Risk factors for gastric cancer in South India

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ABSTRACT

<u>Introduction</u>: Stomach cancer is the third most common cancer in South India. A higher incidence has been reported from certain states in northern India, where potential risk factors have been identified. Similar data is available only to a limited extent from southern India. The aim of this case-control study was to evaluate the effects of lifestyle habits and dietary factors on the risk of gastric cancer in South Indians.

<u>Methods</u>: A hospital-based case-control study of matched pairs was conducted in Chennai, India, from 2002 to 2006 in a large tertiary care referral centre in South India. We studied 89 gastric cancer patients and 89 age- and gender-matched healthy controls of the same socioeconomic status. All subjects were interviewed face-to-face by a trained interviewer using a structured questionnaire to collect data about lifestyle habits, such as cigarette smoking, alcohol consumption, tobacco chewing and dietary factors, with special attention to known factors like salted fish, smoked and pickled foods as well as intake of vegetables and fruits.

<u>Results</u>: The response rate was 100 percent. There were 64 male and 25 female patients. The male to female ratio was 2.6:1. The demographic characteristics were similar in the case and control populations. Less than ten percent of patients were below the age of 30 years. Approximately 50 percent were between 30 and 60 years of age, and the rest were over 60 years of age. Multivariate logistic regression models indicated that alcohol consumption (odds ratio [OR] 2.3, 95 percent confidence interval [CI] 1.1–4.9, p-value is 0.04) and consumption of pickled food (OR 1.8, 95 percent CI 1.2–3.9, p-value is 0.05) are independent risk factors for the development of gastric cancer. A protective effect of the consumption of pulses (OR 0.4, 95 percent CI 0.2–0.9, p-value is 0.05), showing a 55 percent reduction in risk, was also identified; this could be of use for possible control and prevention of this cancer. Tobacco chewing and cigarette smoking did not emerge as high risk factors for stomach cancer.

<u>Conclusion</u>: The study showed alcohol and pickled food consumption as independent risk factors for the development of gastric cancer, while consumption of pulses were protective. Cigarette smoking did not predict an increased risk of contracting the disease.

Keywords: cancer risk factors, dietary factors, gastric cancer, stomach factors

INTRODUCTION

Gastric cancer (GCA) remains one of the most common cancers in Asia.[1,2] GCAs are the third most common cancer in India and the second leading site of cancer occurrence worldwide.[3] Multiple factors contribute to the pathogenesis of GCA. Marked differences in GCA incidence among different ethnic groups living in the same geographical area have been observed, pointing to host genetic factors or socioenvironmental factors peculiar to a particular racial group.[4] Environmental factors, including dietary habits, are important in its development.[5,6] Consumption of salted, smoked, pickled and preserved foods rich in salt, nitrite and preformed N-nitroso compounds have been reported to be associated with an increased risk of GCA. High intake of fresh fruits, vegetables and antioxidants has, in contrast, provided a beneficial effect for reducing the risk of GCA.[7]

Smoking and alcohol consumption have been proposed as risk factors for GCA in some epidemiological studies, but their role has been inconsistent.[8,9] Similarly, dietary factors have been studied in some epidemiological studies from northern India, but their role has not been consistently proven.[8] Although the incidence of GCA is comparatively lower in India than in other countries, a high incidence has been noted in southern India, particularly in Chennai.[9] Few studies from South India have looked into dietary factors and social habits in the development of GCA. A study from the Cancer Institute,

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Chennai, identified smoking as the only independent risk factor in the development of GCA, while neither alcohol consumption nor dietary factors influenced the development of GCA.[10] A study population was, however, heterogeneous, consisting of patients from other states within the country, as the institute is a major referral centre. The present case-control study attempted to investigate the effects of dietary factors and social habits on the development of GCA in a large tertiary care referral centre in South India.

METHODS

89 patients with GCA and 89 age-, gender- and socioeconomic status-matched controls were the subjects of this hospital-based case-control study. Cases were all histologically confirmed from January 2002 to January 2006 at Stanley Hospital, Chennai, India. Our hospital is a large tertiary care referral centre for gastrointestinal (GI) diseases in South India. Consecutive patients with histologically-proven GCA were recruited for the study. GCA patients who had coexisting chronic diseases affecting dietary patterns were excluded. Control subjects were selected from an identical population with dyspepsia and who had normal upper endoscopy. In order to increase the compatibility between cases and controls, the controls that were selected belonged to the same socioeconomic status. Individuals with a history of cancer or chronic diseases affecting their dietary pattern were excluded from the control group. We did not perform *Helicobacter pylori (H. pylori)* serology for our patients, since the lower frequency of GCA among Indians despite high *H. pylori* prevalence has been highlighted by a number of studies.[11-13] Ethical committee approval was obtained from the institution and every subject provided their written informed consent for the study.

The first and second authors interviewed every patient using a structured questionnaire (Appendix 1) either in an outpatient or inhospital setting. Dietary details included the frequency of intake and portion size of the food items prior to the illness. These food items were classified as cereals (including rice and wheat), pulses, green vegetables, tamarind, fresh fruits, tubers, salted and pickled foods, meat, cups of tea, coffee and other beverages. A detailed history of smoking and alcohol consumption was also recorded. Odds ratios (OR) of GCA in the presence of a particular factor were used as a measure of the strength of association, and were presented with 95% confidence intervals (CI). Variables with a p-value < 0.20 were then subjected to multivariate analysis using multiple logistic regression

Table I. Basic demographic data and characteristics of gastric cancer patients and control subjects.

Demographics	Cases (n = 89)	Controls (n = 89)
Mean age	56.91 ± 12.93	49.52 ± 15.33
Male:female ratio	64:25	64:25
Residence		
Urban	51	60
Rural	38	29
Educational level		
High	29	17
Medium	23	29
Low	37	43
Religion		
Hindu	82	74
Muslim	5	4
Christian	2	11
Family history of cancer		
Yes	1	1
No	88	88
Per capita income		
High	59	67
Medium	27	16
Low	3	6
Smoker	36	31
Alcohol consumption	32	20
Betel nut chewer	9	9

analysis. The Statistical Package for Social Sciences version 11.0 (SPSS Inc, Chicago, IL, USA) was used for analysis. Logistic regression analysis was done with the development of GCA as the dependent variable and other measured variables significant on univariate analysis.

RESULTS

The mean age and standard deviation was 56.91 ± 12.93 years for cases and 49.52 ± 15.33 years for controls. There were 64 men and 25 women for both cases and controls. The demographics of the study subjects and controls is shown in Table I. Univariate analysis showed alcohol intake, consumption of rice, meat, pickles and tubers as significant risk factors; pulses and fruits were found to be protective for GCA (Table II). Following multivariate analysis using multiple logistic regression analysis, alcohol consumption (OR 2.3, 95% CI 1.1–4.9, p = 0.04) and consumption of pickled food (OR 1.8, 95% CI 1.2–3.9, p = 0.05) were identified as independent risk factors for the development of GCA, while a high intake of pulses (OR 0.4, 95% CI 0.2–0.9, p = 0.05) was protective against GCA.

DISCUSSION

In this study, we have shown that the characteristics of GCA patients are very similar to those reported in the developing world. There was a slight male

Table II. Univariate analysis of risk factors for gastric carcinoma.

Intake of:	GCA cases (n = 89)	Controls (n = 89)	p-value
Rice			
Frequent	89	89	0.001#
Low/none	0	0	
Wheat			
Frequent	40	47	0.22*
Low/None	49	42	
Pulses			
Frequent	61	72	0.001#
Low/None	28	15	
Vegetables			
Frequent	58	53	0.81*
Low/None	31	36	
Fruits			
Frequent	39	38	0.04#
Low/None	50	51	
Tamarind			
Frequent	70	73	0.2*
Low/None	19	16	
Tubers			
Frequent	49	36	0.001#
Low/None	40	53	
Salted fish			
Frequent	49	42	0.200*
Low/None	40	47	
Salted meat			
Frequent	58	41	0.01#
Low/None	31	48	
Salted pickles			
Frequent	56	40	0.03#
Low/None	33	49	
Egg			
Frequent	52	41	0.62*
Low/None	37	48	

GCA: gastric cancer
*p > 0.05; not significant
#p < 0.05; significant

preponderance, and the mean age at diagnosis was 56.9 ± 12.9 years. In our carefully conducted case-control study, we have identified alcohol consumption as an independent risk factor. Studies of the relation between alcohol consumption and the risk of GCA have been largely inconclusive, and case-control studies from India have not identified alcohol intake as an independent risk factor for GCA in India.[8,10] Beer specimens obtained from several Indian cities in South India have been shown to contain N-nitrosodimethylamine in large amounts,[14] and this may be an important factor for the high risk of GCA associated with alcohol consumption in our part of the country. With regard to environmental factors, diet has always been a subject of interest, particularly for GI cancers. In general, an Indian (especially a South Indian) consumes curries rich in spices during all courses of his meals. Curcumin, which is an active ingredient of turmeric powder used in curries, has been shown to have a protective effect against GCA.[15,16]

We also took a careful history for the intake of fresh fruits and vegetables, as well as salted fish, salted pickles and vegetables. A high intake of fresh fruits and vegetables was found to be protective against GCA on univariate analysis, but did not show significance on logistic regression analysis, while the intake of salted pickles was found to be a significant independent risk factor for GCA. The protective role of fresh fruits and vegetables has been noted for a long time and has been postulated for the north–south difference in GCA within a particular country such as China, where the tropical southern parts with a year-round consumption of fresh fruits and vegetables have a lower incidence of cancer than the temperate northern parts.[17] Studies have shown salted and preserved foods to be carcinogenic.[18-20] The present study showed that long-term consumption of pickled food with a high salt content is an independent risk factor for GCA. Salt also enhances H. pylori colonisation, a gastric carcinogen. It can lead to atrophic gastritis, making gastric mucosa more susceptible to the development of carcinoma. Nitrosamine contamination of pickled foods may also be a contributing factor.

In the present study, a low risk of GCA was observed in patients who have a high intake of pulses. This could be the reason for the low incidence of GCA in North India, where pulses are consumed in larger amounts compared to South India, where the consumption of pulses is much lower. The staple food for the people of South India is rice and it has been shown to be an independent risk factor for GCA in another case-control study from the southern part of India.[21] However, we did not identify rice as a risk factor for GCA. Smoking as a variable risk factor for GCA has been reported from India.[8,10] However, smoking did not predict the development of GCA in the present study. The results were contradictory in another study from the same city, which however consisted of a heterogeneous population.[10] This could probably be attributed to cigar smoking rather than cigarette smoking being more common in this part of the country, and explain the non-contribution of smoking as a major risk factor. In addition, there was no significant association between betel quid chewers and GCA.

In a study of risk factors in the development of GCA from South India,[11] a high consumption of rice, high consumption of chilli and consumption of high-temperature foods were found to be independent risk factors. However, we did not consider the consumption of food served at a high temperature as a contributing factor in our study, and rice and chilli consumption were not found to be significant. There are also potential limitations of the study. We did not conduct H. Pylori serology in our study population, as H. pylori as the cause of GCA is uncommon in India.[11-13] The other limitation is the presumption of the adequacy of dietary recall prior

to the illness. However, the dietary pattern of people in South India has remained unchanged for decades (personal observation by VJ) and we do not think this recall bias could have influenced our study.

In conclusion, our study provides further evidence that alcohol consumption and consumption of pickled food are independent risk factors for the development of GCA, while consumption of pulses is a protective factor against its development. In addition, this study also suggests that cigarette smoking may not predict an increased risk of contracting the disease in our population. Efforts to detect cancer early in developing countries would go a long way in reducing the disease burden and improving the outcome.

ACKNOWLEDGEMENT

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APPENDIX 1. Demographics and dietary factors in gastric cancer.

1. Name:

2. Age (years):

3. Inpatient no.:

4. Med GE no.:

5. Gender: (Male: 1; Female: 2)

6. Resident of Chennai (> 5 years): Urban (city dweller): 1; Village (rural): 2

7. Address:

8. Phone no.:

9. Current occupation: homemaker/labourer/retired/others:

10. Alcohol consumption: Yes/No (No: never/< 5 years); (Yes: current/≥ 5 years in the past)

11. Smoking: Yes/No (No: never/< 5 years); (Yes: current/≥ 5 years in the past)

12. Betel nut chewing: Yes/No (No: never/< 5 years); (Yes: current/≥ 5 years in the past)

13. Education: Classification was modified to suit the local population catering to the low and middle classes of population:

    High: Middle/secondary (years 6–12)
    Medium: Primary (up to year 5)
    Low: Illiterate (no education)

14. Per capita income: High: > Rs 3,000/month; medium: Rs 1,001–2,999/month; low ≤ Rs 1,000/month.

15. Family history of cancer: Yes: 1; No: 2

16. Religion: Hindu: 1; Muslim: 2; Christian: 3; others: 4

17. Food item	Normal / high frequency (daily / ≥ 3 times per week)	Moderate frequency (Once per week / once every fortnight)	Low frequency (Once a month / never)
Rice			
Wheat			
Pulses			
Green vegetables			
Fruits			
Tamarind			
Tubers			
Salted fish			
Salted meat			
Eggs/day			
Pickles			
18. Beverage consumption	High (> 400 ml/day)	Moderate (200–400 ml/day)	Low (< 200 ml/day)
Coffee			
Tea			
Milk			
Others (soda/fruit juice)			

19. Upper endoscopy: (findings)

20. Histopathology: (findings)

Signature of patient/subject   Signature of attending physician

Date: Date: