend was not statistically significant (P = 0.098). The cumulative amount of arrack drinking was calculated as the product of the amount of daily arrack consumption in ml and the duration of the habit in years (mL-year). No significant increase in GC risk was associated with the ml-year of arrack consumption (P = 0.377).

DISCUSSION

The present study showed that bidi smoking was associated with a higher risk of GC. GC risk increased with the increased number of bidis smoked daily (P = 0.012) and with a longer duration of bidi smoking (P = 0.036). Bidi smoking that started at 22 years old or younger was shown to be significantly associated with a higher risk of GC. Cigarette smoking or tobacco chewing was not significantly associated with GC risk. Alcohol drinking was not significantly associated with

Table 5 Gastric cancer risk in relation to alcohol drinking among men

	Person-years	Gastric cancer cases	RR	95%CI	*P* value
Type of alcohol					
Never drinker	454152	51	1.0	Reference	> 0.5[1]
Former drinker	98248	16	0.9	0.5-1.7	
Toddy	10404	3	2.3	0.7-7.3	
Arrack	60956	12	1.7	0.9-3.3	
Foreign	63835	7	1.4	0.6-3.3	
Combination	209740	27	1.2	0.7-1.9	
Other	3384	0	0.0		
Duration of alcohol consumption					> 0.5[2]
Never	454553	51	1.0	Reference	
1-14	148811	14	1.8	1.0-3.3	
15-29	176222	19	1.0	0.5-1.6	
30-44	71460	26	1.4	0.9-2.3	
⩾ 45	11079	1	0.3	0.0-2.5	
Unknown	38596	5	1.3	0.5-3.2	
Age at start of alcohol drinking					0.179[2]
< 25	146010	15	1.0	0.5-1.7	
⩾ 25	166508	29	1.6	1.0-2.6	
Never	454553	51	1.0	Reference	
Unknown	35400	5	1.5	0.6-3.7	

[1]The *P* for heterogeneity; [2]The *P* for trend (those in unknown categories were excluded).

GC risk either.

Three previous Indian studies examined the relation between bidi smoking and GC risk[11-13]. Among them, two studies (a case-control study and a cohort study) found no association[12,13]. However, the case-control study compared the risk among current smokers with the risk among never smokers and former smokers[12]. In the cohort study[13], we cannot deny the possibility that non-bidi smokers included a significant number of cigarette smokers.

In the present study, we did not see an increase in GC risk in current cigarette smokers; however, an increase in risk, although non-significant, was observed among former smokers. Notably, an increase in GC incidence was observed in those individuals who had quit smoking during the 10 years before the survey. The risk of developing GC for those individuals who stopped smoking less than 5 years before the survey was 2 times the risk for current smokers (RR = 2.0; 95%CI: 0.9-4.3), and the RR increased to 2.4 (95%CI: 1.0-5.6) for those individuals who had stopped smoking between 5-9 years before the survey. This excess risk could be a result of quitting smoking due to experiencing symptoms of chronic atrophic gastritis, intestinal metaplasia or gastro-duodenal ulcers. The same phenomenon has been mentioned as the reason for the decrease in the RR estimates often observed in studies in the highest exposure category possibly due to a lower tolerance of people suffering from symptoms such as chronic indigestion due to the above-mentioned conditions[30].

In the present study, GC risk increased among alcohol drinkers, but the association was not statistically significant. Among the types of alcoholic beverages used, toddy had the largest RR. However, the analysis was based on only three GC cases with a toddy drinking habit. Three previous Indian case-control studies were conducted in Madras, Mumbai and Trivandrum. None of these studies found a significant association between alcohol drinking and GC risk[11,12,16]. In the case-control study performed by Gajalakshmi *et al*[11] in Madras, the estimated odds ratio (OR) was 0.8 (95%CI: 0.41-1.77) for the comparison between current and never drinkers and was 1.4 (95%CI: 0.54-3.40) for ex-drinkers versus never drinkers. Among the types of alcoholic beverages used, statistically significant increases in risk were observed for arrack (OR = 2.6; 95%CI: 1.49-4.40) and foreign liquors (OR = 3.0; 95%CI: 1.49-5.96) but not for toddy (OR = 0.4; 95%CI: 0.09-2.20)[11]. In this alcohol-type specific analysis, the values for former drinkers and current drinkers were combined. The results obtained in the present study were consistent with those findings except for toddy. Indeed, the present study showed statistically non-significant elevated RRs for arrack drinkers (RR = 1.7) and foreign liquor drinkers (RR = 1.4).

The association between tobacco chewing and GC risk has been studied in epidemiological studies from different regions of India, including Madras, Mumbai, Trivandrum and Mizoram[11,12,15,16]. Among these studies, only the hospital-based case–control study in Mizoram found an evident risk increase among tobacco chewers; this study reported an OR of 2.6 (95%CI: 1.1-4.2) for those individuals chewing tobacco alone and an OR of 2.0 for those individuals chewing tobacco with betel nuts (95%CI: 1.3-5.3)[15]. Although the cohort study in Mumbai showed an association of GC risk with smokeless tobacco use, the relation was not statistically significant, and the observed RR was not

large (RR = 1.28; 95%CI: 0.68-2.43)[13].

A recent meta-analysis of 36 studies on socioeconomic position (SEP) and GC risk cited in PubMed and EMBASE from 1966 to 2013 observed a significant increase in GC risk among the lowest SEP categories in occupation and education[31]. The present study showed significant heterogeneity in GC risk among occupational groups (P = 0.008). Those findings most likely indicate that SES factors are related to dietary habits, which are known to be related to GC[32-34].

Helicobacter pylori (*H. pylori*) infection is the most important risk factor of GC and is known to trigger a consequence of pathological changes leading to GC[35]. Risk factors such as tobacco use and alcohol drinking can modify the risk of GC induced by *H. pylori*. The evidence showing that tobacco smoking remains a risk factor among individuals infected with *H. pylori* supports this notion[36]. However, studies in India have not shown a strong association between GC risk and *H. pylori* infection, although its prevalence is high. The high prevalence of *H. pylori* infection in India, despite relatively low GC incidence, is known as the Indian enigma[37]. Taken together, in the results of the present study suggests that bidi smoking increases the risk of *H. pylori*-related GC. However, we cannot deny the possibility that bidi smoking also increases *H. pylori*-unrelated GC risk because we do not have any information on *H. pylori* infection in the present study population.

We do not have any information regarding GC pathology; therefore, we could not distinguish the intestinal and diffuse types. However, the diffuse type is considered only weakly related to lifestyle-related factors such as smoking and dietary habits[38]. Thus, the relations between bidi smoking and GC observed in this study were primarily from the associations with the intestinal type. However, we cannot tell whether bidi smoking increased the risk of both subtypes, although to different magnitudes, or only increased the risk of the intestinal type.

Another limitation of this study is the lack of data regarding dietary habits. A case-control study by Mathew *et al*[16] conducted at Regional Cancer Centre, Trivandrum, South India, found that GC risk was not associated with the consumption of dried fish, which is the primary food item with a high concentration of salt in our study area. Moreover, the consumption of dried fish was not common in the study population. Therefore, we believe that our study results regarding the association between bidi smoking and GC risk is unlikely to be substantially affected by salt intake, which was not considered in the present study.

Mathew *et al* also found that GC risk was related to more frequent rice intake (OR = 3.9; 95%CI: 1.6-10.0 for daily users), hot chili consumption (OR = 7.4; 95%CI: 4.0-13.5) and high-temperature food use (OR = 7.0; 95%CI: 3.7-12.9). The ORs for hot chili and high temperature foods are relatively large in this study, but their CIs are wide. In addition, those habits are less common in the study area; therefore, the percentage of stomach cancer cases related to those habits is expected to be small although the ORs are relatively high. Notably, the association of those factors with bidi smoking is unlikely to be large enough to be able to explain the association between bidi smoking and GC completely. However, the weak associations of cigarette smoking and alcohol drinking with GC risk may be explained by the associations with dietary habits. Regarding rice eating, this habit is so common that everybody eats it; the amount of rice consumption is unlikely to be strongly associated with bidi smoking.

To summarize, in the present cohort study, bidi smoking emerged as a risk factor of GC with a positive dose-response relation with the number and duration of bidi smoking.

COMMENTS

Background

In south Asia, bidi smoking is a popular form of tobacco smoking. Bidi smoking has been shown to cause various cancers. However, the association between bidi smoking and the risk of cancers in the lower digestive tract remains unclear.

Research frontiers

Bidi smoking has been shown to cause cancers of the respiratory tract and upper digestive tract by several epidemiological studies, including the Karunagappally cohort study, one of the most important cohort studies in south Asia. To date, only a few case-control studies have examined the relation between bidi smoking and gastric cancer (GC) risk.

Innovations and breakthroughs

This study is the first cohort study in India to investigate the association of bidi smoking with GC incidence, which has not been shown to date.

Applications

From a public health viewpoint, revealing the associations of bidi smoking with all the major cancers in Asia is important for establishing effective and efficient preventive measures. The information obtained by this study will be useful for this purpose.

Terminology

Bidi: Bidi smoking is a common form of tobacco use in South Asia. A bidi consists of 0.15-0.25 g of sun-dried tobacco flakes hand-wrapped in a temburni leaf. Arrack: Arrack is an alcoholic beverage that is common in South Asia. This distilled beverage is made from paddy, wheat, or palm sap and contains approximately 25%-45% alcohol. Toddy: Toddy is an alcoholic beverage that is common in India. This beverage is prepared locally from the sap of coconut flowers or palm trees and has an alcohol content of approximately 5%-10%.

Peer-review

In the present retrospective cohort study, authors analyzed tobacco smoking and alcohol intake as risk factors for GC. The main limitation is that it has been conducted on a population with a wide variety in socio-economic conditions. Moreover, the type of smoking (bidi) and alcoholic beverage (toddy and arrack) are widespread only in India, and their preparation may change according to the city where the recipe was formulated.

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