

# Nutritional factors in carcinoma oesophagus: a case-control study

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A case control study was conducted on 170 patients with oesophageal cancer. An equal number of healthy persons (attendants of patients) were included in the study as controls to identify nutritional risk factors for oesophageal cancer. The majority (55%) of the patients were of low socio-economic status and from Northern parts of India. They were predominantly male (66%). Increase in risk was associated with low consumption of green leafy vegetables, other vegetables and fresh fruits, milk and milk products. Heavy use of spices and use of very hot tea or food were also associated with increased risk. Differences in the past dietary consumption patterns of oesophageal cancer patients and controls suggest a role for nutritional factors in oesophageal cancer pathogenesis. At the same time substance abuse by cigarette or bidi smoking, alcohol consumption, paan and tobacco chewing also increased risk. After multivariate analysis, green leafy vegetables, other vegetables spices, bidi usage and fresh fruits provided protection against oesophageal cancer.

**Key words: Oesophageal carcinoma, nutrition, green leafy vegetables, fresh fruit, bidi smoking, paan chewing, India**

## Introduction

India has a low to medium incidence of oesophageal cancer according to the National Cancer Registry in Delhi. The incidence rates vary from 1.4 to 11.5 per 100,000 persons in various regions of the country. Oesophageal cancer is the 4th commonest cancer in males and the 5th commonest in females<sup>1</sup>. Oesophageal cancer has been reported to be more common amongst people with poor nutritional status and also amongst low socio-economic groups<sup>2</sup>.

Limited data are available in India on the possible nutritional risk factors for oesophageal carcinoma. Hence, the present study was undertaken to assess the nutritional risk factors.

## Subjects

A case-control study was carried out at the All India Institute of Medical Sciences, New Delhi, India. The study group constituted 170 cases of oesophageal carcinoma, attending the Outpatient Department of Surgery and the Cancer Clinic. Each patient had endoscopic, radiological and histopathological assessments to establish the diagnosis. An equal number of apparently healthy attendees constituted the control group and were matched for age, sex and socio-economic status. Socio-economic status was stratified into 5 groups (lower, upper-lower, lower-middle, upper-middle, upper) based on a modified Kuppuswamy classification dependant on 3 variables: occupation, education and monthly income<sup>4</sup>.

A pretested, semi-structured questionnaire was administered to each case and control to elicit information regarding their (i) socio-economic profile (ii) personal habits of smoking, paan\* chewing, tobacco and alcohol consumption (iii) consumption of beverages (like tea and coffee) at high temperatures and their frequency. The investigators' personal criteria of assessment of hot, warm and/or cold temperature was considered as reference (iv) Past dietary history (15 years before the diagnosis of disease),

assessed by food frequency method. The food frequency questionnaire included enquiry about consumption of the major food groups, with special reference to specific food items. Assistance of parent or spouse was sought wherever possible to further validate past dietary consumption.

## Criteria for Selection

i) First attendance at the hospital outpatient department (ii) Subjects were interviewable (proxy interviews were not accepted) (iii) Neither patient nor control should have suffered a major illness which changed their dietary habits.

## Data Analysis

The "odds ratio" (OR) was used to estimate relative risk, with their 95% confidence intervals (CI) and deviance chi-squared tests for effects<sup>3</sup>. A forward step wise procedure was used to construct a multivariate model of risk, eliminating those habits which had no effect on risk when adjusted for other habits.

## Results

One hundred seventy oesophageal cancer patients were included with an equal number of controls. The majority (55%) of the patients were from the northern parts of India. Of the total cases studied, two thirds (66.4%) were male. Nearly 89.5% of the patients were aged 40 years and above. More than half of the cases (55.2%) belonged to the lowest socio-economic group. All patients complained of dysphagia at the time of their first visit to the hospital. The average duration of dysphagia was  $3.6 \pm 2.3$  months and the range of dysphagia varied from 15 days to 1 year. The majority (54.7%) of patients had lesions in the middle part of the oesophagus, followed by the lower oesophagus (37.6%). Histologically, 79% of the patients had squamous cell carcinoma and the rest had adenocarcinoma.

\*Note: Paan consists of a green leaf (the leaf is from betel vine tree, *piper betel*) in which sliced betel-nut, slaked lime, liquefied catechu and varying amounts of a number of spicy agents are rolled. In India, this is often chewed with tobacco.

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Table 1 gives the relationship between risk for oesophageal cancer and past food consumption pattern. Less frequent consumption (< 3 times per week) of green leafy vegetables (GLV), other vegetables, fresh fruits, milk and milk products was associated with significantly higher risk of oesophageal cancer. Risk was more than 3 fold for low consumption of green leafy vegetables (5.46), other vegetables (4.91), fresh fruits (3.08) and milk products (3.04).

**Table 1.** Effects of dietary variables which decrease oesophageal cancer risk.

Frequencies of consumption	Control n=170	Cases n=170	Odds ratio (95% CI)
<b>Other vegetables</b>			
High: $\geq 3$ times/wk	158	101	1.00
Low: < 3 times/wk	22	69	4.91*** (2.78-8.84)
<b>Green leafy vegetables</b>			
High: $\geq 3$ times/wk	122	54	1.00
Low: < 3 times/wk	48	116	5.46*** (3.35-8.93)
<b>Fresh Fruits</b>			
High: $\geq 3$ times/wk	77	36	1.00
Low: < 3 times/wk	93	134	3.08*** (1.87-5.12)
<b>Milk</b>			
High: $\geq 3$ times/wk	110	91	1.00
Low: < 3 times/wk	60	79	1.59* (1.01-2.52)
<b>Milk Products</b>			
High: $\geq 3$ times/wk	120	75	1.00
Low: < 3 times/wk	50	95	3.04*** (1.9-4.88)

\*  $p < 0.05$ ; \*\*\*  $p < 0.001$

**Table 2.** Effect of dietary variables which increase oesophageal cancer risk.

Variable	Controls n=170	Cases n=170	Odd ratio (95% CI)
<b>Spicy food</b>			
Mild	95	47	1.00
Moderate	57	53	1.88** (1.09-3.24)
Heavy	18	70	7.86*** (4.05-15.56)
<b>Type of tea consumed</b>			
Hot	131	112	1.00
Very hot	39	58	1.74** (1.65-2.89)
<b>Type of food eaten</b>			
Warm	150	119	1.00
Hot	20	51	3.21** (1.76-6.00)

\*\*  $p < 0.01$  \*\*\*  $p < 0.001$

The effect of other dietary variables is shown in Table 2. Risk was increased to almost 8 times when heavily spiced foods were consumed and risk was 3.21 times and 1.74 higher when food and tea were consumed at high temperatures, respectively.

Increase in the risk for oesophageal carcinoma was also observed for cigarette and bidi\* smoking (Table 3). Smoking more than 10 bidis in a day had significantly higher (4.17 fold) risk. Smoking more than 10 cigarettes per day had 2.39 times higher risk. More than 3 fold risk was observed when the alcohol consumption was more than 5 times in a week.

There was increase in the risk with paan chewing, but a significant increase in the risk (2.38 times) was observed for paan chewing containing tobacco. Use of more than 5 paan quid per day had more than 3 times the risk for cancer of oesophagus.

For the purpose of multivariate analysis, milk and milk products were combined together, and were treated as one variable and then all the variables were regressed step-wise. A model of 5 factors was thus obtained including (i) low consumption of other vegetables (ii) heavy use of spices (iii) low consumption of GLV

(iv) number of bidis smoked (v) low consumption of fruits. Low consumption of other vegetables and low consumption of GLV (3 times in a week), had 4.63 times and 2.37 times the risk, respectively, bidi smoking had 2.24 times the risk, low fruit consumption had 1.98 times the risk for oesophageal cancer.

**Table 3.** Effect of cigarette, bidi smoking, alcohol and betel liquid consumption on oesophageal cancer risk.

Variable	Controls n=170	Cases n=170	Odds ratio (95% CI)
<b>Cigarette smoking</b>			
Never	141	131	1.00
$\leq 10$ per day	20	19	1.02 (0.49-2.12)
11+ per day	9	20	2.39*** (1.00-6.17)
<b>Bidi smoking</b>			
Never	139	100	1.00
$\leq 10$ per day	13	16	1.71 (0.73-4.05)
11+ per day	18	54	4.17*** (2.24-8.00)
<b>Alcohol</b>			
Never	144	121	1.00
$\leq 4$ times/wk	17	22	1.55 (0.75-3.26)
> 5 times/wk	9	27	3.60*** (1.56-9.00)
<b>Paan + tobacco chewing</b>			
Never	144	158	1.00
$\leq 5$ paan per day	14	9	1.71 (0.66-4.61)
5+ paan per day	12	3	4.39*** (1.15-24.62)

\*\*\*  $p < 0.001$

**Table 4.** Relative risk estimates and their level of significance for the factors resulting from multivariate analysis.

Variable	OR	P Value
1. Other vegetables	4.63	0.001
2. Quantity of spices used		
Mild	1.19	0.001
Heavy	4.73	0.001
3. Green leafy vegetable	2.37	0.001
4. Bidi	2.24	0.001
5. Fresh fruits	1.98	0.05

## Discussion

Poor nutrition is suspected to be a cause of oesophageal cancer. It is difficult to quantify the possible contribution of diet to the risk of cancer. The present case-control study reveals that decreased consumption (< 3 times in a week) of other vegetables, green leafy vegetables (GLV) and fresh fruits is associated with a significant increase in the relative risk for cancer of the oesophagus. It is 4.63 times for other vegetables, 2.37 times for GLV and 1.98 times for fruits. Several earlier studies have also showed the protective effect of intake of vegetables and fruits for a number of geographic locations<sup>5-7</sup>. Vegetables and fruits are the principal sources of  $\beta$ -carotene, vitamin C and several other micronutrients and various potential anti-tumour phytochemicals. Vitamin C and carotenoids are considered to be antioxidants and are free radical scavengers. These antioxidants can block or repair the free radical damage caused by oxidative events, which is central in cancer causation<sup>8</sup>. Vitamin C is known to block the formation of N-nitroso compounds, these are the carcinogens that can be formed in food or in the digestive tract, once nitrite is present<sup>9</sup>. Several epidemiological studies have reported lower risk with higher intake of vegetables and fruits, with concomitant higher intakes of vitamin C and a range of carotenoids<sup>9-11</sup>.

Ingestion of foods and drinks at high temperature, burning hot, has been shown to increase the risk of oesophageal cancer in many studies<sup>12</sup>. In the present study preference for foods and tea at high temperatures carried 3.21 times and 1.74 times the risk, respectively. Heavy consumption of spicy food was found to convey more than 7 times the risk for oesophageal cancer. Similar findings have been reported by Notani *et al*<sup>13</sup>. Experimental evidence is available for red chillies which contain capsaicin,

\* Note: Bidi is an item which is commonly smoked in India which contains a small amount of tobacco (0.2g to 0.3g) rolled in a dried leaf. This leaf is usually of the Temburni tree, *Diospyros melanoxylon*.

mutagenic in a bacterial test system<sup>14,15</sup> tumour promoting *in vivo*<sup>16</sup>.

Alcohol and tobacco are known major risk factors for oesophageal cancer<sup>17</sup>. Earlier studies from India have identified bidi smoking, paan chewing and paan with tobacco chewing as major risk factors for oesophageal cancer<sup>18,19</sup>. The present study supports previous findings.

Risk with bidi smoking increased 2.24 times smoked ( $p < 0.001$ ). Alcohol consumption is a risk factor for oesophageal cancer, in part because it has adverse effect on nutritional status for a number of reasons. Alcohol consumption can lead to deficiency of certain micronutrients. Certain dietary deficiencies increase the vulnerability of the oesophagus to carcinogens<sup>20</sup>. In the present study alcohol consumption ( $> 5$  times/ week) increased risk 3 times more than those who did not consume alcohol.

The risk was increased significantly when tobacco was present in the quid; risk was 4.39 times when more than 5 quids with

tobacco were consumed in a day. A mechanism by which betel quid could cause cancer is by nitrosation in the mouth of certain components of the quid to form nitrosamines. The major constituents which are likely to be involved in carcinogenesis are the alkaloids, nitrosamines which may be formed in the oral cavity from alkaloids, polyphenols and tannins. In addition, the effect of quid chewing in humans could be potentiated by malnutrition and poor oral hygiene<sup>20</sup>.

To summarise, the present case-control study revealed significant differences in the food consumption pattern between cancer patients and controls indicating the importance of nutritional factors in the aetiology of oesophageal cancer.

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## 食道癌的營養因素：病例—對照的研究

### 摘要

作者選用 170 位食道癌病人為對象，並用相同數目的正常健康人為對照，祈求識別食道癌的營養危險因素。

病人來自印度北部，主要為男性(佔 66%)，且有 55% 屬於社會低收入人群，研究發現凡進食綠葉青菜，其它蔬菜和新鮮水果少者，食道癌發病危險性增加。大量應用調味品，特別是紅辣椒和持續吸煙者發病危險性也增加。該文研究表明，食道癌病人與對照人群過去膳食模式不同，提示了營養因素可能助長食道癌的發生。

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