

Bronchogenic carcinoma in Northern India

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ABSTRACT A study of 336 patients with bronchogenic carcinoma was carried out in Chandigarh, Northern India. The findings suggest that its epidemiology differs in several respects from that in Western countries. Almost a third of all patients and 94.4% of the 54 women had never smoked. The peak frequency of bronchogenic carcinoma occurred between the ages of 51 and 60 years, 14.6% of the patients being aged less than 41 years. Of the 232 smokers and ex-smokers, 48.3% had smoked only cigarettes, 28.4% only bidis (made of naturally cured tobacco), 19.8% both cigarettes and bidis, and 3.4% hukkas. There was a clear association between duration of smoking and frequency of carcinoma. Tumours were classified in 287 (85%) of the patients. Squamous-cell carcinoma was relatively more frequent (32.4%) than any other tumour type and occurred almost exclusively in smokers. Adenocarcinoma was found in 13.2% of patients and was the most frequent tumour in non-smokers. No differences of histological type were found between cigarette smokers and bidi smokers.

Bronchogenic carcinoma is being diagnosed in India with increasing frequency but it is uncertain whether this reflects a rise in its incidence or a greater availability of improved facilities for diagnosing it. Little is known about epidemiological aspects of the disease in India or whether it differs from Western countries in its age and sex distribution, the relative frequency of its histological types, and the contribution made by smoking to its aetiology.

To obtain answers to these questions we carried out a study of patients with bronchogenic carcinoma who were seen at the Postgraduate Institute for Medical Education and Research at Chandigarh, the capital city of the States of Punjab and Haryana, about 250 km north of Delhi. A preliminary report on the findings in 150 patients, seen from 1973 to 1977, has been published elsewhere.¹ During the following two years a further 186 patients were seen; this paper reports our findings in the whole series of 336 patients, which we have compared with those reported in Western countries.

Methods

We reviewed the case notes of every patient in whom a diagnosis of bronchogenic carcinoma had been recorded during the years 1973-9. The major-

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ity of patients lived in Chandigarh or the surrounding district but a few had travelled long distances to reach the institute.

Patients were classified as non-smokers if they denied having ever smoked; those classified as smokers comprised current smokers and ex-smokers. A smoking index was calculated for every smoker; this was the product of the average number of cigarettes or bidis smoked per day and the duration of smoking in years. Three categories of smokers were distinguished by smoking index—those in whom it was not more than 100, those in whom it was 101-300, and those in whom it was more than 300.

In the analysis of the findings smokers were further classified by their form of smoking—that is, whether they had smoked cigarettes, bidis, or hukkas.* The amount smoked by hukka smokers could not be estimated, but because of the large amount of tobacco used and the length of time taken over

**Bidis* are handmade from locally grown tobacco in a cottage industry. After the leaves have been dried in the sun, the tobacco is packed loosely inside a rolled leaf of a tendu plant and secured by a thread. Bidis are cheaper than cigarettes and are smoked widely by both townspeople and villagers in Northern India. A *hukka* comprises a receptacle containing 50-100 g of tobacco mixed with molasses connected to a basin filled with water, from which smoke is drawn through a long pipe. Hukkas in this part of India are of large size and several people participate in smoking them; but in other regions small, portable hukkas are smoked by individuals. Hukka smoking is more common among elderly people and in rural areas.

Distribution of bronchogenic carcinoma by age, sex, and smoking habit

Age (y)	Never smoked				Smokers				Total				Smoker: non-smoker ratio									
	Males No	Females No	Total No	M:F ratio	Males No	Females No	Total No	M:F ratio	Males No	Females No	Total No	M:F ratio										
21-30	2	0.6	4	1.2	6	1.8	0.5:1	5	1.5	—	—	5	1.5	—	7	2.5	4	7.4	11	3.3	1.8:1	0.8:1
31-40	10	3.0	9	2.7	19	5.6	1.1:1	19	5.6	—	—	19	5.6	—	29	10.3	9	16.7	38	11.3	3.2:1	1.0:1
41-50	12	3.6	13	3.9	25	7.4	0.9:1	58	17.3	2	0.6	60	17.9	29:1	70	24.8	15	27.8	85	25.3	4.7:1	2.4:1
51-60	18	5.4	16	4.8	34	10.1	1.2:1	91	27.1	1	0.3	92	27.4	91:1	109	38.6	17	31.4	126	37.4	6.4:1	2.7:1
61-70	8	2.4	7	2.1	15	4.5	1.1:1	42	12.5	—	—	42	12.5	—	50	17.7	7	13.0	57	17.0	7.1:1	2.8:1
≥71	3	0.9	2	0.6	5	1.5	1.5:1	14	4.2	—	—	14	4.2	—	17	6.1	2	3.7	19	5.7	8.5:1	2.8:1
Total	53	15.8	51	15.2	104	31.0	1.0:1	229	68.1	3	0.9	232	69.0	76:1	282	83.9	54	16.1	336	100.0	5.2:1	2.2:1

smoking hukkass they were included in the category of smokers with a smoking index greater than 300.

Histological examination was performed on specimens of sputum, bronchial aspirate obtained at bronchoscopy, pleural fluid, or tissue obtained at bronchoscopy or by needle aspiration of the tumour, biopsy specimens of regional lymph nodes or pleura, and specimens of tumour obtained at thoracotomy or necropsy. The WHO International Histological Classification² was used to classify the tumours.

Results

During the seven years under review a diagnosis of bronchogenic carcinoma was made in 336 patients and was confirmed histologically in 287 (85%). In the remainder, who had terminal illness, the diagnosis was made on clinical and radiographic findings alone.

SEX AND AGE DISTRIBUTION

There were 282 men and 54 women (M:F, 5.2:1), the sex ratio rising progressively from 1.8:1 in the youngest to 8.5:1 in the oldest age group (table). The mean age of the patients was 53.3 years. In both sexes the highest frequency of carcinoma occurred at 51-60 years. Forty-nine patients (14.6%) were aged less than 41 years, and almost a quarter (24.1%) of the women were in this age range. Smoking habit differed greatly between the sexes; whereas 81.2% of the men were smokers only three (5.6%) of the women had ever smoked.

DISTRIBUTION IN NON-SMOKERS AND SMOKERS AND RESIDENCE

Nearly a third of all patients (31%) had never smoked (table). The sex ratio of non-smokers varied only from 0.5:1 to 1.5:1 and did not increase with age as in the whole series.

In the two youngest age groups the number of smokers and non-smokers were almost identical (smoker:non-smoker ratios: 0.8:1 and 1.0:1), but in patients aged more than 40 years the proportion of smokers rose with increasing age.

Of the 232 smokers (including four ex-smokers),

98.7% were men. There was little difference between the age groups in the average amount smoked; hence duration of smoking was the principal factor responsible for the progressive rise in smoking index with increasing age. The majority of smokers (48.3%) had smoked cigarettes only. Of the remainder, 28.4% had smoked bidis only, 19.8% had smoked both cigarettes and bidis, and 3.5% had smoked hukkass only. All three women smokers had smoked bidis.

In 91.3% of the smokers the smoking index was greater than 300. Lower values of smoking index were found only in smokers aged less than 41 years.

The proportion of patients who lived in towns (58.3%) exceeded that of villagers (urban:rural ratio, 1.4:1), but there were no significant differences between them in sex distribution or smoking consumption.

CLINICAL AND RADIOGRAPHIC FINDINGS

The most frequently recorded symptoms were expectoration (62% of patients), haemoptysis (58%), and chest pain (38%). On examination the commonest signs were those of regional collapse (58%), pleural effusion (20%), and superior vena caval compression (17%). Clubbing was present in 20%, and hypertrophic pulmonary osteoarthropathy in 4%. Evidence of chronic obstructive bronchitis or emphysema was found in 24%. Nine patients (2.7%) had neuropathic or myopathic complications of bronchogenic carcinoma. Seven men (2.5%) had gynaecomastia.

The most frequent radiographic findings were opacities with or without collapse (64%), pleural effusion (23%), and widening of the mediastinum (19%). Rib erosion and lymphangitis carcinomatosa were present in a few patients. In 11 (4%) there was radiographic evidence of previous pulmonary tuberculosis.

The commonest sites of metastases were the supraclavicular lymph nodes (26%), the mediastinal nodes (14%), the liver (10%), and the brain (4%).

TREATMENT AND SURVIVAL

Only 10 (3%) of the patients had a resectable

tumour. Chemotherapy, radiotherapy or both were given to 225 patients (77%). The remaining 67 patients (20%) were in a terminal state when first seen and only palliative treatment was given. Because of difficulties in follow-up the survival rate could not be estimated but it was ascertained that at least 34% of the patients had died within a year. Only four patients (1%) were known to have survived for two or more years.

DISTRIBUTION OF TUMOUR TYPES

Histological examination was made of 287 tumours (from 241 men and 46 women). Classification into four main types was possible in 212 tumours (74%). Most of the other 75 tumours, classified as "undifferentiated," were highly anaplastic. In some of the specimens obtained by needle aspiration of the tumour mass changes in cellular morphology made classification impossible.

No association was found between any tumour type and age, though the mean age of patients with squamous-cell carcinoma was significantly higher ($p < 0.01$) than that of any other type. This tumour occurred almost exclusively in smokers; its frequency of 46.7% in 195 smokers was significantly higher than that of 2.2% in 92 non-smokers ($p < 0.001$). Furthermore, its frequency was highest in those smokers whose smoking index was greater than 300. On the other hand, adenocarcinoma (including three tumours of bronchoalveolar type) occurred significantly more frequently ($p < 0.001$) in non-smokers (29.3%) than in smokers (5.6%). This was the most frequently found classifiable tumour in non-smokers. The frequency of this tumour was significantly higher ($p < 0.001$) in the 46 women (34.8%) than in the 241 men (9.1%). The frequency of other tumour types was similar in smokers and non-smokers and in the two sexes.

No differences were found between cigarette smokers and bidi smokers in the frequency of squamous-cell carcinoma or any other tumour type. In only one instance was a tumour (an adenocarcinoma) associated with a fibrous scar due to previous tuberculosis.

Discussion

Increased smoking, urbanisation, and the introduction of new industries has probably led to a rise in the incidence of bronchogenic carcinoma in India. The findings of this study, however, suggest that its epidemiology, at any rate in Northern India, differs in certain respects from that in Western countries. The most noteworthy of these are the younger age range of our patients and the higher proportion of non-smokers.

In smokers and non-smokers of both sexes we found the peak frequency to be 51–60 years, whereas in England and Wales it has been moving steadily upwards and by 1971 it was 75–84 years.³ Contemporary surveys in Western countries have shown that only a small proportion of patients develop the disease before the age of 40 years, except in the special context of young military populations in the United States.^{4–6} In Britain Belcher and Anderson⁷ and, in the United States, Ochs *et al.*⁸ (and Ochs, personal communication) found, respectively, only 1.8% and 2.4% of patients aged less than 40. The findings of surveys carried out during the 1930s, however, suggest that formerly the disease used to occur more frequently in young people. In 1931 Fischer⁹ found that in 13% of 1888 collected cases the age was less than 40, and in 1939 Ochsner and De Bakey¹⁰ reported that in 13.6% of 4307 collected cases the age was 20–39. Thus our own finding of 14.6% of patients aged less than 41 years and the finding of 9% in this age range in another study from India¹¹ point to a similarity between the contemporary epidemiology in India and that in Western countries about 40 years ago.

The overall sex ratio of bronchogenic carcinoma in our patients (5.2:1) was similar to that found in other surveys in India—4.4:1 by Jussawalla *et al.*¹² and 6.9:1 by Viswanathan *et al.*¹¹ Belcher,¹³ in a review made in 1971 of worldwide differences in sex ratio, reported that it ranged from 1.0:1 to 13.5:1. There is some evidence that the sex ratio has undergone changes in Western countries. Adler¹⁴ in 1912 found it to be 3.7:1 and Simon¹⁵ in 1937 reported it to be 4.1:1. Writing in 1939, Ochsner and De Bakey¹⁰ predicted that if women increased smoking the sex ratio should eventually fall. Such a trend was, however, counterbalanced by the great increase in incidence among men, and in Western countries the sex ratio has remained high. In 1958 Burford *et al.*¹⁶ in the United States reported it to be 5.0:1, while in 1972 Bignall and Martin¹⁷ in Britain reported a sex ratio of 4.6:1. The recent increase in incidence among women in the West, which has been associated with a great increase in their smoking, may now give rise to the fall in sex ratio which Ochsner and De Bakey¹⁰ anticipated. Belcher¹⁸ found that it had fallen in Britain from 5.4:1 in 1950 to 4.9:1 in 1970.

Although the overall sex ratio which we found is similar to that in the West, clearly this cannot be explained by a similarity of the contributions made to it by women smokers, since only three (5.6%) of the 54 women in our series had ever smoked. The explanation must lie in the fact that a relatively high proportion (18.8%) of our male patients were also non-smokers. The high proportion of non-smokers

among our patients of both sexes (30.9%) was reflected in a much lower smoker:non-smoker ratio (2.2:1) than those reported in the West. In another study from India Notani and Sanghvi¹⁹ also found a low smoker:non-smoker ratio (3.9:1). These findings from India contrast with those from the United States, in which smoker:non-smoker ratios of 16:1 and 14:1 have been reported.^{20,21}

The findings of our study suggest that smoking, at any rate in men, is as important an aetiological factor of bronchogenic carcinoma in India as in the West. Probably the progressive rise in sex ratio that we found with increasing age was a reflection of the duration of smoking necessary to induce carcinoma in the smokers, of whom 98.7% in our series were men.

In India the smoking of manufactured cigarettes is less common than in Western countries. Of the smokers whom we studied, 28.4% had smoked bidis exclusively and an additional 19.8% had smoked them as well as cigarettes. Not only do bidis contain less tobacco than the common types of Indian cigarettes but the tobacco is dried naturally and in this respect resembles cigar and pipe tobacco. Bidi smokers generally inhale deeply and Jindal and Malik²² showed that as great a rise in carboxyhaemoglobin concentration may occur after smoking a bidi as after a cigarette.

Notani and Sanghvi¹⁹ found no difference in the relative risks of bronchogenic carcinoma from bidi smoking and cigarette smoking. Possibly therefore the lower risk of carcinoma associated with pipes and cigars is due not to their containing naturally cured tobacco (as opposed to the flue-cured tobacco of cigarettes) but rather to the fact that pipe and cigar smokers generally do not inhale. There is little information about the risks of bronchogenic carcinoma from hukka smoking but one study in India has reported an association.²³

Squamous-cell carcinoma in our series occurred almost exclusively in smokers. Because of the smaller proportion of smokers in our series, its relative frequency (32.4%) was lower than that reported in four series from the United States and Britain,^{7,16,24,25} in which it varied from 49.1% to 55.0%. On the other hand, the relative frequency of adenocarcinoma which we found (13.2%) agrees closely with the range of 10.0–15.8% found in those surveys. In our patients this tumour was significantly associated with non-smokers and women.

Our finding that the relative frequency of adenocarcinoma was similar to that in Western countries is difficult to reconcile with the view of Kreyberg,²⁶ who considered that if adenocarcinoma is not caused by smoking an inverse relation should exist in any country between the total incidence of

bronchogenic carcinoma and the proportion of adenocarcinomas. Belcher,¹³ however, has pointed out that this postulate does not always hold true and is inconsistent with the high frequency of adenocarcinoma in Taiwan (38%), where there has been a 10-fold rise in incidence.

The high proportion (30.9%) of our patients who were non-smokers points to the possible existence of some carcinogenic factors other than smoking. Enstrom²⁷ has drawn attention to a rise in mortality from bronchogenic carcinoma among non-smokers in the United States and suggested various factors that might have been responsible. In India domestic air pollution, to which women are particularly liable to be exposed, may be one such factor. It has recently been suggested that kerosene, which is widely used for cooking in towns and villages in India, may be carcinogenic.^{28,29}

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