Review

Lung Cancer Related to Environmental and Occupational Hazards and Epidemiology in Chiang Mai, Thailand

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The causes of lung cancer in northern Thailand have not been completely understood, but it is strongly believed that they are multi-factorial. The environmental and occupational factors have played a significant role on lung cancer. They can be categorized as physical, chemical, and biological. In the northern region of Thailand, specifically Chiang Mai province, it has been recognized that the incidence of lung cancer is among the highest in Thailand. For example, in the year 2007, the age-standardized incidence rate in males was 31.3 and that in female was 22.9 per 100,000 population. The district ranked the highest was Muang district, Chiang Mai. The previous studies showed that, apart from smoking, the indoor radon, air pollution and genetic factors might be the causes.

Key words: air pollution, gene, lung cancer, polycyclic aromatic hydrocarbon, radon, Thailand

Introduction

Lung cancer is the leading cause of cancer death worldwide. In Thailand, lung cancer has ranked first for new cancers among males in Chiang Mai since the first population-based registration in 1983 (1). Although smoking is the major cause of lung cancer, this factor alone could not explain the high incidence in northern Thailand (2). In this article, the environmental and occupational hazards related to lung cancer have been reviewed, including the epidemiology of lung cancer in Thailand and northern Thailand. Finally, the risk factors of lung cancer in the area have been postulated.

Environmental and Occupational Hazards

Among cancers that are associated with occupational exposures, cancer of the lung is the most common (3). Although the causes of lung cancer are almost exclusively environmental, it is likely that there is substantial individual variation in the susceptibility to lung cancer (4). Environmental and occupational hazards can be broadly divided into 3 categories: physical, chemical, and biological. The followings are the details of each category.

Physical hazards: There have been epidemiological studies showing that exposure to high doses of radiation

is associated with lung cancer especially ionizing radiation (4). However, the risks of low-dose radiation, which are more relevant to contemporary workers and the general population, have proven difficult to characterize (5). So far, radon—produced naturally from uranium in the decay series of uranium and categorized as high linear energy transfer (LET) radiation—is the second cause of lung cancer after smoking in many countries (6). It is quite clear that two of the decay products of radon emit α particles, which are high in energy and mass, causing damage to the DNA of cells of the respiratory epithelium. Even though epidemiologic studies of underground miners of uranium (7) and residents living near uranium milling and mining (8) have established that exposure to radon daughters is a cause of lung cancer, exposure to indoor radon also is assumed to cause lung cancer, but the magnitude of the risk is unclear (9–11). In contrast, the risk of lung cancer associated with exposure to lower doses of low-LET (e.g., x-rays and gamma rays) is small (12,13).

Chemical hazards: Cigarette smoking is by far the leading cause of lung cancer, accounting for approximately 90% of lung cancer cases in many countries where cigarette smoking is common (14). According to the evaluations by the International Agency for Research on Cancer, compounds for which there is “sufficient evidence for carcinogenicity” in either laboratory animals or humans are: polycyclic aromatic hydrocarbons (PAH) (such as: benzo[*b*]fluoranthene, benzo[*j*]fluoranthene, benzo[*k*]fluoranthene, dibenzo[*a,i*]pyrene, indeno[1,2,3-*cd*]pyrene, dibenz[*a,h*]anthracene, 5-methylchrysene), dibenz[*a,h*]acridine, 7H-dibenzo[*c,g*]carbazole, *N*-nitrosodiethylamine, 4-(methyl-nitrosamino)-1-(3-pyridyl)-1-butanone, 1,3-butadiene, ethyl carbamate, nickel, chromium, cadmium, polonium-210, arsenic, and hydrazine (15,16).

Apart from chemical carcinogens in tobacco smoke,

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other chemicals related to lung cancer are silica (17), asbestos (18), beryllium (19), bis-chloromethyl ether (20), and polyvinyl chloride (21).

Biological hazards: Researches looking at microorganism as a possible cause of lung cancer are still in the beginning. Infectious agents that have been associated with lung cancer in newer studies include: *Chlamydia pneumoniae* (22), human papilloma virus (23), measles virus (24), and pneumocystis (25). However, more studies are needed to link these microorganisms to lung cancer.

Cancer in Thailand

Thailand is located in the Southeast Asia between latitudes 5:37 N and 20:27 N and between longitudes 97:22 E and 105:37 E. It is bordered to the north with Laos and Myanmar, to the east with Laos and Cambodia, to the south with the Gulf of Thailand and Malaysia, and to the west with the Andaman Sea and Myanmar. The total area is 513,155 km². The climate of the country as a whole is tropical and characterized by monsoons. Thailand is divided into 77 provinces, within four geographical regions: the Northern, Northeastern,

Fig. 1. Map of Thailand and the 4 provinces in northern Thailand (marked as black dots).

Fig. 2. Thailand age-standardized incidence rates per 100,000 population (ASR), all sites, 1995–2003.

Fig. 3. ASRs of all cancer sites in northern Thailand, 2003–2007, compared to Japan and the US. *The incidence is in 2008.

Table 1. The 10 leading cancers in males and females of Thailand, 2001–2003

Males	ASR	Females	ASR
Liver and bile duct	38.6	Breast	20.9
Trachea, bronchus and lung	24.9	Cervix uteri	18.1
Colon and rectum	11.3	Liver and bile duct	14.6
Prostate	5.5	Trachea, bronchus and lung	9.7
Non-Hodgkin lymphoma	5.0	Colon and rectum	7.9
Leukemia	4.9	Ovary	5.1
Bladder	4.6	Leukemia	3.7
Oral cavity	4.5	Oral cavity	3.7
Stomach	4.1	Thyroid	3.7
Esophagus	3.2	Non-Hodgkin lymphoma	3.2

Southern, and Central (see Fig. 1).

For cancer incidences in 2001–2003 according to the National Cancer Institute of Thailand (26), there were 121,986 new cancer cases in males with an age-standardized incidence rate per 100,000 population per annum (ASR) of 143.3 and there were 119,065 new cancer

cases in females with an ASR of 118.6. Figure 2 shows the trend of ASRs by gender during 1995–2003. During 2001–2003, the most common cancer type in males was liver and bile duct cancer, totally 33,313 cases with an ASR of 38.6 followed by trachea, bronchus, and lung cancer totally 20,602 cases with an ASR of 24.9. The most common cancer type in females was breast cancer, totally 21,967 cases with an ASR of 20.9 followed by cervical and uterine cancer, totally 19,011 cases with an ASR of 18.1. Table 1 shows the 10 leading cancers in males and females in Thailand.

Cancer Incidence in Northern Thailand

Regarding cancer incidences in northern Thailand, based on the data of 4 provinces: Chaing Mai, Lampang, Lamphun and Phitsanulok, during 2003–2007 (27), there were 40,872 new cancer cases in males with an ASR of 125.7 and there were 44,190 new cancer cases in females with an ASR of 119.4. ASRs of males and females in northern Thailand were slightly lower than those in Thailand as illustrated in Fig. 3.

Among these 4 provinces, the region with the highest cancer incidence in males was Lampang province (ASR of 170.5) and that in females was Lamphun province

Table 2. The 10 leading cancers in males and females of northern Thailand, 2003–2007

Males	ASR	Females	ASR
Lung	30.0	Breast	20.8
Liver	24.4	Cervix	19.4
Colorectal	10.4	Lung	16.7
Lymphoma	5.8	Colorectal	7.9
Leukemia	5.2	Liver	7.9
Prostate	4.6	Ovary	4.7
Stomach	4.5	Leukemia	3.9
Bladder	4.0	Lymphoma	3.7
Skin	3.5	Skin	3.3
Oral cavity	3.2	Thyroid	3.1

(ASR of 163.8). These ASR values of males and females are higher than those of Thailand in 2008, respectively. However, they are lower than those of Japan (ASR of 247.3 in males and 167.6 in females in 2008) or those of the US (ASR of 335.0 in males and 274.4 in females in 2008) (28) (see Fig. 3).

Lung Cancer in Northern Thailand

In northern Thailand (see Fig. 1) during 2003–2007, the total number of new lung cancers was 15,604 cases, 9,603 in males and 6,001 in females. The sex ratio of males and females was approximately 1.6:1. The ASRs of lung cancer were 30.0 in males (ranking the first among cancers) and 16.7 in females (ranking the third among cancers) (see Table 2). Among 4 provinces in northern Thailand, the province with highest incidence of lung cancer of males and females was Lampang (ASRs of 48.4 in males and 25.4 in females), which was

Fig. 4. ASRs of lung cancer by region in northern Thailand, 2003–2007, compared to Japan and the US. *The incidence is in 2008.

Fig. 5. Age-specific ASRs in northern Thailand, 2003–2007.

the highest among those of 77 provinces in Thailand (26), where the ASR in males was 26.8 and that in females was 12.1 in 2008 (28). However, the incidences of lung cancer in both genders are lower than those in the US in 2008 (ASR of 49.5 in males and 36.2 in females); although they are higher than those in Japan in 2008 (ASR of 38.7 in males and 13.3 in females) (28) (see Fig. 4). Figure 5 shows the age-specific ASRs of lung cancer. It can be clearly seen that the incidences in both genders are exponentially increasing after the age of 45 and peaked at the seventh decade.

Lung Cancer in Chiang Mai

The lung cancer incidences in Chiang Mai, shown in Fig. 6, tend to be slightly decreasing over the years 2001–2007. In 2007, the ASR in males was 31.3 and that in females was 22.9 (1). Chiang Mai comprises 25 districts and, according to the lung cancer registration in district level, the district with the highest incidence of lung cancer in both genders was Muang followed by

Mae On with the ASRs of 82.1 and 78.6, respectively (see Fig. 7). However, the highest incidences in males and females were in Mae On and Hang Dong districts with the ASRs of 100.5 and 73.7, respectively. The most common histopathological type of cancer cell was adenocarcinoma (49.2%), followed by squamous cell carcinoma (27.2%) (see Table 3).

Risk Factors of Lung Cancer in Northern Thailand

The epidemiological study of Wiwatanadate *et al.*

Table 3. The histopathology of lung cancer in Chiang Mai, 2007

Cell type	%
Adenocarcinoma	49.2
Squamous cell carcinoma	27.2
Small cell	10.3
Large cell	8.6
Others	4.7

Fig. 6. ASRs of lung cancer in Chiang Mai, 2001–2007.

Fig. 7. The 5 leading districts with highest ASRs of lung cancer in Chiang Mai, 2007.

(29)—performed in Saraphi district, Chiang Mai, Thailand relating the indoor radon and lung cancer—found that smoking was significantly the main factor of lung cancer followed by the levels of indoor radon. In 2006, the prevalence of tobacco use among males in Thailand, Japan, and the US were 43%, 42%, and 25%, respectively, whereas those among females were 2%, 13%, and 19%, respectively (30). The statistics surveyed by the National Statistical Office of Thailand in 2007 (31) showed that smoking situation in Thailand has been improved continuously; the smoking rate declined from 32.0% in 2001 to 21.2% in 2007. The smoking rate in the northern part of Thailand (22.2%) is the third highest after that in the south (25.0%) and the northeast (23.8%); however, the smoking rate in females is highest in the north (5.0%) and the top five provinces having highest smoking rates in females are all in the northern region (Tak, Lamphun, Chiang Rai, Chiang Mai, and Mae Hong Son ranging from 13.4–6.3%). The statistics implies that smoking alone could partially explain the high incidence of lung cancer in northern Thailand. Previously, there were surveys of indoor radon in Thailand nationwide revealing that the range of radon levels was 1–1,974 Bq/m³ and that the radon levels in northern area were among the highest in Thailand (32–44). In Japan, nationwide surveys of indoor radon during 1993–1996 showed the mean value of 15.5 Bq/m³ (ranging from 3.1 to 208 Bq/m³) (45), compared to the mean value of 48.1 Bq/m³ (ranging from 1 to 1,851.9 Bq/m³) in the US (46). However, there might be other risk factors related to the air pollution in northern Thailand. The severe air pollution from hazes of northern Thailand had been empirical from the air quality data of the Pollution Control Department's monitoring stations in Chiang Mai showing that, in March 2010, the levels of particulate matter less than 10 μ m in aerodynamic diameter (PM₁₀) exceeded the 24-h average standard level of 120 μ g/m³ every day. The highest level was on 18 March 2010 at 518.5 μ g/m³, which is the all-time record (47). The sources of hazes were forest fires, open burnings in the agricultural settings followed by garbage and dry leave and stick burnings, traffic and constructions. The study of Rayanakorn *et al.* (48) in Chiang Mai and Lamphun provinces showed that PAH compositions of PM₁₀ were highest in dry season (December–March), which corresponded to the amounts of PM₁₀ contaminated in the atmosphere. Furthermore, among the PAH components, the proportion of carcinogenic PAHs was as high as 74.2%. Therefore, it is possible that the causes of high incidence of lung cancer in northern Thailand might be the synergistic effects of smoking, indoor radon, and air pollution including individual variation in the susceptibility to lung cancer. Furthermore, the genetic factor might play a significant role on lung cancer as Heepchantree *et al.* found the sig-

nificantly higher frequency of micronucleus (49) and longer tail length (comet assay) (50) in Saraphi (high lung cancer incidence area) compared to Chom Thong (low lung cancer incidence area) districts in Chiang Mai, Thailand. Peripheral blood lymphocytes from people residing in two districts of Chiang Mai, Thailand were used in the two studies.

Conclusion

The high incidence of lung cancer in northern Thailand is a challenging problem. Epidemiological study demonstrated that smoking and indoor radon might be the main risk factors. This article postulates that there might be other risk factors related to air pollution, specifically the PAHs. Nevertheless, more studies are needed to illuminate the real causes of lung cancer.

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