



SELECTED DIETARY HABITS AND RISK OF ESOPHAGEAL CANCER

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Abstract

Esophageal cancer is one of the least studied and one of the main health issues in Mizoram. The objective of this article is to assess the relationship between esophageal cancer and selected dietary habits. A hospital based case control study was carried out, comprising 138 cases with histologically confirmed diagnosis of esophageal cancer and 276 controls that were cancer disease free. Cases and controls matched by gender and age (± 2 years). Ratio of cases and controls was 1:2. A questionnaire was used to collect possible risk factors of esophageal cancer. The odds ratios and 95% confidence interval were calculated by conditional logistic regression.

Most of the cases are from middle income group and their education level is lower than controls. After adjustment for smoking, consumption of alcohol, betel quid, tobacco, family history on cancer, income and education level, higher risk of esophageal cancer was found for fermented soya bean, fermented pig fats, fermented fish and pickled vegetables. After controlling for other food items that were associated with esophageal cancer and smoking, consumption of alcohol, betel quid, tobacco, family history of cancer, income and education level, frequent consumption of fermented soya bean (OR=5.35, 95% CI=1.45-19.71), fermented pig fats (OR= 9.61, 95% CI=3.79-24.30), fermented fish (OR=20.03, 95% CI=6.29-63.81) and pickled vegetables (OR=6.88, 95% CI=3.67-12.90) was significantly associated with the increased risk of esophageal cancer. Consumption of shrimp paste, smoked vegetables and ajinomoto leads to increase risk of esophageal cancer, however, this increase was not statistically significant.

In conclusion, higher risk was found for consumption of fermented food items.

Key Words: Ash Filtrate, Ajinomoto, Fermented Fish, Fermented Pig Fats, Fermented Soya Bean, Dietary Habits, Esophageal Cancer, Shrimp Paste.

Introduction

Esophageal cancer (EsC) is one of the least studied and deadliest cancers worldwide because of its extremely aggressive nature and poor survival rate. Esophageal carcinoma affects more than 450,000 people worldwide and the incidence is rapidly increasing^[1]. It is the eight most common incident cancer in the world because of its extremely aggressive nature and poor survival rate^[2]. It exhibits an epidemiologic pattern distinct from all other cancers^[3]. Incidence of esophageal adenocarcinoma has increased sharply over the past few decades, both by period and birth cohort.

Esophageal cancer is the second most common cancer among males and the fourth most common cancer among females according to combined data from cancer registries in India^[4]. Various foods and food additives have been studied for their association with this disease^[5].

The dietary habit of the Mizo people is wholly rice-based, i.e. rice is the staple food and any other foods such as vegetables and meats are considered as side dishes. Spices tend to be used less than in other Indian cuisines^[6].

Mizoram is one of the eight sister states of northeast India^[7] 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^[8]. Majority of the native people inhabiting Mizoram are previously called "Lushai" and now "Mizo"^[9] 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^[10]. Hence, they also possess different traditional techniques of processing foods^[11].

1. *Sa-um* (fermented pig fats): Fats of pigs are mainly collected from the inner abdominal portion (sometimes fats from other parts of the pig's body were also used), cooked and torn/chopped into pieces and are placed in a special container called "sa-um bur" (Fig. 1) which is prepared from the dried fruit of the plant *ûm* (*Lagenaria siceraria*, bottle gourd)^[9]. The container is placed over the fireplace and approximately after three days or even longer, it is ready for use in the preparation of other foods such as bawl, bai, etc.^[12]



Figure 1: Saum Bur Made From Bottle Gourd (Lagenaria Siceraria)

2. *Ching-al* (ash filtrate): This is an ash filtrate and is an important seasoning for food items such as “bai” (This is a mixed vegetable and the Mizos have a number of “bai” and the method of preparation might be different at different places). An inverted conical shaped container with a minute opening at the tip is made from bamboo thinly splitted and woven, which was locally called “chingal thlawrbur”. But, nowadays, chingal thlawrbur is made from tin (Fig. 2). To this, ashes are placed and clean water is poured onto it and it was then hung. The opening at the tip allows the filtrate to pass through which is then collected and stored for further use. Today, this particular seasoning has been replaced largely by cooking soda in cities and towns^[12].



Figure 2: Chingal Thlawrbur for Ash-Filtrate Preparation

4. *Bekang um* (fermented soyabean): Soya-bean (*Glycine max*) 8 seeds are commonly used as a side dish and most often as a seasoning. The seeds are first cleaned, boiled and are spread evenly on the leaves of “hnahkiah” (*Callicarpa arborea* Roxb.)^[13] placed over the sieve locally known as “chhihri”. Ashes from the fireplace/mantelpiece are spread evenly and then covered with the leaves of “hnahkiah”. They are kept un-opened for three days over the fireplace and sometimes outside in the sun after which it is ready for consumption (Fig. 3). They can be consumed directly and can also be dried in the sun and stored for further use. The seeds are also fried, grounded and added to the tea which is considered as a special tea in some places^[12].



Figure 3: Fermented Soybean Locally Known as Bekang Wrapped with the Leave of Callicarpa Arborea Roxb



Materials and Methods

The study was based on hospital-base matched case-control study, which was carried out at Civil hospital, Aizawl during march 2015 to march 2016. The study included 138 patients, who had histologically confirmed diagnosis of esophageal cancer. Controls were individually matched to case-patients by gender and age (± 2). Ratio of cases and controls was 1:2. Totally, we had 276 controls that were cancer free.

A structured questionnaire was developed, which included questions on dietary habits, diet (13 items) lifetime smoking habits, lifetime consumption of alcohol, betel nut consumption and tobacco consumption. In addition, we asked questions regarding lifetime occupation history and family history of cancer.

The patients were asked to fill the questionnaire by themselves, if they have a problem. They were interviewed by interviewers. Three interviewers were trained and were not aware of the study hypothesis. Cancer patients were asked to refer about some lifestyle habits a year before the disease was diagnosed.

Diet was assessed according to consumption frequency (never, 1 time a week, 2-4 times a week, more than 4 times a week, 0-6 times a week and daily) of different food items. Cigarette smoking was measured in pack-years (number of cigarettes smoked per day/20 x smoking time (in years))^[14]. Alcohol consumption was assessed by never drinkers, current drinkers and those who had given up as past drinkers.

A conditional logistic regression was used to calculate odds ratios (OR), and corresponding 95% confidence intervals (CI) for esophageal cancer in relation to exposure of interest. The Chi-square test was carried out to calculate the difference between proportions. The level of significance was set at 5%. All the calculations were performed with the SPSS version 20 software.

Results

Table 1: Distribution of Socio-Economic Characteristics in Cases and Controls

Variables	Category	Cases		Controls		p-value
		n	%	n	%	
Age	<45	19	13.77	38	13.77	matched
	45_54	60	43.48	119	43.12	
	55_64	39	28.26	75	27.17	
	65_74	14	10.14	32	11.59	
	75<	6	4.35	12	4.35	
Gender	Male	95	68.84	182	65.94	matched
	Female	43	31.16	94	34.06	
Residence	Rural	33	23.91	45	16.30	0.062
	Urban	105	76.09	231	83.70	
Education	Primary	20	14.49	16	5.80	<0.000
	Middle	21	15.22	18	6.52	
	High School	32	23.19	32	11.59	
	Higher Secondary School	10	7.25	30	10.87	
	College and above	55	39.86	180	65.22	
Income(Rs)	<8000	31	22.46	103	37.32	<0.000
	8000-300000	84	60.87	111	40.22	
	30000 and above	23	16.67	62	22.46	
Occupation	Office worker	45	32.61	107	38.77	0.310
	farmer	37	26.81	72	26.09	
	business	17	12.32	40	14.49	
	other	39	28.26	57	20.65	
Family History of Cancer	Yes	88	63.76	125	45.28	<0.001
	No	50	36.23	151	54.71	

The distribution of socio-demographic variables among cases and controls is shown in Table 1. Cases had significantly lower education level than controls group. Among 138 cases, 68.84% are male. Most of the cases (60.87%) and controls (40.22%) group are from middle income group. There were more controls without history on cancer as compared to cases. Therefore, education level, income level and family history on cancer were included in the logistic regression model like smoking, alcohol consumption, tobacco consumption and betel nut consumption as variables to adjust for.



Table 2: Selected Dietary Habits and Risk of Esophageal Cancer

Variables	Category	Cases	Controls	OR ¹ (95% CI) p for trend	OR ² (95% CI) p for trend	OR ³ (95% CI) p for trend
Bekang (Fermented soya bean)	Never	23	124	1(reference)	1(reference)	1(reference)
	1time/week	62	122	2.71	2.82	3.93
	2-4times/week	42	22	10.03	9.55	11.93(499-
	>4times/week	11	8	6.61	6.66	5.35
Sa-um (Fermented pig fats)	Never	25	127	1(reference)	1(reference)	1(reference)
	1time/week	52	103	2.53	2.30	2.37
	2-4times/week	34	12	3.42	3.43	3.47
	>4times/week	27	34	12.96	13.31	9.61
Dangpuithu (fermented fish)	Never	59	203	1(reference)	1(reference)	1(reference)
	1time/week	34	61	2.24	2.20	2.76
	2-4times/week	17	7	8.32	7.05	6.41
	>4times/week	28	5	21.61	23.61	20.03
Nghapih (shrimp paste)	Never	83	197	1(reference)	1(reference)	1(reference)
	Never	35	64	1.41	1.40(0.81-	1.83(0.96-
	1time/week	8	9	1.49	1.10	1.14
	2-4times/week	12	6	3.75	3.36	3.55
Green leafy vegetable	0-6times/week	42	131	1(reference)	1(reference)	1(reference)
	Daily	96	145	0.45	0.43	0.61
Non-leafy vegetables	0-6times/week	55	55	1(reference)	1(reference)	1(reference)
	Daily	83	221	0.36	0.41	0.39
Smoked vegetables	Never	49	121	1(reference)	1(reference)	1(reference)
	0-6times/week	53	131	1.05	0.91	1.37
	Daily	36	24	3.31	2.75	4.32
Pickled vegetables	Never	41	166	1(reference)	1(reference)	1(reference)
	>1times/week	97	110	5.05	6.42	6.88
Fruits	0-6times/week	123	208	1(reference)	1(reference)	1(reference)
	Daily	15	68	0.91	0.92	0.89
Ajinomoto	0-6times/week	77	193	1(reference)	1(reference)	1(reference)
	Daily	61	83	1.52	1.38	1.14
Chingal (ash-filtrate)	0-6times/week	124	254	1(reference)	1(reference)	1(reference)
	Daily	14	22	1.37	1.12	0.81

OR¹-Adjustment for smoking, consumption of alcohol, betel quid, tobacco and family history on cancer.

OR² – further adjustment for income and education level.

OR³ - further adjustment for fresh meats (beef, pork, mutton and fish), smoked meats (pork, beef and fish), dried meats (fish and prawn), salted meats (fish and prawn), pickled meat (beef) and tinned meats (beef and fish).

All the esophageal cancer patients (n = 138) were confirmed by histology. Of the 136 cases, 83.33% consumed fermented soybean. Consumption of fermented soya bean, fermented pork, fermented fish, shrimp paste, green leafy vegetables, non-leafy vegetables, smoked vegetables, pickled vegetables and fruits was associated with risk of esophageal cancer in univariate logistic regression model. After controlling for smoking, alcohol consumption, betel nut consumption, tobacco consumption and family history of cancer, consumption of fermented soya bean(OR, 6.61;95% CI,1.96-16.04), fermented pork(OR,12.96; 95% CI,5.69-29.53), and pickled vegetables(OR, 5.05; 95% CI, 3.06-8.34) was associated with the increased risk of esophageal cancer. However, consumption of non-leafy vegetables (OR, 0.36; 95% CI, 0.22-0.59) significantly related with decreased risk of esophageal cancer (Table 2). There was increased association between consumption of Ajinomoto((OR, 1.52; 95% CI, 0.96-02.39) and ash filtrate(OR, 1.37; 95% CI, 0.64-2.93) and risk of esophageal cancer though they were not



statistically significant, The ORs remained statistically significant for fermented poor, fermented soya bean, fermented fish and pickled vegetables after adjustment for education level and income level.

Finally, we used multivariate logistic regression model that included all dietary variables (fermented soya bean, fermented pork, fermented fish, shrimp paste, green leafy vegetables, non-leafy vegetables, smoked vegetables, pickled vegetables, fruits, ajinomoto and ash filtrate that were associated with the disease, and smoking, alcohol consumption, betel quid consumption, tobacco consumption and family history on cancer. A significant increase in risk was observed at higher consumption of fermented soya bean (OR=5.35), fermented pork (OR=9.61), fermented fish (OR=2.76) and pickled vegetables (OR=6.88). Though they are not statistically significant, consumption of fruits and chingal(ash filtrate) leads to decrease risk of esophageal cancer.

Discussion

Consumption of fermented food items is very popular in Mizoram. The present study has demonstrated an increased risk of esophageal cancer with selected dietary habits. This study revealed that increased consumption of bekaang (fermented soya bean) leads to the increased risk of esophageal cancer. These findings were consistent with work done by Y. Chen^[15]. An individual who frequently ate fermented pork fat, a traditional Indian food, had a 9.61-fold increased risk of developing esophageal cancer. The data also showed that a significant increase in risk of esophageal cancer for people with frequent consumption of dangpuithu (fermented fish). And also showed increase, but not significant, OR for esophageal cancer with frequent consumption of nghapih(shrimp paste).

Inverse associations between a high intake of fresh leafy vegetables and non-leafy vegetables in esophageal cancer have been observed. It has been suggested that the anti-carcinogenic effect of vegetables is attributed in part to the effect of antioxidant vitamins, especially vitamin C and beta-carotene, which inhibit the intra gastric formation of carcinogens such as N-nitroso compounds from secondary amines and nitrite. This inhibition might be caused by the reduction of nitrites into nitric oxide in the presence of reducing equivalents, such as vitamin C, or the combination of antioxidant vitamins with amines^[16-18]. Another possible mechanism for the anti-carcinogenic effects of antioxidants is the neutralization of reactive oxygen free radicals that can damage DNA^[18, 19]. Fresh vegetables contain a larger amount of antioxidant vitamins, such as vitamin C and beta-carotene, than processed vegetables^[21-23]. However, few prospective studies have looked at associations between vegetarian diets and cancer risk^[24-26].

Our finding also indicated that higher consumption of fruits leads to decrease risk of esophageal cancer, but it is not statistically significant. These findings are consistent with data reported by other authors^[27-31]. Anti-carcinogenic factors found in those foods include ascorbic acid, vitamin E, carotenoids, flavonoids, phytosterols, indoles, fiber, among others^[32]. Moreover, a larger consumption of vegetables and fruits may be an expression of a more generally healthy attitude towards diet and other lifestyle habits^[33].

Higher consumption of smoked vegetables is highly related with increased risk of esophageal cancer. Frequent intake of Ajinomoto also leads to increase risk of esophageal cancer. In another study, it was shown that ajinomoto added to food leads to cancer^[34]. Though it is not significant, frequent use of Chingal (ash filtrate) also related to decrease risk of esophageal cancer.

An attempt was made to explore the effects of consumption of pickled vegetables. Since, the consumption of pickled vegetables is quite common, it may have a great interest for public health. The present study found a significant association between increased consumption of pickled vegetables with increased risk of esophageal cancer. The findings are consistent with most of the epidemiological studies^[35-39]. While in the highest esophageal cancer risk area of north central China no association between pickled consumption and cancer has been noted in multiple studies^[37, 39, and 40].

Ethical Clearance: The study has been cleared by Mizoram Ethics Committee and all participants gave informed consent.

Conflict of Interest: The author has no conflict of interest.

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