

## Review Article

# LUNG CANCER AND SMOKING IN ASIA

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## Abstract

The incidence of lung cancer is rising dramatically in Asia. Cancer is currently placed 6<sup>th</sup> to 9<sup>th</sup> in the common causes of mortality in the SAARC region. The most common cancers in Asia are the cancers of head, neck and thorax, which can be directly attributed to the smoking and tobacco chewing habits in the region especially SAARC region. The pattern of cigarette smoking changed globally during last three decade. It is slowly decreasing in developed countries, at a rate of 1% annually and rising in developing countries, at a rate of 2%. Recent studies have shown in addition to the direct tobacco smoking, environmental tobacco smoke has a proven lung carcinogenic effect. As the single most important cause for lung cancer is tobacco smoke, every effort should be taken to control this menace.

**Key Words:** Lung cancer, Asia, Tobacco Smoking

## Epidemiology

Lung cancer is the most frequent malignant disease and most common cause of cancer death in the world with 1.18 million deaths.<sup>1</sup> Almost half (49.9%) of the cases occur in the developing countries, a big change since 1980, when it was estimated that 69% were in developed countries.<sup>2</sup> Worldwide, it is the most common cancer in men, with the highest rates observed in North America and Europe (especially Eastern Europe). In women, incidence rates are lower with a global rate of 12.1 per 100,000 compared to 35.5 per 100,000 in men.<sup>2</sup> Mortality from lung cancer remains very high in the world. The average survival at five years in the United States is 15%, in Europe is 10% and in developing countries is 8.9%.<sup>2</sup> The situation is similar in SAARC countries. In India one year survival has been reported as 9.8 percent.<sup>3</sup>

## Burden of Lung Cancer in Asia

In 2000, there were 1.2 million deaths from cancer of trachea, bronchus and lung globally.

The rate in males was 28.8/100000, and in females 10.8/100000, with considerable regional variation. In Asia, age standardised mortality rates from lung cancer was the highest in China and the lowest in the South Pacific Islands with rates of 29.1 and 13.8/100000 in males and 14.5 and 7.7/100000 in females respectively.<sup>4</sup>

## Trends in lung cancer mortality and incidence in Asia

In many developed countries, lung cancer mortality has declined since 1980s.<sup>5</sup> In developing countries, lung cancer is primarily a problem of males whereas the rates in females are low in all populations, except for those of Chinese origin. Chinese women have relatively high incidence of lung cancers compared with other ethnic groups in the region.<sup>6</sup>

A recent report from China shows a gradual increase in lung cancer rates in the past decade, mostly in men.<sup>7</sup>

In South Korea, the age adjusted mortality rate from lung cancer increased from 3.7 in 1980 to 17.8/100000 in 1994 in males and from 1.4 to 7/100000 in females.<sup>8</sup>

In India lung cancer is the leading cancer of both sexes in three of the Urban Cancer Registries (Bhopal, Delhi and Mumbai).<sup>9</sup>

A study done in Kashmir, India, using 321 lung cancer patients revealed that there was a preponderance of males (91.9%) as compared to females (8.1%) with male to female ratio of

11.3:1.<sup>10</sup> In India other studies show that male to female ratio varies from 5.76:1 to 6.7:1.<sup>11</sup>

### Cancer pattern among males in South Asian Region

The Age Standardized Rate (ASR) per 100,000 of top ten cancers among males in different countries in South Asia is given in Table 1

**Table 1 Top Ten Cancer in South Asian Countries, Males, Year 2000**

India		Pakistan		Bangladesh		Sri Lanka	
Site	ASR	Site	ASR	Site	ASR	Site	ASR
Oral cavity	12.8	Lung	20.1	Lung	22.4	Oral cavity	36.1
Other Pharynx	9.6	Oral cavity	14.7	Larynx	15.4	Oesophagus	8.2
Lung	9.0	Bladder	8.8	Oral cavity	13.4	Other Pharynx	6.1
Oesophagus	7.6	Larynx	8.5	Other Pharynx	12.5	Leukaemia	5.5
Larynx	6.2	Other Pharynx	6.7	Oesophagus	6.9	Larynx	4.5
Stomach	5.7	Oesophagus	6.3	NHL	2.8	Lung	1.9
Colon/Rectum	4.7	Liver	5.6	Stomach	1.6	Bladder	1.9
Prostate	4.6	NHL	5.1	Liver	1.3	Colon/Rectum	1.8
Leukaemia	3.1	Colon/Rectum	5.0	Testis	0.9	Thyroid	1.3
NHL	3.2	Leukaemia	3.4	Leukaemia	0.9	Stomach	1.2

*Source: Cancer Awareness, Prevention and Control; Strategies for South Asia-A UCII Hand book.*

According to table 1, lung cancer is the commonest in Bangladesh and Pakistan with not much of a difference in the incidence rates between themselves but double the times higher than India and ten times more than Sri Lanka.

### Smoking and lung cancer in Asia

Tobacco use, especially cigarette smoking, accounts for up to 90% of all lung cancer deaths worldwide.<sup>12, 13</sup> Fewer than 20% of cigarette smokers, however, develop lung cancer, suggesting that other factors play a role in the disease.<sup>14</sup> Other causes of lung cancer include environmental factors such as tobacco smoke, radon and various occupational exposures. Diet and pre-existent non malignant lung disease also have been associated with the risk for developing lung cancer.<sup>15</sup>

Before the 20<sup>th</sup> century, tobacco usually was chewed or inhaled in the form of snuff. Therefore lung cancer was rare before the 20<sup>th</sup> century. Majority of lung cancer cases have been convincingly proved to be associated with smoking habits. The first epidemiological study on the relationship between tobacco and lung cancer was published in 1939 by several German physicians.<sup>16</sup>

After that several prospective studies worldwide have shown significantly higher cancer mortality rates among smokers than non smokers, table 2.

**Table 2 Relative Risk for death from lung cancer for Men: Major Prospective studies in the World**

Study	Smoking Status	Relative Risk
Cancer Prevention Study II (1982 – 1988)	Never smoked	1.0
	Former smokers	9.4
	Current smokers	20.3
Kaiser Permanent Medical Care Programme Study (1979 – 1987)	Never smoked	1.0
	Current smokers	8.1
Japanese study of 29 health districts (1966 – 1982)	Non smokers	1.0
	Current smokers	3.8
Swedish study (1963 – 1979)	Non smokers	1.0
	Current smokers	7.0
British doctor's study (1951 -1973)	Non smokers	1.0
	Current smokers	14.0

Source: US Department of Health and Human Services. A Report of the Surgeon General, Centre for Disease Control and Prevention, Office on Smoking and Health, 2001.

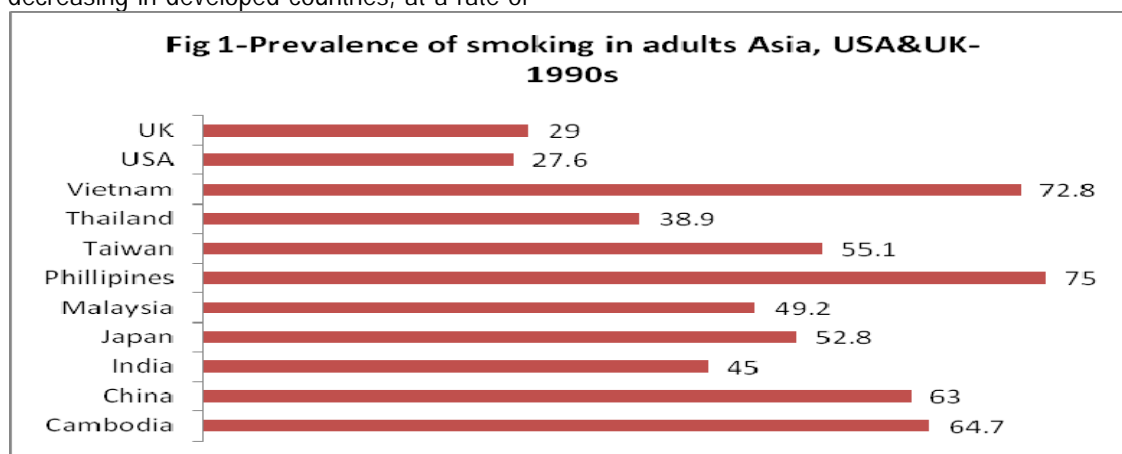
Table 2 shows in current male smokers, relative risk for death from lung cancer compared with non smokers varies from about 3.8 times to more than 20 times.<sup>17</sup>

Tobacco smoke is a complex mixture of over 4000 different chemicals, of which over 40 compounds have been evaluated by the International Agency for Research on Cancer (IARC) in animals as carcinogens. Polycyclic aromatic hydrocarbon in tobacco smoke have been shown carcinogenic to animals.<sup>18</sup>

The pattern of cigarette smoking changed globally during last three decade. It is slowly decreasing in developed countries, at a rate of

1% annually and rising in developing countries, at a rate of 2%.<sup>19</sup> With this trend, tobacco companies are directing aggressive marketing campaigns in developing countries in both Asia and Africa, targeting not only men but also women and young people.<sup>20</sup>

Figure 1 shows prevalence of smoking in adults and adolescents by sex in selected Asian and in the US and UK in the 1990s. In adults the prevalence of smoking in many Asian countries now exceeds those of the US and UK.<sup>21</sup>



Source: Centre for Disease Control and Prevention. National Tobacco Information Online System (NATIONS), Atlanta, GA, CDC

### Epidemiology of Smoking in Asia

Annual per capita cigarette consumption and prevalence of smoking in adult male and

female in SAARC countries -2001 are listed in the Table 3.

**Table 3 Annual per capita cigarette consumption and prevalence of smoking in adult male and females in SAARC countries -2001**

Country	Prevalence of adult smoking			Cigarette consumption(Annual per person)
	Total (%)	Male (%)	Female (%)	
Afghanistan	No Data	No Data	No Data	98
Bangladesh	38.7%	53.6%	23.8%	245
India	No Data	29.4%	2.50%	129
Maldives	26%	37%	15%	1441
Nepal	38.5%	48%	29%	619
Pakistan	22.5%	36%	9%	564
Sri Lanka	13.7%	25.7%	1.7%	374

Source: Machael J, Eriksen M. (2001) The Tobacco Atlas, World Health Organization

According to the table 3, the highest per capita cigarette consumption in the region is seen in Maldives, Nepal and Pakistan.

The smoking habits of Indians are different from that observed in the Western society. In India tobacco is used in various forms such as the cigarette, bidi, hooka, chutta, chillum and pan masala.<sup>22</sup>

Bidi smoking, which is extremely common in rural India, carries a higher risk of lung cancer compared to cigarette smoking.<sup>23</sup> (In India seven bidis are sold for every one cigarette).

In China, the estimated consumption of cigarettes per adult increased by 260% between 1970 and 1990. The rates of smoking are very high in both urban and rural areas in men, with rates of 60% and 64% and 15% and 9% in women respectively.<sup>24</sup>

Smoking cessation has been associated with a declining risk for lung cancer. The relative risk for lung cancer among former smokers begins to drop 5 years after they quit smoking and continues to drop thereafter; however, the relative risk in former smokers never reaches the risk of life-long non smokers.<sup>25</sup>

### Passive smoking (Environmental Tobacco Smoke (ETS))

ETS consists of side stream smoke and the exhaled smoke of the smoker. Some known carcinogens such as benzo(a)pyrene, nitrosamine and  $^{210}\text{Po}$  are present in higher concentration in side stream smoke.<sup>26</sup> ETS is now classified as a class A carcinogen, responsible for 20% of lung cancers in non-smokers.<sup>27</sup>

The association between passive smoking and lung cancer risk is biologically plausible because of the similar chemical composition of smoke inhaled directly from a cigarette and smoke from a burning cigarette and the demonstration of absorption of a tobacco

specific carcinogen in the urine of non-smokers exposed to cigarette smoke.<sup>28</sup>

Hirayama<sup>29</sup> from Japan in 1981 reported that age – adjusted lung cancer mortality rates were lowest for wives of non-smokers, intermediate for wives of light or ex-smokers and highest for wives of heavy smokers. A meta analysis of 35 case- control and 5 cohort studies showed that the relative risk among lung cancer among non-smoking women ever exposed to ETS by their husbands was 1.2 (1.05-1.28)<sup>30</sup> Rapiti *et al*/from Chandigarh India recently reported high risk of lung cancer among those who exposed to ETS in childhood.<sup>31</sup> Because of the low prevalence of smoking in Asian women, any misclassification bias should be small, and the Asian evidence for causal relationship between passive smoking and lung cancer is particularly strong.<sup>32</sup>

As in active cigarette smoking, the risk for lung cancer from exposure to ETS also may be influenced by genetic factors. Using archival tumour tissue from 106 women with lung cancer who were lifelong non smokers, Bennett *et al* revealed that those patients with significant exposure to ETS were statistically more likely to be deficient in glutathione S-transferase M1 (GSTM1), an enzyme believed to be important in the detoxification of tobacco smoke carcinogen, when compared with patient without such exposure (OR-2).<sup>33</sup>

### Histological types of lung cancer

Based on the biology, therapy and prognosis, lung cancer is broadly divided in to two categories.

1. Non small cell lung cancer (NSCLC)
2. Small cell lung cancer (SCLC)

Squamous cell carcinoma, adeno carcinoma and large cell carcinoma are classified as NSCLC and account for 75% to 80% of all lung cancer cases.<sup>34</sup>

Before 1980, the predominant cell type in lung cancer worldwide was Squamous cell carcinoma. Since then there has been gradual increase incidence of adeno carcinoma, with a corresponding decline in squamous cell cancers in many developed countries .The same changing pattern is observed in some Asian countries. In Taiwan, a study of over 10000 lung cancer cases over the period1970-1993 showed that the incidence of squamous cell carcinoma decreased from 46.4% to 36.2% in men, whereas adenocarcinoma increased from 30% to 36% in men.<sup>35</sup> A similar pattern was found in Singapore, Japan, Korea and Hong Kong.<sup>36-39</sup>

However, clinical profile and histological type of lung cancer in India is different from the developed countries, in that Indian patients present almost 15-20 years earlier, in the 5<sup>th</sup> and 6<sup>th</sup> decade of life<sup>40</sup> and squamous cell carcinoma continues to be the commonest histological type.<sup>41</sup>

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