

Risk factors of esophageal cancer in Turkmen Sahra of Iran

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ABSTRACT

Present study was carried out in three years' duration (2002-2004) to investigate the risk factors of esophageal cancer in Iranian Turkmens (Northeast of Iran; where the esophageal cancer is the most common world wide). Concerning registered cases of esophageal cancer in the region, 139 cases were selected. Controls matching in terms of age and sex were 500 healthy individuals. Furthermore, a questionnaire was designated with several questions including: personal characteristics, family history of cancer, possible disease background, and addiction to cigarettes or drugs, and presence of any particular dietary habits. The questionnaires filled with free will (voluntarily) by cases and controls. The collected data was analyzed by SPSS 10.0 software. The mean age of people under study was 60 years. The studied cases were significantly correlated with their first line relatives in term of cancer contraction ($P=0.001$ and $OR=7.6$). It was also significant in second and third line relatives ($P=0.042$ and $OR=3.38$). There was a significant correlation considering the consumption of stale food and butter with esophageal cancer. As a conclusion, in addition to mentioned risk factors, some other factors as mode of nourishment, employment status, special hygienic habits and inheritance were important factors in esophageal cancer etiology among the studied subjects. [Turk J Cancer 2007;37(1):16-21]

KEY WORDS:

Iran, Turkmen Sahra, esophageal cancer, nutrition

INTRODUCTION

Esophageal cancer is the fourth cancer of digestive system that constitutes two up to five percent of all identified malignancies (1). One of the main characteristics of this lethal disease is its specific geographical distribution. For instance, its incidence has been reported to be 3/100,000 in Europe and USA (2). However, this is in some parts of central Asia, which is known as esophageal cancer belt including Turkmen Sahra of Iran and China have been reported to be 115/100,000 and 130/100,000, respectively (2,3). Esophageal cancer in the north east of Iran, (Turkmen Sahra in Golestan Province) was reported to be 165 and 195/100,000 for females and males, during 1980s (4-12). Furthermore, in 1995 the number of registered esophageal cancer cases in Mazanderan province was reported to be 115 that denoted 28% of total of the district and 56% of the whole esophageal cancers of the country (13). When Golestan in northeast of Mazanderan was announced as a new province in 1996 with the total population of 1,466,289 comprising 710,287 men and 716,001 women, the docu-

mented total number of cancer was 465 consisting of 244 males and 221 females. In that time, the registered patients as esophageal cancer were 125, i.e. accounting to be 26.8% of whole cases (n=465) within newly generated province. However, involved people were 93 in 1998 (27.6% of all malignancies). Hence, smoking cigarettes, drinking alcohol, malnourishments, bacterial, fungal, viral agents and inheritance are regarded as some etiologic factors of cancer (4,6,7,14,15). There are several studies carried out concerning epidemiology of esophageal cancer as nutritional states, state of gene expression of P53 protein, esophageal cancer and Papillomaviruses, Cytomegalovirus and Epstein-Barr virus as etiologic factors, in Iran (16-20). Furthermore, there are other studies about esophageal cancer conducted by Tehran University of Medical Sciences, and Health Research Institute in Babol and Europe concerning nutrition, hygienic practices, cultural, economical and environmental

factors (4-12). According to an estimation carried out by World Health Organization (WHO) about health care and population, structure considering lifestyle and environmental changes, globally the involved cancer patients will increase by 50% from 2000 and mortality will increase to exceed 8 million deaths by 2020. Hence, this can be quite critical to take crucial initiatives for proper health care after controlling the infectious and nutritional diseases, especially in developing countries. This cross-sectional descriptive study was designated to assess certain risk factors associated with esophageal cancer particularly in nutritional points of view.

MATERIALS AND METHODS

The cases were selected from the cancer referral center pathology laboratory located in Gorgan (northeast of Iran) between the 2002-2004 period. From the registered lists,

Table 1
Frequency of some relative risk factors for esophageal cancer in cases and controls, northeast of Iran, Turkmen Sahra

	Cases	Controls
Sex		
Male	98	354
Female	41	146
Mean age	60	60
Family history of cancer	25.2%	0.98%
Fresh vegetables and fruits	57%	62.6%
Drink hot tea	62.6%	44.6%
Use spices	10.8%	3.2%
Employment status		
Farmer	52.5%	35%
Government staff	4.3%	3%
Business	43.2%	62%
Bread		
Home baked	36%	19%
Village bakery	10.1%	6.4%
City bakery	38.1%	47.4%
Meat consumption		
Lamb and goat	44.6%	31.4%
Beef	7.2%	18.8%
Cooking oil		
Saturated oil	80.6%	69.8%
Animal fat	2.9%	3%

after recording the addresses of cases, trained personnel performed house visits. A total number of 139 cases were selected including 109 cases of squamous cell carcinoma, 18 cases of adenocarcinoma and 12 cases of undifferentiated carcinoma types. The controls were 500 healthy individuals (chosen in random) similar to cases in terms of age, sex and place of residence. A questionnaire concerning several information as personal characteristics, history of cancer in the family, disease in past, any particular addiction to drugs or cigarettes, stale food, existing dietary habits of the patients before commencement of clinical symptoms were filled for each case and control. The collected data was analyzed by Chi-square and Fisher tests using SPSS 10.0 software.

RESULTS

The cases consisted of 41 women and 98 men, whereas the control group consisted of 146 females and 354 males, respectively. The mean age for both groups was 60 years. Cases were 52.5% farmers, 4.3% government employees and 43.2% in business, while these figures for controls were 35%, 3% and 62%, respectively (Table 1).

Amongst cases and controls, 10.8% and 3.2% had used spices as pepper with their meals. Concerning bread provision, amongst the cases 36% used home baked bread, 10.1% from village and 38.1% from city bakeries. In controls, they were 19%, 6.4% and 47.4%, respectively. There was a significant difference between type of bread and esophageal cancer ($P=0.001$). Considering meat consumption, 44.6% of the cases used to consume lamb, goat and 7.2% beef, while among controls, the records were 31.4% and 18.8%, respectively. Another factor compared between cases and controls was the type of cooking oil they consumed. In cases, 80.6% used saturated oil, while 2.9% utilized animal fat for cooking purposes. Though amongst control group, the figures were 69.8% and 3%, respectively ($P=0.001$). Moreover, within patients with cancer, 38.1% used to take red meat, 41% white meat and 6.5% used both; while the rates were 41%, 24.4% and 6.4% in controls, respectively. In consideration of addiction to cigarettes (three or more per day), of the cases, 19.8% were smokers and this was 17.3%, in controls. Furthermore, 53.2% of

the cases, used to take fresh vegetables and fruits; while it was 57% in controls. Besides, 62.6% of the cases and 44.6% of controls used to drink hot tea, the latter finding showed significant relationship between hot edibles (both tea and meals) and esophageal cancer ($P=0.001$). The findings showed that 25.2% of the cases had family history of cancer; while in controls, only 0.98% of them had such record, hence there was significant difference between the two findings ($P=0.0001$). Furthermore, in cases, 21.6% showed esophageal cancer in first line relatives, but controls did not, so the concluding result by accurate Fisher's test, indicated meaningful relationship between the two groups ($P=0.001$). As a result, we did find a noteworthy interaction between esophageal cancer and consumption of stale food and butter ($P=0.004$).

DISCUSSION

According to present study, it seems that the dietary patterns in both groups are almost identical i.e. of consumption of animal proteins. Although it is worth mentioning that when a nutritional factor changes, it obviously influences other diet categories. For instance as a result of reduction in animal protein intake, ingestion of fat and cholesterol also decreases correspondingly and according to the combination of the meals, there might be elements that accelerates carcinogenicity (21). Another finding of this study was that almost 44.6% of cases used to take lamb and goat as a part of their dietary habit. This figure is concerning, since higher red meat intake naturally induces higher fat ingestion. It appears that, fat plays critical role in development of the tumors due to the fact that fat in presence of ionized bile acids and fatty acids in form of toxicogenics can persuade changes in epithelial tissues (22). In former studies, consumption of home baked bread was reported as one of the possible risk factor of cancer in Turkmen Sahra; because the local population used to keep the wheat in their basements and possibility of contamination with fungi and production of materials such as aflatoxins and silica fibers were regarded as possible risk factors (6,8,12). Therefore in our study, use of home baked bread prepared from local wheat exhibited significant difference between two groups; so the latter finding was assumed as a likely risk factor for the disease. Another study in China pointed out other risk

factors including water in causation of esophageal cancer (23). Further investigations documented the role of diets in etiology of such malignancy; but with various rates (24). As a result of remarkable regional incidence of esophageal cancer, it necessitates demographical studies between different ethnic groups. For instance in the United States, different dietary habits between the whites and the blacks have marked various effects in esophageal cancer manifestations (25). Similarly, another investigation concerning esophageal cancer in north of France, has reported that one third of the involved cases were related to butter overuse (26). Since there is evidence of dysfunction of homeostasis in cancer, the patients are not utilizing glucose and subsequently capable of using up stock fat to fulfill their requirements; so the latter, causes anomalous conditions (21). In esophageal cancer incidence rate studies that were carried out in Italy, the relationship between the unsaturated fatty acids with such malignancy was reported to be significant (7). In the present study the association between the type of cooking oil and the cancer was also shown. On the other hand the relevant studies have documented that as the consumption of animal protein increases, the use of salt increases, too. The latter aspect is regarded as one of the major hazardous factors in inflammation of mucous membrane of the digestive system and its subsequent alteration (27). In addition, the salted meat (as a type of regional conservation method) is a source of nitrosamines which is believed as the pathogenic agent for esophageal cancer that besides its reaction with methemoglobin, causes certain abnormalities (28,29). The role of nitrosamines in etiology of esophageal cancer has been demonstrated; although deficiencies of other micronutrients and vitamins (A, C and B2) were also included in population under study (29). According to the causes stated above, the emergence of the disease is not regarded critical unless and until the consumption of beverages like tea or coffee (with sugar) or even the meals are all taken very hot on a regular basis which can hurt esophagus altogether (27). This is quite clear that inappropriate dietary habits would stimulate the outcome of the disease, e.g. in France taking hot drinks and high amount of butter look upon as an esophageal carcinogenic factor (30). As a matter of fact, our study does

not rule out this as a possible risk factor either; but in general taking stale food and highly spiced meals which contain stimulants, can cause dystrophy of esophageal tissue due to their nature. Some reports have revealed that, there is meaningful association between esophageal cancer and salted food, meals contaminated with mycotoxins, aflatoxins and nutritional deficiencies (31). The past nutritional history of the patients should be noted and the influential factors in dietary habits of them must be adjusted. The epidemiological studies have proven that, there are certain intervening fundamentals in esophageal cancer like economical, social and nutritional conditions; so life styles of peoples at risk can contribute to the progression of the disease in the future (32). Neither cases nor controls took adequate amount of fresh vegetable and fruits, which are known to contain extraordinary nutritional value. Fruits and vegetables do possess inhibitory role on cancer; because of valuable nutrients and vitamins, specially antioxidants. There is also extensive literature pointing out the effects of micronutrients as: retinol, zinc, riboflavin, niacin, and other vitamins, molybdenum, beta carotene and selenium in reduction of mortality rate due to esophageal cancer (33,34). An article reported that ingestion of micronutrients and occurrence of esophageal cancer especially in people who suffer from nutritional insufficiency are closely linked and even more shortage of certain nutrients act as predictor indices in etiology of this particular malignancy (35). As mentioned earlier, due to incidence of esophageal cancer in Turkmen Sahra and more importantly its frequency in family relatives, it is quite obvious that inheritance plays a key role and must be considered seriously. The latter phenomenon was identical to our findings i.e. there was a significant relationship between esophageal cancer and rate of its occurrence in relatives. Another issue of concern is addiction to drugs and use of hot beverage, stale food, alcohol and tobacco as stimulants for esophageal cancer that do necessitate further studies (31,16). Peculiar attitudes of local population, for example: smoking Hubble-Bubble and tobacco (or pipe tobacco) which are commonly practiced without detoxification, as part of behavioral patterns, might put people at risk for disease even with satisfactory nourishment states (24). As a conclusion, in addition to men-

tioned risk factors, some other factors as mode of nourishment, employment states, special hygienic habits and inheritance were important factors in esophageal cancer etiology among the studied subjects.

The authors believe that the results of this investigation could contribute to further studies for better identification

of etiological agents and other risk factors responsible for esophageal cancer in order to control the disease in both the country and the region under study.

References

- 1- Tosato F, Passaro U, Vasapollo L, et al. Epidemiology of Esophageal Cancer. *G Chir* 1996;17:449-52.
- 2- Allen JW, Richardson JD, Edwards MJ. Squamous cell carcinoma of the esophagus: a review and update. *Surg Oncol* 1997;6:193-200.
- 3- Cortes Gonzalez R, Villasenor Caloca R.. Esophageal Cancer. *Rev Gastroenterol Mex* 1997;62:149-59.
- 4- Ghadirian P. Thermal Irritation and esophageal cancer in North Iran. *Cancer* 1987;60:1909-14.
- 5- Editorial. Esophageal Cancer in the Caspian Littoral. *Lancet* 1978;1:641-2.
- 6- O'Neill CH, Hodges GM, Riddle PN, et al. A fine fibrous silica contaminant of flour in the high oesophageal cancer area of north-east Iran. *Int J Cancer* 1980;26:617-28.
- 7- Mahboubi E, Kemet J, Cook PJ, et al. Oesophageal cancer studies in the Caspian Littoral of Iran: the Caspian cancer registry. *Br J Cancer* 1973;28:197-214.
- 8- Cook-Mozaffari PJ, Azordegan F, Day NE, et al. Oesophageal cancer studies in the Caspian Littoral of Iran: results of a case-control study. *Br J Cancer* 1979;39:293-309.
- 9- Munoz N, Crespi M, Grassi A, et al. Precursor lesions of oesophageal cancer in high-risk populations in Iran and China. *Lancet* 1982;1:876-9.
- 10- Crespi M, Munoz N, Grassi A, et al. Esophageal lesions in Northern IRAN: A premalignant condition? *Lancet* 1979;2:217-21.
- 11- Kmet J, Mahboubi E. Esophageal cancer in the Caspian littoral of Iran: initial studies. *Science* 1972;17:846-53.
- 12- Hormozdiari H, Day NE, Aramesh B, et al. Dietary factors and esophageal cancer in the Caspian Littoral of Iran. *Cancer Res* 1975;35:3493-8.
- 13- The cancer Institute publication No. 3, The Imam Khomeini Medical Center, Hospital based cancer registry 1377 (1998).
- 14- Moses FM. Squamous cell carcinoma of the esophagus. Natural history, incidence, etiology, and complications. *Gastroenterol Clin North Am* 1991;20:703-16.
- 15 - Parkin DM, Pisani P, Lopez AD, et al. At least one in seven cases of cancer is caused by smoking. Global estimates for 1985. *Int J Cancer* 1994;59:494-504.
- 16- Siassi F, Pouransari Z, Ghadirian P. Nutrition intake and esophageal cancer in the Caspian littoral of Iran: a case-control study. *Cancer Detect Prev* 2000;24:295-303.
- 17- Behnam B, Salehian P, Attar K. P53 protein Expression and DNA ploidy in squamous cell carcinoma of the esophagus in Iran. *Arch Anat Cytol Path Clin Exp Pathol* 1998;46:388.
- 18- Salehian P, Behnam B, Attar K, et al. P53 protein expression and DNA ploidy in ethnic and non-ethnic esophageal squamous cell carcinoma in Iran. *Arch Anat Cytol Path Clin Exp Pathol* 1998;46:411.
- 19- Moradi A, de Villiers EM, Mokhtari-Azad T, et al. Detection of Human Papillomavirus DNA by PCR in Esophageal Squamous Cell Carcinoma from Turkmen Sahra, North-east of Iran. *Iranian Biomedical Journal* 2002;6:19-24
- 20 - Natgeh A, Attarzaden B, Aramesh D, et al. Anti-body to viral capsid antigens of Epstein-Barr virus and Cytomegalovirus in patients with carcinoma of the esophagus. In: *Viruses in naturally occurring cancers (BookA)*. Cold Spring Harbor Laboratory Press, 1980;Vol 7:55-61.

- 21- Laquatra, I, Gelach, M. Nutrition in Clinical Nursing. Delmar Publisher Inc, 1990;679-95.
- 22- Mahan LK, Arlin MT. Krause's Food Nutrition and Diet Therapy. 8th ed. Philadelphia, PA: WB Saunders Co, 1992.
- 23- Yokokawa Y, Otha S, Hou J. Ecological study on the risks of esophageal cancer in Ci-Xian, China: the importance of nutritional status and use of the well water. *Int J Cancer* 1999;83:620-4.
- 24- Hill MJ. Nutritional and metabolic aspects of gastrointestinal cancer. *Curr Opin Clin Nutr Metab Care* 1998;1:405-7.
- 25- Brown LM, Swanson CA, Gridleg G. Dietary factors and the risk squamous cell esophageal cancer among black and white men in the United States. *Cancer Causes Control* 1998;9:467-74.
- 26- Gamliel Z. Incidence, epidemiology and etiology of esophageal cancer. *Chest Surg Clin Nutri Am* 2000;10:441-50.
- 27- Castellsague X, Munoz N, De Stephani E. Influence of mate drinking, hot beverages and diet on esophageal cancer risk in South America. *Int J Cancer* 2000;88:658-64.
- 28- Rogers MA, Vaughan TL, Davis S. Consumption of nitrate, nitrite, and nitrosodimethylamine and the risk of upper aerodigestive tract cancer. *Cancer Epidemiol Biomarkers Prev* 1995;4:29-36.
- 29- Yang CS. Vitamin nutrition and gastroesophageal cancer. *J Nutr* 2000;130(2s Suppl):338-9.
- 30- Launog G, Milan C, Day NE. Diet and squamous cell cancer of the esophagus: a French multicenter case-control study. *Int J Cancer* 1998;76:7-12.
- 31- Sharma D. Carcinoma of esophagus etiological factors and epidemiology: an overview. *J Ind Med Assoc* 1999;97:360-9.
- 32- Tretli S, Robsahm TE. Height, weight and cancer of the esophagus and stomach: a follow-up study in Norway. *Eur J Cancer* 1999;8:115-22.
- 33- Zhang ZF, Kurtz RC, Yu JP. Adeno carcinoma of the esophagus and gastric cardia: the role of diet. *Nutr Cancer* 1997;37:298-309.
- 34- Hill MJ. Nutrition and human cancer. *Ann Nutr Acad Sci* 1997;833:67-87.
- 35- Brown LM, Swanson CA, Gridleg G. Adeno carcinoma of the esophagus: role of obesity and diet. *J Natl Cancer Inst* 1995;87:874-8.