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RISK OF LUNG CANCER AMONG PAST ALCOHOL DRINKERS: A CASE CONTROL STUDY

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Abstract
There is clear evidence that smoking causes lung cancer, but much about the etiology of lung cancer is not well understood, including why some nonsmokers develop lung cancer.

A hospital-based case-control study was carried out to identify the influence of alcohol consumption on the risk of developing lung cancer, which included 106 cases and 212 controls. A questionnaire was designed to collect information on possible risk factors of lung cancer. The odds ratios (OR) and 95% confidence interval (CI) was calculated by using conditional logistic regression.

Cases had lower education level; most of the cases are from middle income group and married. After adjustment for family history of cancer, body mass index (BMI) and smoking, higher risk of lung cancer was found among consumption of 26 g/day (OR, 1.12; 95% CI, 0.55-2.30), consumed for ≥ 31 years and start drinking before 15 years also associated with increased risk of lung cancer. After controlling for previous medical history, environmental tobacco smoke at home and work, Cooking fuels and workplace exposure that were associated with the disease and family history of cancer, BMI, smoking, residence, education level, income level, occupation and marital status, duration (OR, 1.39; 95% CI, 0.33-5.77), dose (OR, 1.23; 95% CI,1.39-6.32) and age when started (OR,1.97;95% CI, 0.60-6.46) also significantly associated with the increased risk of lung cancer.

In conclusion, heavy intake of alcohol associated with higher risk of lung cancer.

Key Words: Alcohol, Cooking Fuels, Lung Cancer, Mizoram, Smoking.

Introduction

Lung cancer has been the most common cancer in the world since 1985. With a total number of 1.3 million new cases and 1.1 million deaths per year estimated worldwide, lung cancer is ranked highest with respect to morbidity and mortality among malignant neoplasms. In the year 2002, lung cancer made up 12.4% of cancer cases and accounted for 17.6% of all cancer related deaths on the world scale[1].In Mizoram, it was ranked 4th during the last five years[2].

Tobacco smoking is the major cause of lung cancer, accounting for 80% of the worldwide lung cancer burden in males and 50% in females[3]. There is increasing evidence that women present different clinical patterns of lung cancer from men: they are more likely to develop adenocarcinoma, tend to be younger than men and experience better survival rates[4,5]. These gender differences raised the question of the possible role of female hormones in lung cancer carcinogenesis and found support by studies that have identified steroid receptors in lung cancer cell lines and tumour tissue[6]. However, the significance of oestrogens and progesterone receptor expression in lung cells is still unknown as these receptors are expressed in many other organs [7]. Oestrogens could also interact with cigarette smoking by accelerating the metabolism of smoking-derived carcinogens[8,9].

There is clear evidence that smoking causes lung cancer, but much about the etiology of lung cancer is not well understood, including why some nonsmokers develop lung cancer and why only a portion of smokers do so. It has been suggested that some of this variation may be explained by alcohol consumption [10,11]. Alcohol is oxidized to acetaldehyde, a known carcinoge [12]. There is evidence that alcohol can act as a prooxidant in tissues, including lung tissue[13,14] and on lipids, including lung membrane lipids[13,15]. Alcohol can induce the expression of enzymes that are related to carcinogen metabolism [16] and compounds other than ethanol that are contained in alcoholic beverages may have carcinogenic effects. In studies of alcoholics, morbidity and mortality due to lung cancer have been shown to be high[17-21] but the greater risk may be explained, in part or entirely, by the fact that the people in these populations were also more likely to smoke.

Mizoram is one of the eight sister states of northeast India[22] and lies between 21°56'N latitude, and 92°16'E and 93°26'E longitude. The state has an area of 21,081 sq km, and shares an international boundary with Bangladesh in the west and Myanmar in the east and south. It also shares interstate boundary with Tripura in the northwest, Assam in the north and Manipur in the northeast[23]. Majority of the native people inhabiting Mizoram are previously called “Lushai” and now

"Mizo" and they are known to have a unique tradition and ethnicity when compared with other states of India. The major tribes of Mizo are Lusei, Ralte, Hmar, Pawi, Paite and other groups[24].

Mizoram is an agricultural state and most of the population is engaged in agriculture activities. In 2003 census, 53.91% are cultivators[25]. During the old age time, their parents advised to smoke meizial (mizo cigarette) to protect them from mosquitos and sand fly bites when they are working in the jhoom.

Materials and Methods

A hospital based case control study has been carried out at Aizawl Civil Hospital situated in Aizawl. This hospital serves as tertiary heath care facility and is the only hospital having facility to treat cancer in the state. The study included 108 patients aged 30–86 years who had histoligically confirmed diagnosis of lung cancer admitted during in the hospital during March 2015 to March 2016.Controls were selected from the same hospital from an individual's come for medical checkup during the same period. Ratio of cases and controls was 1:2. Controls were matched for age (±5 years) and sex and ethnicity. Totally, we had 212 controls that were cancer and any lung diseases free.

A structured questionnaire was developed to use in this study. It includes data regarding sociodemographic characteristics, family history of cancer, lifetime smoking habits, previous medical history, family smoking, passive smoking from workplace, cooking fuels used and workplace exposure.

All subjects were asked to fill out a questionnaire by themselves. If there were some reasons not to do that, they were interview by interviews and were not aware of the study hypothesis. Cancer patients were asked to refer about some past lifestyle alcohol consumption habits.

Family history of cancer, lifetime smoking habits, previous medical history, family smoking, passive smoking from workplace, cooking fuels used and workplace exposure was categorized into two categories: yes and no. Alcohol consumption was assessed by sum of the products that were calculated by multiplying consumption frequency of beer, wine and strong alcohol (local alcohol, vodka, whisky, etc) by standard alcohol units (SAU), where 1 SAU is 10 g of pure alcohol found in 250 ml of beer or 120 ml of wine or 32 ml of vodka[26]; body mass index (BMI) grouped into two groups: ≤ 24.9 kg/m^2 and ≥ 25 kg/m^2 ; educational level was categorized into five categories: illiterate, middle school, high school, higher secondary school(HSS) and under graduate (UG) and above; residence assessed by living in rural and urban; income level was grouped into three groups: low income, middle income and high income; occupation was categorized into four categories: office worker, farmer, business and others; marital status was grouped into married and unmarried.

A conditional logistic regression [27] was used to calculate odds ratios (OR), and 95% confidence intervals (CI) for lung cancer in relation to exposures of interest. Statistical significance trends for matching pairs were calculated by categorizing the exposure variable and treating the score variable as a continuous variable. The Chi square test was utilized to calculate the similarity of demographic factors. The level of significance was set at 5%. All the calculation was performed with SPSS version 20 and R version 3.1.2 version.

Results

All the lung cancer patients (n = 106) were confirmed by histology. The age and sex profile of the cases and controls is shown in Table 1. The mean age of the cases and controls was 62.51 years and 62.24 years, respectively. The minimum and maximum ages among cases are 30 years and 86 years. There were no statistically differences between the age of the cases and controls, suggesting that age matching was effective. Of the cases, 60.38% were male and majorities (39.62%) of the lung cancer were in the group 60 – 69 years at the time of diagnosis of lung cancer. Cases had significantly lower education level and mostly resided in rural area. Generally, most of the cases are from middle income group, farmer and married. Therefore, residence, education level, income level, occupation and marital status on cancer were included into the logistic model like smoking, physical activity, family history of cancer and BMI as variables to adjust for.

There was a statistically significant relationship between the risk of lung cancer and consumption of alcohol in univariate logistic regression model. ORs were calculated using non-drinker as reference group to observe the association with alcohol consumption (Table 2). After controlling for family history of cancer, BMI and smoking, dose (OR=1.12, 95% CI =0.55-2.30) and duration (OR =1.26, 95% CI = 0.53-2.97) of alcohol consumption was significantly related with the increase risk of lung cancer. The ORs remained statistically significant and after adjustment for residence, education level, income level, occupation and marital status.

The risk of lung cancer is associated with many other factors, finally, we used multivariate conditional logistic regression model that included all the items like alcohol consumption, previous medical history (asthma, TB, bronchitis and other respiratory illness), environmental tobacco smoke at home and work, Cooking fuels(gas, wood or charcoal and electric stove/oven) and workplace exposure(diesel/petrol smoke, paints or thinner, welding equipment, pesticides and wood dust) that were associated with the disease, and family history of cancer, BMI, smoking, residence, education level, income level, occupation and marital status. A significant increase in risk was observed at alcohol past drinkers, age when started and duration. The significant dose-response relationship also found between consumption of alcohol and risk of lung cancer.

Table 1: Demographic Distribution of Lung Cancer into Cases and Controls

Variable	Category	Cases		Controls		p-value
		n	%	n	%	
Age	≤49	12	11.32	26	12.26	matched
	50-59	23	21.70	45	21.23	
	60-69	42	39.62	84	39.62	
	≥70	29	27.36	57	26.89	
	Mean ± SD	62.51±11.21		62.24±11.37		
Sex	Male	64	60.38	135	63.68	matched
	Female	42	39.62	77	36.32	
Residence	Rural	56	52.83	52	24.53	**<0.000**
	Urban	50	47.17	160	75.47	
Education level	Illiterate	10	9.43	5	2.36	**<0.000**
	Middle School	31	29.25	8	3.77	
	High School	24	22.64	49	23.11	
	Higher secondary	33	31.13	54	25.47	
	UG & above	8	7.54	96	45.28	
Income level	Low income	32	30.19	38	17.92	**<0.001**
	Middle income	64	60.38	119	56.13	
	High income	10	9.43	55	25.94	
Occupation	Office worker	14	13.21	35	16.51	**<0.000**
	Farmer	49	46.23	44	20.75	
	Business	20	18.87	69	32.55	
	Others	23	21.70	64	30.19	
Marital Status	Married	102	96.23	151	71.23	**<0.000**
	Unmarried	4	3.77	61	28.77	

Table 3: Odds Ratios (OR) and 95% Confidence Interval (CI) for Lung Cancer in Relation to Alcohol Consumption

Variable	Category	Cases		Controls		OR^1 (95% CI) p for trend	OR^2 (95% CI) p for trend	OR^3 (95% CI) p for trend
		n	%	n	%			
Alcohol drinking status	Non drinkers	73	68.87	146	68.87	1(reference)	1(reference)	1(reference)
	Past drinkers	33	31.13	66	31.13	0.95 (0.56-1.61) **<0.000**	1.01 (0.53-1.92) 0.008	1.39 (0.61-3.17) 0.021
Dosage (g/day)	Non drinkers	73	68.87	146	68.87	1(reference)	1(reference)	1(reference)
	≤25	18	16.98	39	18.40	0.88 (0.46-1.67)	0.99 (0.46-2.20)	0.98 (0.57-4.21)
	≥ 26	15	14.15	27	12.74	1.12 (0.55-2.30) **<0.000**	1.03 (0.43-2.43) 0.008	1.23 (1.39-6.32) 0.020
Age when started (year)	Non drinkers	73	68.87	146	68.87	1(reference)	1(reference)	1(reference)
	≤15	21	19.81	40	18.87	0.98 (0.46-2.11)	1.22 (0.49-3.06)	1.97 (0.60-6.46)

	≥16	12	11.32	26	12.26	0.94 (0.50-1.75) **<0.000**	0.89 (0.41-1.93) 0.007	1.14 (0.43-3.01) 0.019
Duration (year)	Non drinkers	73	68.87	146	68.87	1(reference)	1(reference)	1(reference)
	≤20	11	10.38	26	12.26	0.74 (0.33-1.64)	0.67 (0.24-1.81)	1.12 (0.31-4.06)
	21-30	10	9.43	17	8.02	0.99 (0.45-2.17)	1.12 (0.44-2.84)	1.63 (0.52-5.12)
	≥31	12	11.32	23	10.85	1.26 (0.53-2.97) **<0.000**	1.47 (0.49-4.41) 0.008	1.39 (0.33-5.77) 0.020

OR^1-adjusted for family history of cancer, BMI and smoking.
OR^2-further adjustment for residence, education level, income level, occupation and marital status.
OR^3- adjusted for previous medical history (i.e. asthma, TB, bronchitis and other respiratory illness), environmental tobacco smoke at home and work, Cooking fuels(i.e. gas, wood or charcoal and electric stove) and workplace exposure(i.e. diesel/petrol smoke, paints or thinner, welding equipment, pesticides and wood dust).

Discussion

Primary lung cancer in India was rare during the early 20th century. But now with increased life span and increasing prevalence of smoking, lung cancer has reached an epidemic proportion in India[28]. It has become a major health problem in Mizoram. In the present study, patients over 50 years of age were found to have higher risk of lung cancer. Cases of this disease start to be diagnosed from the age of 30 years onwards, reaching a peak at about 70 years of age[29-31].

Living in a rural area was found to be a risk factor for lung cancer in this study. Other studies in high-incidence regions have also shown that patients living in rural areas are more likely to develop lung cancer[30]. The risk of lung cancer is higher in famer of middle income group with low education level. It was also observed that increased risk of lung cancer was found among those who got married [30, 32-34].

The study also showed that consumption of alcohol leads to the increased risk of lung cancer. In meta-analysis of 10 case-control studies; there was an increase in lung cancer risk associated with alcohol consumption in hospital-based but not population-based case-control studies[35].These finding are consistent with the data reported by other authors[11,36-40].

The association between amount of alcohol intake and lung cancer was evaluated in several prospective studies; some investigators observed an elevated risk of lung cancer among subjects who consumed alcohol [35, 41], whereas others did not [32, 42-44].

In addition to the suspected carcinogenic effect of acetaldehyde, chronic alcohol consumption increases cytochrome P-450 level and microsomal enzyme activity, which can accelerate the activation of carcinogens[45, 46]. Ethanol might act in the later stages of carcinogenesis[48, 13]. However, the effect of ethanol on the lung might be cumulative; thus, assessing ethanol intake only at recruitment could lead to underestimation of the association between ethanol intake and lung cancer [13].

We observed a lower risk of lung cancer for moderate and low ethanol intake than non-drinkers. In two US studies, the risk of lung cancer was lower among moderate drinkers than among nondrinkers at baseline[47, 48] also observed. In the pooled analysis[36], a lower risk of lung cancer for low and moderate drinkers as compared with nondrinkers was observed, which was confined to women. However, there was no inverse association between moderate ethanol intake and lung cancer in two reviews[11, 35]. Despite alcohol's detrimental effects on health when consumed in large amounts, several investigations have shown an inverse association of moderate alcohol consumption with mortality, mainly based on the inverse association with coronary heart disease [49].

In a meta-analysis, alcohol (ethanol) intake of ≥2,000 g/month (~67 g/day) was associated with an elevated risk of lung cancer [35]. In a pooled analysis of seven cohort studies (including 3,137 lung cancer cases), a non-significantly higher risk was also seen for an intake of ≥30 g/day compared with no intake [36]. Other study mentioned that the increased risk was again primarily confined to those drinking ≥30 g alcohol/d [36]. Our data also showed increased consumption of alcohol also associated with the increased risk of lung cancer. A significant dose-response relationship with total alcohol intake has been reported in two case-control studies [50, 51] and three cohort studies [11, 37, 52]. The studies that reported an association found risk estimates ranging from 1.6 for ≥41 drinks/week to 2.2 for ≥176 ml of pure ethanol/day (almost 3liters of beer/day) [53].

The study revealed that longer intake of alcohol increased the risk of lung cancer. However, other studies cited that no statistical significant association between lifelong exposure to alcohol and lung cancer was seen in two US case-control studies [36, 54]. Years of drinking were related to the risk of lung cancer in a Turkish case-control study [51] but not in a US cohort study [11].

In conclusion, years of drinking with higher consumption of alcohol for a long period are significantly associated with the increased risk of lung cancer. However, low and moderate consumption of alcohol can reduce lung cancer.

Ethical Clearance: This study was approved by Mizoram Ethics Committee.

Conflict of Interest: None declared.

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