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A CASE-CONTROL STUDY OF STOMACH CANCER IN MUMBAI, INDIA

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Stomach cancer incidence rates are much lower in India than elsewhere, but the stomach remains one of the 10 leading sites of cancer in both sexes in most of the metropolitan registries. This is an unmatched case-control study of stomach cancer carried out at Tata Memorial Hospital (TMH), Mumbai. Our purpose was to identify the association of tobacco and alcohol use, occupational hazards, diet, consumption of beverages like tea and coffee, the living environment, cooking media and literacy with stomach cancer. Our study included 170 stomach cancer cases and 2,184 hospital controls interviewed during the period 1988–1992. Tobacco chewing, bidi or cigarette smoking and alcohol drinking did not emerge as high risk factors for stomach cancer. Consumption of dry fish at least once a week compared to never or once a every 2 weeks showed a 12-fold excess risk (OR = 12.4, 95% CI 7.0–22.1, $p < 0.0001$) for stomach cancer among the nonvegetarian food items considered. A protective effect of tea consumption (OR = 0.4, 95% CI 0.2–0.9, $p = 0.03$), showing 59% reduction in risk, was identified, which could be of use for possible control and prevention of this cancer.

Key words: *alcohol; tobacco; diet; dry fish; stomach cancer; India*

The stomach is one of the 5 leading sites of cancer in both sexes in developing and developed countries, but there has been a declining trend in the incidence and mortality of this cancer.[1,2] In India, the stomach was estimated to be the fifth leading site in males and the seventh in females in 1991 with age-standardized rates (ASRs) of 5.0 and 2.8 per 100,000 in males and females, respectively.[3] With the establishment of the National Cancer Registry Programme, cancer incidence data are available for 5 metropolitan areas and 1 rural area in India since 1982. From 1988 through 1992, the stomach was the leading site of cancer in males in Chennai (ASR = 15.9 per 100,000) and Bangalore (ASR = 10.3), fifth in Mumbai (ASR = 7.7) and fourth in Trivandrum (ASR = 6.8); among females, it was the fourth leading site in Chennai (ASR = 7.0), fifth in Bangalore (ASR = 5.1) and sixth in both Mumbai (ASR = 3.8) and Trivandrum (ASR = 2.5).[4] High ASRs for stomach cancer (36.7 for males, 9.9 for females) have been reported in Kashmir Valley, northern India.[5] Rates in India are lower than in other countries around the world.[4] Very few studies in India were carried out to identify the risk factors for stomach cancer. Tobacco smoking (but not tobacco chewing), high-temperature food intake, spicy food and rice eating have been shown to be high risk factors in India.[6,7] The purpose of our case-control study was to identify the association of tobacco usage, alcohol drinking, nonvegetarian dietary items, consumption of beverages like tea and coffee and living environment (type of house, cooking media, source of drinking water) with stomach cancer in India.

MATERIAL AND METHODS

Two social workers routinely interviewed patients attending the hospital before being clinically examined in the Out Patient Department. The questionnaire covered demographic factors, occupation, family history of cancer, use of tobacco and alcohol (including frequency, duration and cessation of these habits) and dietary practices. Medical records were subsequently scrutinised for diagnosis and entered in the forms. This hospital, being a comprehensive cancer centre for diagnosis and treatment, attracts patients from all parts of India; in general, over 30–40% of these patients are found to be free from cancer in 1 year. These cancer-free patients were considered as controls by scrutinising their medical history and diagnosis. During the period 1988–1992, 1,356 patients with gastrointestinal tract cancers were interviewed and 2,914 controls (unmatched) were chosen among patients diagnosed as being free from cancer. There were 170 stomach cancer cases (12.9%) among the interviewed cancer patients. Only cancer patients and hospital controls in the age group 30–75 years were selected for analysis. Among 2,914 hospital controls, 730 who had either infectious disease or benign lesion or age above 75 years or below 30 years were excluded. Based on these criteria, there were 170 cases and 2,184 controls. Of the 2,184 controls, 2,106 were diagnosed as having no evidence of disease. The remaining 78 controls were diagnosed as suffering from inflammatory conditions, including cervicitis, mastitis and fibrosis. Except the above-mentioned criteria, no other matching factor was considered. Histologic confirmation was about 90.6%, 84% being adenocarcinoma type. In general, chewers take pan, betel nut, lime and tobacco with some spices and condiments and smokers smoke Indian cigarettes called *bidis* (obtained by wrapping 0.2–0.3 g of tobacco in tendu leaf), cigarettes, chutta (a kind of cigar), hukka and chilum (clay pipe). Bidi smoking and cigarette smoking are the commonest smoking habits. Alcohol is locally brewed liquor, mostly from palm trees (ethanol content 40–60%). No distinction was made between types of alcohol and it is generally classified as being of local or foreign make.

At a later part of the study, a questionnaire was used to collect additional data on the use and consumption of fruits and vegetables, intake nonvegetarian dietary items, environmental factors like type of house (flat, thatched, chawl etc.), source of drinking water (tap system, well, river, etc.) and cooking media (liquid petroleum gas, kerosene, charcoal, wood, etc.). Consumption of dietary variables was recorded at least once a week, once every 2 weeks, or never. Risk estimates were obtained for those who used items at least once a week compared to other categories. Consumption of beverages was categorised as daily, rarely and never. Risk estimates were obtained for daily users compared to other categories. These additional data were available for 119 cases (70%) and 1,591 (72.8%) hospital controls (data set II). Some sections of the population, mostly among Hindus, consume a strict vegetarian diet (no poultry, fish or other animal products) and were classified as "vegetarians."

Mantel-Haenszel summary χ^2 and unconditional logistic regression were used to estimate the odds ratio (OR), confidence interval (CI) and significance levels.

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TABLE I – GENERAL CHARACTERISTICS OF CANCER PATIENTS AND CONTROLS

	Cases	(%)	Controls	(%)
Total number	170		2,184	
Male	121	71.2	1309	59.9
Female	49	28.8	875	40.1
Average age (years) ± SD	51.9 ± 11.1		48.1 ± 11.4	
30–39	24	14.1	561	25.7
40–49	36	21.2	586	26.8
50–59	62	36.5	558	25.5
60–69	35	20.6	391	17.9
70+	13	7.6	88	4.0
Residence				
Mumbai	57	33.5	1,033	47.3
Maharashtra	57	33.5	564	25.8
Others	56	33.0	587	26.9
Religion				
Hindu	149	87.7	1,753	80.3
Muslim	14	8.2	322	14.7
Christian	3	1.8	64	2.9
Others	4	2.3	45	2.0
Education				
Illiterate	79	46.5	901	41.3
Literate	89	52.4	1,282	58.7
Unknown	2	1.1	1	0.04
Type of habit				
No habit	68	40.0	1,020	46.7
Chewer only	50	29.4	539	24.7
Smoker only	25	14.7	294	13.4
Chewer + smoker only	8	4.7	139	6.4
Alcohol only	3	1.8	19	0.9
Alcohol + chewer only	1	0.6	56	2.6
Alcohol + smoker only	9	5.3	79	3.6
Alcohol + chewer + smoker	6	3.5	37	1.7
Unknown	—	—	1	0.04

RESULTS

The general characteristics of patients and controls regarding age, residence, religion, education and tobacco/alcohol habits are shown in Table I. There were 121 males and 49 females among cases and 1,309 males and 875 females among controls. The average age of patients was 51.9 years (SD = 11.1), whereas among controls the average was 48.1 years (SD = 11.4). A majority of patients and controls belonged to the Hindu community (cases 87.7%, controls 80.3%). About 52.4% of cases and 58.7% of controls were literate. The habit pattern among cases and controls did not vary much and only 3 cases (1.8%) and 19 controls (0.9%) reported alcohol as a single habit. Sixteen cases (9.4%) and 172 controls (7.9%) had combined habits of either chewing or smoking or both along with alcohol. Alcohol use was not reported among female cases and hence, analysis was restricted to males only.

Table II shows the OR for tobacco and alcohol habits, 95% CIs and tests of significance. Risk estimates for different habits were obtained after adjusting for sex and 5 age groups (30–39, 40–49, 50–59, 60–69 and 70+) (Table II). Neither smoking nor chewing emerged as a significant risk factor. The OR for chewers was 1.01 (95% CI 0.7–1.4), whereas for smokers it was 0.9 (95% CI 0.6–1.3). Neither smoking nor tobacco chewing showed a statistically significant association with stomach cancer and the risk level was the same for bidi and cigarette smokers. Alcohol use also did not show any significant association with stomach cancer. The average duration of these habits, particularly tobacco chewing (controls 21.8 ± 12.4 years, cases 26.1 ± 14.5 years), bidi smoking (controls 25.6 ± 12.1 years, cases 27.3 ± 10.4 years) and alcohol drinking (controls 15.5 ± 9.9 years, cases 17.0 ± 10.0 years) did not vary among cases and controls. Dose-response and trend analyses were carried out for tobacco chewing, bidi and cigarette smoking and alcohol, but ORs and trends were not significantly different from unity.

TABLE II – OR ESTIMATES FOR CHEWERS, SMOKERS AND ALCOHOL USERS AND TESTS OF SIGNIFICANCE ADJUSTED FOR 5 AGE GROUPS AND SEX

Factors	Total		
	Cases/controls	OR (95% CI)	*p*
Any habit			
No	68/1,020	1.0	
Yes	102/1,163	1.01 (0.7–1.4)	0.5
Chewers[1]			
Nonchewers	105/1,412	1.0	
Chewers	65/771	1.01 (0.7–1.4)	0.5
Tobacco chewers			
Non-tobacco chewers	109/1,470	1.0	
Tobacco chewers	61/714	1.03 (0.7–1.4)	0.5
Smokers			
Nonsmokers	122/1,634	1.0	
Smokers	48/549	0.9 (0.6–1.3)	0.3
Bidi smokers[1]			
Non-bidi smoker	137/1,780	1.0	
Bidi smoker	33/403	0.8 (0.5–1.2)	0.2
Cigarette smokers[1]			
Non-smoker	156/2,051	1.0	
Cigarette smoker	14/132	1.2 (0.6–2.1)	0.4
Alcohol drinkers[1]			
Nondrinkers	156/1,992	1.0	
Alcohol drinkers	14/191	0.8 (0.4–1.3)	0.2

[1]One control unknown.

TABLE III – OR ESTIMATES AND 95 CIs FOR LITERACY AND 3 OCCUPATIONAL CATEGORIES AFTER ADJUSTING FOR 5 AGE GROUPS, RESIDENCE AND HABIT, FOR MALES ONLY[1]

	Cases	Controls	OR (95% CI)	*p*
Literacy[2]				
Literate	44	439	1.0	
Illiterate	75	868	1.1 (0.7–1.6)	0.4
Agriculture[3]				
No	75	1,006	1.0	
Yes	40	287	1.5 (1.1–2.6)	0.013
Labourer[4]				
No	103	1,143	1.0	
Yes	12	150	1.1 (0.5–2.1)	0.4
Mill[5]				
No	109	1,201	1.0	
Yes	6	90	0.9 (0.3–2.0)	0.5

[1]Adjusted for residence (Mumbai, 1; non-Mumbai, 0) and habit (yes, 1; no, 0).–[2]Two cases and 2 controls unknown.–[3]Six cases and 16 controls unknown.–[4]Six cases and 16 controls unknown.–[5]Six cases and 18 controls unknown.

Factors such as literacy and occupation, which were available for the entire data set, were tested for an association with stomach cancer (Table III). Literacy status was not a risk factor for males. As most of the females did not have an occupation other than as housewives, the analysis was restricted to males only. In the data set, there were 3 main occupational categories: agricultural worker, unskilled laborer and mill or textile worker. ORs, 95% CIs and statistical significance are shown in Table III. Male agricultural workers had a 50% excess risk (OR = 1.5, 95% CI 1.1–2.6) compared to other occupations, whereas laborers and mill/textile workers did not show as high a risk.

OR estimates for dietary factors, beverages and commonly used cooking oil as well as 95% CIs and significance values for data set II are shown in Table IV. OR estimates were obtained after adjusting for 5 age groups, sex and habits. About 28 cases (23.5%) and 469 controls (29.6%) were classified as vegetarians. The percentage of vegetarians (21.8% cases, 27.5% controls) did not differ much in the entire data set. Consumption of nonvegetarian items at least once a week was reported for mutton in 73% of cases and 64.9% of controls, dried fish in 54.6% of cases and 20.6% of controls and chicken in 52.1% of cases and 41.9% of controls;

TABLE IV – OR ESTIMATES AND 95% CIs FOR DIETARY FACTORS, BEVERAGES AND TYPE OF OIL USED FOR COOKING AFTER ADJUSTING FOR HABITS, 5 AGE GROUPS AND SEX (DATA SET II)[1]

Dietary factors	Cases	Controls	OR (95% CI)	*p*
Dry fish				
Never or once in 2 weeks	54	1,262	1.0	
At least once a week	65	329	4.59 (3.1–6.8)	<0.001
Fresh fish				
Never or once in 2 weeks	49	798	1.0	
At least once a week	70	793	1.4 (0.95–2.0)	0.055
Mutton				
Never or once in 2 weeks	32	558	1.0	
At least once a week	87	1,033	1.4 (0.9–2.2)	0.067
Chicken				
Never or once in 2 weeks	57	925	1.0	
At least once a week	62	666	1.4 (0.9–2.1)	0.04
Liver				
Never or once in 2 weeks	93	1,132	1.0	
At least once a week	26	459	0.7 (0.4–1.0)	0.03
Tea[2]				
Never/rarely	14	64	1.0	
Daily	105	1,513	0.28 (0.2–0.5)	0.0003
Coffee[2]				
Never/rarely	116	1,542	1.0	
Daily	3	35	1.2 (0.3–3.5)	0.5

[1]Mumbai, 1; non-Mumbai, 0; habit, 1; no habit, 0; male, 1; female, 0.–[2]Fourteen controls unknown.

TABLE V – OR ESTIMATES AND 95% CIs FOR SELECTED HOUSEHOLD FACILITIES AFTER ADJUSTING FOR RESIDENCE[1], 5 AGE GROUPS AND SEX FOR DATA SET II

	Cases	Controls	OR (95% CI)	*p*
Type of house[2]				
Nonflat	80	524	1.0	
Flat/bungalow/ chawl	39	1,045	0.26 (0.2–0.4)	<0.0001
Cooking medium[3]				
Non-gas	81	1,089	1.0	
Gas	38	483	0.23 (0.1–0.3)	<0.0001
Tap water[4]				
No	54	363	1.0	
Yes	65	1,211	0.4 (0.2–0.5)	<0.0001

[1]Residence (Mumbai, 1; non-Mumbai, 0).–[2]Twenty-two controls unknown.–[3]Nineteen controls unknown.–[4]Seventeen controls unknown.

TABLE VI – LOGISTIC REGRESSION MODEL USING 14 FACTORS ADJUSTED FOR 5 AGE GROUPS, SEX, RESIDENCE, RELIGION AND LITERACY (DATA SET II)[1]

Factors	OR	95% CI	*p*
Bidi	0.7	(0.4–1.3)	0.2
Cigarette	0.7	(0.2–2.1)	0.5
Tobacco chewing	0.7	(0.5–1.2)	0.2
Alcohol	0.7	(0.3–1.7)	0.5
Dry fish	12.4	(7.0–22.1)	<0.0001
Fresh fish	1.3	(0.7–2.4)	0.3
Chicken	1.3	(0.7–2.5)	0.4
Mutton	0.6	(0.3–1.2)	0.2
Liver	0.9	(0.5–1.7)	0.7
Sausages	0.02	(0.01–0.04)	<0.0001
Tea	0.4	(0.2–0.9)	0.03
Agriculture (yes, 1; no, 0)	1.2	(0.7–2.0)	0.5
Labour (yes, 1; no, 0)	1.1	(0.5–2.3)	0.9
Mill	0.8	(0.3–1.9)	0.6

[1]Adjusted for sex (male, 1; female, 0), residence (Mumbai, 1; non-Mumbai, 0), religion (Hindu, 1; non-Hindu, 0), literacy (illiterate, 1; literate, 0) and 5 age groups (30–39, 40–49, 50–59, 60–69, 70+). Beverages categorised as daily *vs.* rarely or never. Dietary items categorised as once a week at least = 1 *vs.* never or once in 2 weeks = 0.

consumption of pork (10.9% of cases and 9.0% of controls), sausages (1.7% of cases and 1.1% of controls) and beef (3.4% of cases and 5.3% of controls) was not common among cases and controls. Intake of dry fish showed an over 4-fold excess risk for stomach cancer (OR = 4.6, 95% CI 3.1–6.8). Consumption of chicken at least once a week compared to once every 2 weeks or never had a 40% excess risk for stomach cancer and a 30% protective effect was found for consumption of liver. Consumption of fresh fish did not show any excess risk for stomach cancer.

Tea and coffee consumption varies in the different regions of India. Tea drinking is generally more prevalent in northern India, whereas coffee drinking is more common in southern regions. In our study, tea drinking was reported in 105 cases and 1,513 controls, whereas coffee drinking was reported in only 3 cases and 35 controls. After adjusting for 5 age groups, sex, residence and habits, tea drinkers had a protective effect for stomach cancer (OR = 0.28, 95% CI 0.2–0.5) compared to non-tea drinkers. Consumption of coffee, though not common, showed a 20% excess risk for stomach cancer, but this was not statistically significant.

The living standard of cases and controls was evaluated by 3 criteria: house type (accommodation), source of drinking water and type of cooking medium (Table V). Residential accommodation was classified as "flat" if it was an apartment, bungalow or chawl (common bath/toilet) and as "nonflat" if it was a thatched house, hut, etc. Thirty-nine cases (32.8%) and 1,046 controls (65.7%) had a flat type of accommodation; an approximately 74% (OR = 0.26, 95% CI 0.2–0.4) reduction in risk was observed for those living in flat accommodation and a 60% (OR = 0.4, 95% CI 0.2–0.5, $p < 0.001$) reduction in risk for those with drinking water supplied by a governmental agency. Use of liquid petroleum gas as cooking medium showed a 77% reduction in risk (OR = 0.23, 95% CI 0.1–0.3) for stomach cancer.

Logistic regression analysis for 14 factors was carried out for data set II and the results are presented in Table VI. After adjusting for confounding variables such as sex, age group, religion, literacy and residence, a 12-fold excess risk was observed for consumption of dry fish (OR = 12.4, 95% CI 7.0–22.1). Alcohol, tobacco chewing and bidi and cigarette smoking did not emerge as risk factors in the final analysis. The protective effect of tea consumption was confirmed in the regression model (OR = 0.4, 95% CI 0.2–0.9, $p < 0.03$).

DISCUSSION

We carried out an unmatched case-control study to identify risk factors for stomach cancer in India. Our study did not include all

stomach cancer patients registered in the hospital during the period 1988–1992 for various reasons. Social workers routinely interviewed patients prior to diagnosis and this, to some extent, controlled the interviewer bias generally associated with case-control studies. The additional data items introduced in the questionnaire during the course of the study and subsequent restriction of cases and controls for analysis may have affected the risk level for some items. In Mumbai, stomach cancer rates are intermediate and not as high as in southern parts of India. Our study did not show tobacco use (chewing and smoking) and alcohol as risk factors for stomach cancer, though other studies conducted in India have shown that bidi and cigarette smoking are significant risk factors for stomach cancer.[6] Hukka smoking among Kashmir Muslim males has been associated with a high incidence of stomach and esophageal cancers.[5] Several studies conducted elsewhere have failed to conclusively establish the association of cigarette smoking and alcohol drinking with stomach cancer.[8] The intestinal histologic type of stomach cancer, but not the diffuse type, has been associated with smoking habit.[9]

In India, alcohol is country-made liquor generally consumed among low socioeconomic strata and hard liquor may not be consumed as frequently as country-made liquor.

In our study, the duration of the alcohol habit, not the quantity consumed during the lifetime, was analysed for a possible dose-response effect. Alcohol drinking did not emerge as a risk factor. Similar findings have been reported from studies conducted in high-risk populations in Chennai, Kerala and the Kashmir.[5,6] Similar findings that did not show alcohol as a risk factor for stomach cancer have been reported.[8,10,11] Wine consumption was positively associated with stomach cancer, whereas consumption of chilled beer, brandy, rum and tequila in Mexico was not associated with stomach cancer.[12,13]

Racial, ethnic and religious differences have been associated with the occurrence of cancer at certain sites, in particular stomach cancer.

In India, the ASRs in Mumbai for the years 1973–1978 revealed that there were variations among religious communities in general for all sites and in particular for digestive tract cancer. Higher incidence rates (ASRs) for stomach cancer in both sexes were observed among Christians (males 16.6, females 9.1) than among Hindus (males 9.4, females 6.1) and Muslims (males 9.1, females 6.6) and this was attributed mainly to differences in the tobacco habit. Further, stomach cancer rates were higher than esophageal cancer rates among Christians and Parsis compared to Hindus and Muslims in Mumbai.[14–16] Parsis generally do not indulge in tobacco chewing and smoking. Dietary practices may play a major role in these observed differences.

The role of diet in stomach cancer has been analyzed previously.[17,18] Consumption of nonvegetarian food, *e.g.,* mutton, chicken, beef, pork, liver and sausages and its association with stomach cancer has not been reported from India. Intake of dry fish has been conclusively shown to be a high risk factor for stomach cancer in other studies,[19–23] and our present findings are in agreement with this.

A study carried out in Korea indicated that meat and fish prepared by pan frying decreased the risk, whereas stewing and broiling of the same food increased the risk.[24] Further studies are required to consolidate these findings.

Data regarding consumption and frequency of intake of green vegetables, root vegetables, sprouts and fruits were also collected; but the analysis on these could not be carried out due either to a small number of cases or controls or to all cases and controls reporting use of these items, preventing calculation of ORs. Many studies have reported that consumption of fruits and vegetables has a protective effect for stomach cancer.[25]

In our study, dietary factors were evaluated individually instead of considering the total dietary intake in terms of average calories and other related biochemical parameters between cases and controls.

It has been shown that Japanese from Japan and Chinese from China settled in the United States have high stomach cancer rates compared to rates in the host country.[4,16] Similar observations have been reported among Indians settled in Natal, South Africa and in Singapore. These migrant populations were mostly from the southern part of India, where high stomach cancer rates are observed. This was attributed to continuation of tobacco habits and dietary practices (staple diet of rice) from the host country.[26]

Consumption of *Brassica* vegetables, red chilies and salted tea among people in Kashmir leads to high intake of dietary amines and nitrate and this is a possible cause of the high incidence of stomach cancer in that region.[27]

Occupational hazards associated with the risk of stomach cancer have been reported. In our study, farmers did not show a statistically significant excess risk in the regression model. Occupations like newspaper publishing and printing, those involving lead exposure, grinding operations (exposure to mineral oil or ethanolamine-based fluids), excavators and pavers, forestry, electric and electronics, sailors and allied groups, motor transport and the food industry have been suggested to be associated with stomach cancer.[28–30]

Helicobacter pylori infection has been postulated as one of the risk factors for stomach cancer. An association of the infection with gastritis and gastric ulcer, precursors of stomach cancer, has been reported.[31] One of the sources of infection may be common water supply systems. A significant negative relationship between drinking water hardness and gastric cancer mortality has been reported from China.[32] In our study, drinking water provided by governmental agency was shown to be protective for stomach cancer, possibly due to the control or absence of *H. pylori* infection.

Consumption of beverages like tea, especially green tea, has been shown to be protective for stomach cancer;[33–35] and our study in a low-risk area confirmed this. Salted tea, commonly consumed by a majority of the population in Kashmir Valley, has been associated with a high incidence of stomach cancer; but no further studies have been carried out to confirm this.[6]

Many other factors, such as body mass index, familial history of smoking habit, high consumption of exogenous nitrosamines and consumption of smoked fish, have been associated with stomach cancer.[36–38] In the absence of conclusive evidence for tobacco and alcohol as risk factors for stomach cancer, dietary factors continue to be the major contributors to either an increased risk or a decreased risk. The general declining trend for stomach cancer all over the world has been largely attributed to sophistication in food-preservation techniques and changes in dietary habits.

The etiology and consequent possible preventive strategy for this cancer still need to be formulated.

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