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Lifestyle and Risk of Stomach Cancer: A Hospital-Based Case-Control Study

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Background. Stomach cancer (SC) is the most frequent cancer among males and third most common cancer among females in Madras, India. The incidence rate of SC is higher in Southern India compared to Northern India.

Methods. A hospital-based case-control study on 388 incident cases of SC was carried out in Madras as part of a multicentre study in India to identify the risk factors for SC. Cases were matched to cancer controls based on age (± 5 years), sex, religion and mother tongue. Categorical variables for income group, level of education and area of residence were included in all models to control for confounding.

Results. Smokers had a twofold risk of SC (95% confidence interval [CI] = 1.25–3.78) compared to non smokers and the risk seen among current smokers (odds ratio [OR] = 2.5; 95% CI : 1.36–4.44) was significantly different from that seen among exsmokers (OR = 1.5; 95% CI : 0.67–3.54). The risk among those who smoke bidi (OR = 3.2; 95% CI : 1.80–5.67) was higher than that seen among cigarette (OR = 2.0; 95% CI : 1.07–3.58) and chutta (OR = 2.4; 95% CI : 1.18–4.93) smokers. Significant dose response relationships were observed with age began smoking bidi ($P < 0.001$) and with lifetime exposure to bidi ($P < 0.001$), cigarette ($P < 0.01$) and chutta ($P < 0.05$) smoking. The habits of drinking alcohol and chewing did not emerge as risk factors. An interaction effect was not seen between the lifestyle habits. Attributable risk (AR) for smoking among exsmokers was 33% and current smokers 60%. Population AR for smoking was 31%.

Conclusion. Smoking tobacco is an independent risk factor for SC.

Keywords: case-control study, risk factors, alcohol drinking, smoking and tobacco, Madras

The Cancer Institute (WIA), Madras, is located in South India. It is one of the major National Centers of cancer research and treatment. A large number of cancer patients seek treatment at the Institute from different parts of India but they come largely from the South Indian States (Tamilnadu, Andhrapradesh and Kerala). Both hospital- (HBCR) and population-based (PBCR) cancer registries which are in the network of the National Cancer Registry Programme (NCRP) of the Indian Council of Medical Research (ICMR), Government of India function at the Institute.

Stomach cancer (SC) is the second most common cancer, next to lung cancer in the world. It ranks first among male and third among female cancers seen in Madras PBCR. The age-adjusted (to world population) incidence rates for SC in PBCR in Madras, Bangalore, Bombay, Bhopal and Delhi are 16.4, 12.6, 8.0, 5.1 and 3.8 respectively per 100 000 male population and 6.5, 5.9, 3.7, 3.6 and 2.0 respectively per 100 000 female population.[1] The HBCR in the NCRP network of ICMR are located in Madras, Bangalore and Thiruvananthapuram in South India and Bombay and Dibrugarh in Northern India. The frequency of SC in relation to all cancers seen ranges from 2.4% in Bombay HBCR to 6.9% in Madras HBCR among males and 1.0% in Thiruvananthapuram HBCR to 4.9% in Dibrugarh HBCR among females.[2] Both frequency and age-adjusted incidence rates are low in Northern India compared to Southern India among males and the highest incidence rate is seen in Madras in both sexes compared to other PBCR in India. Because of the intraregional differences in the occurrence of SC, a case-control study on SC was carried out at the Cancer Institute (WIA), Madras as part of a multicentre hospital-based case-control study in India to identify its risk factors.

METHODS AND MATERIALS

The basic design was a hospital-based matched case-control study. The cases were patients with SC diagnosed at the Cancer Institute (WIA), Madras from June 1988 to August 1990. Those with confirmed diagnosis of SC by histology, endoscopy, barium meal, or surgical

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TABLE 1 *Cases and controls by age, sex, educational level, income group and area of residence*

	Cases		Cancer Control	
	No.	%	No.	%
Age group (years)				
<25	2	0.5	2	0.5
25–34	30	7.7	29	7.5
35–44	64	16.5	67	17.3
45–54	84	21.6	86	22.2
55–64	124	32.0	118	30.4
65–74	68	17.5	72	18.6
75+	16	4.1	14	3.6
Sex				
Male	287	73.9	287	73.9
Female	101	26.1	101	26.1
Education (years)				
Nil	114	29.4	112	28.9
<9	194	50.0	184	47.4
9–12	63	16.2	62	16.0
>12	17	4.4	30	7.7
Income				
Low	288	74.2	263	67.8
Middle	71	18.3	94	24.2
High	29	7.57	31	8.0
Area of residence				
Tamilnadu	180	46.4	220	56.7
Andhra Pradesh	176	45.4	145	37.4
Kerala	22	5.7	17	2.3
Other states	10	2.6	6	1.5

procedures were included in the study. Patients with SC diagnosed only by clinical method were excluded from the study group. Controls were cancer patients diagnosed at the Cancer Institute (WIA), Madras from June 1988 to August 1990 but who did not have cancer at the following sites: oral cavity, pharynx, larynx, lung, urinary bladder, pancreas and gastrointestinal tract. Patients with tobacco-related cancers were not included as controls because this may obscure any association, if it exists, between SC and tobacco. Each case was matched with a cancer control from the control pool, using computer programs, on age (± 5 years), sex, religion and mother tongue. If more than one control was matched with a case, one of them was picked randomly. One control was matched with only one case. The percentage distribution of site of cancer in cancer controls was: penis 23.5%, bone and connective tissue 15.2%, skin 13.1%, cervix 11.9%, leukaemia 6.2%, prostate 6.2%, breast 5.2% and other sites 18.7%. Table 1 shows 46% of cases were from Tamilnadu and 45% from Andhrapradesh, so it was not feasible to take population controls for this study.

A structured questionnaire was prepared and a trained social investigator interviewed both cases and controls at the hospital. The items included in the questionnaire were: demographic data, details of present and past occupations, data on income, medical history, family history of cancer, details of lifestyle habits (smoking, drinking alcohol, chewing and taking snuff) and dietary pattern with average frequency of consumption of each food item. To exclude an effect of disease itself on diet, questions regarding diet and eating habits referred to the period 1 year before the date of diagnosis of cancer. The frequencies of consumption were classified as follows: (1) daily or almost daily, (2) 2–4 times per week, (3) <2 times per week, (4) occasionally i.e. less than once a month and (5) very rarely or never. Frequency of consumption of the following were collected: cereals, pulses, meat (lamb, pork, chicken, beef, seafood and fish), eggs, vegetables (leafy vegetables, roots and tubers and other vegetables), salty food, fruits, milk and dairy products, chillies, papad, chutney, pickles, type of oil used for cooking, drinking coffee and tea. The method (fried or not fried) of preparing dishes using vegetables and meat was also collected. A change in dietary pattern, if any, was noted. The dietary pattern section of the questionnaire was designed in consultation with the National Institute of Nutrition, Hyderabad, India.

Under 'details of habits', the following information was ascertained. For smoking—type of tobacco smoked, namely, bidi, cigarette or chutta; for alcohol drinking—type of alcoholic beverages consumed; and for chewing—type of chewing habit, namely, chewing areca nut alone, quid with or without tobacco, or chewing tobacco alone. In addition to this, for each type of habit, age started and stopping the habit and the frequency per day were noted. For the purpose of the analysis ex-smokers/exdrinkers/exchewers were defined as those who had quit the habit for more than 6 months at the time of diagnosis of cancer.

Bidi is a type of local cigarette made from sun cured tobacco which is rolled in a rectangular piece of dried temburni leaf (*Diospyros melanoxylon*) and tied with cotton thread. The tobacco content in each bidi is about 0.2–0.3 gm[3]. Chutta is a type of small cigar consisting of cured tobacco folded into a dried tobacco leaf.[3,4] Chuttas are also known as Cheroots. Quid contains betel leaf which is a leaf of the vine *Piper betel* (Piperaceae), small pieces of areca nut and a pinch of aqueous lime (calcium hydroxide). Areca nut is the fruit of the *Areca catechu* (Palmaceae) tree. It is chewed either alone or with other components of quid. Snuff is a fine tobacco powder used for deep intranasal inhalation.

The type of alcoholic beverages which are commonly consumed are 'Toddy', 'Arrack' and 'Foreign Liquor'. Toddy is a locally fermented palm sap; arrack is a locally brewed liquor with approximately 40% ethanol content and foreign liquor includes wine, whisky, beer, brandy, gin, and rum.

There were no missing values in the data because it was a prospective study and data were not abstracted from the medical records but collected by interview. All items in the questionnaire were coded manually and checked for typographical errors after entry into the computer. Lifetime exposure (LTE) for smoking was calculated as follows: frequency per year * duration of the habit in years. The variable 'age started' was grouped into three levels: those who were ≤20 years, 21–30 years and >30 years when they started the habit and LTE were categorized into three based on number smoked during lifetime. Univariate analysis was done with individual food items. Food items were divided into groups, e.g. meat fried, meat non-fried, salty food, milk and dairy products etc. A multivariate model was constructed for each food group by including simultaneously the individual food items significant in the univariate analysis to evaluate whether there was any confounding effect between the food items in the given food group. The food items which remained significant in each food group in the above multivariate models were included in the final multivariate regression model to evaluate the confounding effect of food items between the food groups and the effect of these variables on the risk of SC. Significant habits (smoking and alcohol drinking) in the univariate model were included in the final model along with chewing habit and dietary items that emerged as significant in the final multivariate model of the dietary analysis to take care of their confounding effect, if any. Categorical variables for income group, level of education and area of residence were included in all models to control for confounding. Odds ratios (OR) and their corresponding 95% confidence intervals (CI) were computed using conditional logistic regression for matched analysis.[5] Trend tests were performed to evaluate dose response relationships. Attributable risk (AR) and population attributable risk (PAR) were estimated using the method described by Cole and McMahon.[6]

RESULTS

Out of 393 SC cases diagnosed at the Cancer Institute from June 1988 to August 1990, 75% of the diagnoses were confirmed by histological verification and 25% by barium meal, exploratory surgery, or endoscopy. Among the histologically confirmed cases, three squamous cell carcinomas and two lymphomas were excluded from the analysis. Thus the total number of cases analysed was 388. The habits of smoking and drinking alcohol are not common among females in India. They were included in the study to find out the effect of chewing tobacco on the development of SC. The data in Table 1 show similar distribution of age and sex which were matching factors among cases and controls. The distribution of level of education, income group and area of residence which were not matching factors in the study were included in all models to control their confounding effect.

Smoking

The data in Table 2 indicate the risk associated with smoking. Odds ratios were calculated using non-smokers as reference group. The OR of current smokers was higher than exsmokers. The likelihood ratio test showed that the risk associated with current smokers was significantly different from that seen among ex-smokers and OR of exsmokers was not statistically significant in the multivariate model (Table 4). Hence further analysis was done only for current smokers. Among current smokers statistically significant risks were seen for smokers of all types of tobacco (bidi, cigarette and chutta smokers) but higher risks were seen for bidi smokers (OR = 3.2; 95% CI : 1.80–5.67) than smokers of other types of tobacco. Those with the habit of smoking more than one type had higher risk than single type users. The risk associated with bidi and cigarette smoking decreased with increased age at onset of smoking. However this trend was statistically significant only for bidi ($P < 0.001$). A twofold risk was seen regardless of the age started the habit of chutta smoking. Lifetime exposure to smoking was divided into three groups based on the number smoked during lifetime as follows: 'Mild' <50 001, 'Moderate' 50 001–100 000 and 'Heavy' >100 000. The risk of SC increased with increase in the quantity smoked during lifetime and these linear trends were statistically significant for all three types (bidi, cigarette and chutta) of tobacco ($P < 0.05$).

Drinking Alcohol

Table 3 shows the risk of SC seen among drinkers of alcoholic beverages and chewers. Non-drinkers were used as the reference group to compute the risk estimates. A higher risk seen for current drinkers of alcohol was not significantly different from that seen for past drinkers. Among the types of alcoholic beverages used, statistically significant risks were observed for arrack and foreign liquor. The significance of risk seen among exdrinkers and current drinkers disappeared in

TABLE 2 *Smoking and risk of stomach cancer*

	Cases	Controls	Odds ratio[a]	(95% confidence interval)
Any tobacco use				
Non-smokers	185	245	1.0[†]	
Exsmokers	44	46	1.8	(1.05–3.13)
Current smokers	159	97	2.7	(1.79–4.07)
Ex & current smokers	203	143	2.5	(1.67–3.61)
Current smokers				
Bidi	72	40	3.2	(1.80–5.67)
Cigarette	43	33	2.0	(1.07–3.58)
Chutta	31	22	2.4	(1.18–4.93)
Combination	13	2	8.2	(1.74–38.9)
Age began (years)				
a Bidi				
≤20	35	19	3.7	(1.66–8.34)
21–30	27	16	2.7	(1.23–5.86)
>30	10	5	3.6	(0.97–13.53)
	Trend test	$P < 0.001$		
b Cigarette				
≤20	17	12	2.4	(0.94–5.88)
21–30	20	14	2.1	(0.85–5.14)
>30	6	7	1.5	(0.40–5.63)
	Trend test	$P < 0.1$		
c Chutta				
≤20	16	11	2.3	(0.89–6.02)
21–30	12	6	2.4	(0.82–7.24)
>30	3	5	2.2	(0.34–13.54)
	Trend test	not significant		
Lifetime exposure				
a Bidi				
Mild	21	17	2.0	(0.90–4.27)
Moderate	17	11	5.3	(1.56–18.28)
Heavy	34	12	4.5	(1.81–11.28)
	Trend test	$P < 0.001$		
b Cigarette				
Mild	18	16	1.6	(0.68–3.62)
Moderate	13	10	2.0	(0.71–5.40)
Heavy	12	7	3.1	(0.93–10.48)
	Trend test	$P < 0.01$		
c Chutta				
Mild	12	12	2.8	(0.92–8.41)
Moderate	8	7	1.5	(0.50–4.58)
Heavy	8	3	4.4	(1.17–16.10)
	Trend test	$P < 0.05$		

[a] Adjusted for income group, educational level and area of residence.
[†] Non-smokers were reference category.

TABLE 3 *Drinking, chewing and risk of stomach cancer*

	Cases	Controls	Odds ratio[a]	(95% confidence interval)
Alcohol				
(Any alcoholic beverage)				
Non-drinkers	285	324	1.0[†]	
Exdrinkers	37	26	1.9	(1.09–3.39)
Current drinkers	66	38	2.3	(1.43–3.74)
Ex & current	103	64	2.2	(1.44–3.19)
a Type				
Toddy	2	7	0.4	(0.09–2.20)
Arrack	62	31	2.6	(1.49–4.40)
Foreign liquor	30	15	3.0	(1.49–5.96)
Combination	9	11	1.0	(0.41–2.52)
Chewers				
Non-chewers	237	257	1.0[†]	
Exchewers	34	32	1.2	(0.65–2.08)
Current chewers	117	99	1.4	(0.96–1.93)
Ex & current	151	131	1.3	(0.95–1.83)
a Type				
Areca nut	15	16	1.2	(0.54–2.44)
Quid	48	42	1.3	(0.81–2.12)
Quid & tobacco	83	70	1.3	(0.89–1.98)

[a] Adjusted for income group, educational level and area of residence.
[†] Non-drinkers, non-chewers were reference category.

the multivariate model (Table 4). Therefore the detailed analysis on age began the habit and LTE is not presented.

Chewing

The OR were calculated using non-chewers as reference category. Non-significantly elevated risk was seen for the habit of chewing (Table 3).

Taking Snuff

Only two cases, five healthy controls and none of the cancer controls had the habit of taking snuff. Hence this variable could not be analysed.

Independent Effects

The habits of smoking and drinking alcohol were highly correlated. Hence they were included in the model with chewing habit, factors which emerged as significant in the multivariate model of dietary analysis, level of education, income group and area of residence to control their confounding effect and the results are shown in

TABLE 4 *Factors significant in multivariate analysis*

Habits	Cases	Controls	Univariate		Multivariate	
			OR	(95% CI)	OR	(95% CI)
Smoking						
Non-smokers	185	245	1.0†		1.0†	
Exsmokers	44	46	1.8	(1.05–3.13)	1.5	(0.67–3.54)
Current smokers	159	97	2.7	(1.79–4.07)	2.5	(1.36–4.44)
Ex & current	203	143	2.5	(1.67–3.61)	2.2	(1.25–3.78)
Drinking alcohol						
Non-drinkers	285	324	1.0†		1.0†	
Exdrinkers	37	26	1.9	(1.09–3.39)	1.4	(0.54–3.40)
Current drinkers	66	38	2.3	(1.43–3.74)	0.8	(0.41–1.77)
Ex & current	103	64	2.2	(1.44–3.19)	1.1	(0.58–1.95)
Chewing						
Non-chewers	237	257	1.0†		1.0†	
Exchewers	34	32	1.2	(0.65–2.08)	0.6	(0.26–1.49)
Current chewers	117	99	1.4	(0.96–1.93)	1.0	(0.56–1.63)
Ex & current	151	131	1.3	(0.95–1.83)	0.8	(0.51–1.37)
a) Roots & tubers[a]						
Occasionally	43	29	1.0†		1.0†	
<2/week	151	114	0.8	(0.47–1.40)	0.7	(0.30–1.44)
2–4/week	144	146	0.7	(0.40–1.20)	0.4	(0.20–0.97)
Daily	50	99	0.3	(0.19–0.62)	0.4	(0.16–0.91)
b) Fried egg						
Never	128	193	1.0†		1.0†	
Occasionally	221	167	2.1	(1.53–3.0)	1.7	(1.04–2.75)
<2/week	32	20	3.9	(1.86–7.98)	4.9	(1.69–13.97)
2–4/week	7	8	1.9	(0.49–7.24)	3.4	(0.52–22.53)
c) Chillies						
Medium	152	263	1.0†		1.0†	
Hot	236	125	3.5	(2.48–5.01)	2.8	(1.73–4.54)
d) Chutney						
Never	19	23	1.0†		1.0†	
Occasionally	140	310	0.6	(0.26–1.15)	0.5	(0.19–1.04)
Regularly	229	55	5.7	(2.54–12.87)	4.5	(1.94–11.78)

[a] Potatoes, beetroot, carrot, turnip, radish, yam etc.
The variables Smoking and Drinking alcohol were adjusted with chewing habit, factors significant in the multivariate model of dietary item analysis, income group, educational level and area of residence.
† Reference category.

Table 4. There was no appreciable difference seen between risk estimate of current smokers in the univariate and multivariate models and the significance of the risk associated with exsmokers and drinkers disappeared in the multivariate model.

The interactions between smoking and drinking alcohol, smoking and chewing or drinking alcohol and chewing were not significant at the 5% level.

The data in Table 4 were used to compute attributable risk percentage (AR%)[6] and population attributable risk percentage (PAR%)[6] in relation to SC. Attributable risk indicates the proportion of SC cases among those with the specified habit (exposed population) that was due to that habit and this proportion could be avoided by eliminating that habit in the exposed population. The risks attributed to smoking among exsmokers and current smokers were respectively 33% and 60%. The PAR which depends on both odds ratio and prevalence of exposure is defined as the proportion of SC cases among the general population (exposed and unexposed to the specified habit) that is attributable to the exposure. The PAR% for smoking was 31.

TABLE 5 *Family history of cancer*

Family history	Cases	Controls	Odds ratio[a]	(95% confidence interval)
Nil	346	348	1.00[†]	
Gastric cancer	12	2	5.73	(1.26–26.05)
Other cancer	30	38	0.89	(0.52–1.51)

[a] Adjusted for income group, educational level and area of residence.
[†] Reference category.

Family History of Cancer

Table 5 shows a significantly higher risk for those with family history of SC and a non-significant risk for those with family history of other cancers compared to those without family history of cancer. The result should be interpreted cautiously because of the small number of subjects with family history of SC.

DISCUSSION

Our study showed a statistically significant twofold risk among smokers (ex- and current) compared to non-smokers. The risk seen among current smokers was significantly different from that of exsmokers. The magnitude of SC risk associated with cigarette smoking reported from both case-control and cohort studies so far has ranged from 1.3 to threefold. However one case-control study[7] has shown reduced risk (OR = 0.52; 95% CI : 0.3–0.89) among current smokers compared to non-smokers and some of the studies could not detect any significant association between cigarette smoking and the risk of SC.[8–10] Only a few case-control studies[11–16] and cohort studies[17,18] have shown significant dose response relationships with the amount smoked and/or with the age started the habit of smoking. Despite the inconsistent findings in the literature, among current smokers the present study reveals significant elevation in the risk associated with cigarette smoking (OR = 2.0; 95% CI : 1.07–3.58) and the risk increased with increase in the quantity of cigarettes smoked during their lifetime ($P < 0.01$).

Epidemiological studies carried out in India have shown an association between bidi smoking and cancers in the following sites: oral cavity, pharynx, larynx and oesophagus.[19–23] The present study shows threefold SC risk with bidi smoking among current smokers and this risk was higher than that seen for current cigarette smokers. Risk decreased with increased age at starting the habit ($P < 0.001$) and increased with increase in the quantity of bidi smoked during the lifetime ($P < 0.001$). Even though the amount of tobacco in bidi (0.2–0.3 g) is less compared to a cigarette (1.0 g)[24] the risk seen with bidi smoking is higher than the risk associated with cigarette smoking. This may be attributed to poor combustibility, possibly due to low porosity of the wrapper (Tendu leaf), which appeared to result in higher concentrations of volatile phenols (as tumour promoting agents), tar and the carcinogenic hydrocarbons benz(a)anthracene and benzo(a)pyrene.[24]

Among controls, 37% were smokers. This is comparable with the finding of 35% as average tobacco prevalence for men in India in the national level survey conducted by the National Sample Survey Organisation.[25] The AR among current smokers (60%) was higher than that of exsmokers (33%) so it is conceivable that the risk among current smokers could be reduced from 60% to 33% if they quit smoking. The PAR% for SC estimated by Siemiatycki *et al.*[26] in Canada was 35% as against 31% from present study. There does not appear to be any other literature on this.

Segi *et al.*[27] noted more heavy sake drinkers among SC cases compared to controls which was not supported by the prospective study done by Hirayama.[28] Wynder *et al.*[29] found no significant differences either in type or quantity of alcohol consumption among cases and controls in their study in Japan and in three other countries. Our study also could not find any significant association between drinking alcoholic beverages and SC risk.[9,10,12,16,18,30–33]

The Third National Cancer Survey reported a non-significant RR of 1.7 in the highest category of smokeless tobacco use.[34] Kneller *et al.*[18] found non-significant elevated risk (RR = 2.3; 95% CI : 0.98–5.22) among users of smokeless tobacco (chewing or taking snuff) compared to tobacco abstainers. A case-control study carried out in a coal mining region of Pennsylvania could not detect any significant association with smokeless tobacco use.[35] The present study also shows no significant association between chewing habit and risk of SC.

Studies have shown increased familial risk of SC[36–39] and Matsukara *et al.* reported the almost simultaneous occurrence of SC in two monozygotic twins.[40] Increased risk of developing SC was seen among those with a family history of gastric cancer and this finding is consistent with other studies.[36,41–45] However, it cannot be excluded that the higher risk for SC seen among those with family history of SC might also be due to shared environmental factors like smoking and diet.

The principle findings of this study are the excess risks and the dose response gradients for smoking bidi,

cigarette or chutta. No significant association was seen between the habits of alcohol drinking or chewing and risk of SC.

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REFERENCES

[1] Annual Report of Population-Based Cancer Registry of the National Cancer Registry Programme. A Project of the Indian Council of Medical Research, New Delhi, India, 1994.

[2] Consolidated Report of the Hospital Cancer Registries (1993) of the National Cancer Registry Programme. A Project of the Indian Council of Medical Research, New Delhi, India, 1995.

[3] Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Tobacco Smoking. IARC Scientific Publication No.38, International Agency for Research on Cancer, Lyon, France, 1986.

[4] Monograph on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Tobacco Habits other than smoking: Betel-Quid and Areca-Nut Chewing; and Some Related Nitrosamines. IARC Scientific Publication No.37, International Agency for Research on Cancer, Lyon, France, 1985.

[5] Breslow N E, Day N E. *Statistical Methods in Cancer Research. Vol.1. The Analysis of Case-Control Studies*. IARC Scientific Publication No. 5, International Agency for Reasearch on Cancer, Lyon, France, 1980.

[6] Cole P, MacMahon B. Attributable risk present in case-control studies. *Br J Prev Soc Med* 1971; **25:** 242–44.

[7] Boeing H, Frentzel-Beyme R, Berger M *et al.* Case-control study on stomach cancer in Germany. *Int J Cancer* 1991; **47:** 858–64.

[8] Jedrychowski W, Wahrendorf J, Popiela T, Rachtan J. A case-control study of dietary factors and stomach cancer risk in Poland. *Int J Cancer* 1986; **37:** 837–42.

[9] La Vecchia C, Negri E, Decarli A, D'Avanzo B, Franceschi S. A case-control study of diet and gastric cancer in Northern Italy. *Int J Cancer* 1987; **40:** 484–89.

[10] Buiatti E, Pall D, Decarli A *et al.* A case-control study of gastric cancer and diet in Italy. *Int J Cancer* 1989; **44:** 611–16.

[11] Correa P, Fontham E, Pickle L W, Chen V, Lin Y, Haenszel W. Dietary determinants of gastric cancer in South Louisiana inhabitants. *J Natl Cancer Inst* 1985; **75:** 645–54.

[12] You W C, Blot W J, Chang Y-S *et al.* Diet and high risk of stomach cancer in Shandong, China. *Cancer Res* 1988; **48:** 3518–23.

[13] Hu J, Zhang S, Jia E *et al.* Diet and cancer of the stomach : A case-control study in China. *Int J Cancer* 1988; **41:** 331–35.

[14] Wu-Williams A H, Yu M C, Mack T M. Life-style, work place, and stomach cancer by subsite in young men of Los Angeles County. *Cancer Res* 1990; **50:** 2569–76.

[15] Kato I, Tominaga S, Ito Y *et al.* A comparative case-control analysis of stomach cancer and atrophic gastritis. *Cancer Res* 1990; **50:** 6559–64.

[16] Tominaga K, Koyama Y, Sasagawa M, Hiroki M, Nagai M. A case-control study of stomach cancer and its genesis in relation to alcohol consumption, smoking and familial cancer history. *Jpn J Cancer Res* 1991; **82:** 974–79.

[17] McLaughlin J K, Hrubee Z, Blot W J, Fraumeni Jr J F. Stomach cancer and cigarette smoking among US Veterans 1954–1980. *Cancer Res* 1990; **50:** 3804.

[18] Kneller R W, McLaughlin J K, Bjelke E *et al.* A cohort study of stomach cancer in a high-risk American population. *Cancer* 1991; **68:** 672–78.

[19] Sanghvi L D, Rao K C M, Khanolkar V R. Smoking and chewing of tobacco in relation to cancer of the upper alimentary tract. *BMJ* 1955; **i:** 1111–14.

[20] Shanta V, Krishnamurthi S. A study of aetiological factors in oral squamous cell carcinoma. *Br J Cancer* 1959; **13:** 381–88.

[21] Shanta V, Krishnamurthi S. Further study in aetiology of carcinomas of the upper alimentary tract. *Br J Cancer* 1963; **17:** 8–23.

[22] Wahi P N, Usha K, Lahiri B. Factors influencing oral and oropharyngeal cancers in India. *Br J Cancer 1965*; **19:** 642–60.

[23] Jussawalla D J, Deshpande V A. Evaluation of cancer risk in tobacco chewers and smokers: An epidemiological assessment. *Cancer* 1971; **28:** 244–52.

[24] Hoffmann D, Sanghvi L D, Wynder E L. Comparative chemical analysis of Indian bidi and American cigarette smoke. *Int J Cancer* 1974; **14:** 49–53.

[25] Sarvekshan. National Sample Survey Organisation, Ministry of Planning, Government of India, Vol.15, No.1 (Issue 48), 1991.

[26] Siemiatycki J, Krenoski D, Franco E, Kaiserman M. Associations between cigarette smoking and each of 21 types of cancer: A multi-site case-control study. *Int J Epidemiol* 1995; **24:** 504–14.

[27] Segi M, Fukushima I, Fujisaku S *et al.* Epidemiological study on cancer in Japan. *Gann* 1957; **48 (Suppl.):** 1–63.

[28] Hirayama T. Epidemiology of stomach cancer. *Gann Monogr* 1971; **11:** 3–19.

[29] Wynder E L, Kmet J, Dungal N, Segi M. An epidemiological investigation of gastric cancer. *Cancer* 1963; **16:** 1461–96.

[30] Acheson E D, Doll R. Dietary factors in carcinoma of the stomach. A study of 100 cases and 200 controls. *Gut* 1964; **5:** 126–31.

[31] Graham S, Schotz W, Martino P. Alimentary factors in the epidemiology of gastric cancer. *Cancer* 1972; **30:** 927–38.

[32] Nomura A, Grove J S, Stemmermann G N, Severson R K. A prospective study of stomach cancer and its relation to diet, cigarettes and alcohol consumption. *Cancer Res* 1990; **50:** 627–31.

[33] Hoshiyama Y, Sasaba T. A case-control study of stomach cancer and its relation to diet, cigarettes and alcohol consumption in Saitama perfecture, Japan. *Cancer Causes Control* 1992; **3:** 441–48.

[34] Williams R R, Stegens N L, Horm J W. Patient interview study from the Third National Cancer Survey: Overview of problems and potentials of these data. *J Natl Cancer Inst* 1977; **58:** 519–24.

[35] Weinberg G B, Kuller L H, Stehr P A. A case-control study of stomach cancer in a coal mining region of Pennsylvania. *Cancer* 1985; **56:** 703–13.

[36] Macklin M T. Inheritance of cancer of the stomach and large intestine in man. *J Natl Cancer Inst* 1960; **24:** 551–71.

[37] Woolf C M, Isaacson E A. An analysis of five stomach cancer families in the state of Utah. *Cancer* 1961; **14:** 1005–16.

[38] Farinati F, Cardin F, Di Mario F *et al.* Genetic, dietary and environmental factors in the pathogenesis of gastric cancer: study of a high incidence family. *It J Gastroenterol* 1987; **19:** 321–24.

[39] Zanghieri G, Di Gregorio C, Sacchetti C *et al.* Familial occurrence of gastric cancer in the 2-year experience of a population-based registry. *Cancer* 1990; **60:** 2047–51.

[40] Matsukara N, Onda M, Tokunaga A *et al.* Simultaneous gastric cancer in monozygotic twins. *Cancer* 1988; **62:** 2430–35.

[41] Ogawa H, Kato I, Tominaga S. Family history of cancer among cancer patients. *Jpn J Cancer Res* 1985; **76:** 113–18.

[42] Kato I, Kito I, Nakazato H, Tominaga S. Second malignancy in stomach cancer patients and its possible risk factors. *Jpn J Clin Oncol* 1986; **16:** 373–81.

[43] Kato I, Tominaga S, Ito Y *et al.* A comparative case control analysis of stomach cancer and atropic gastritis. *Cancer Res* 1990; **50:** 6559–64.

[44] Yu G P, Hsieh C C. Risk factors for stomach cancer: A population-based case control study in Shanghai. *Cancer Causes Control* 1991; **2:** 169–74.

[45] La Vecchia C, Negri E, Franceschi S, Gentile A. Family history and the risk of stomach and colorectal cancer. *Cancer* 1992; **70:** 50–55.

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