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10-Year Trends in Dietary Intakes in the High- and Low-Risk Areas for Esophageal Cancer: A Population-Based Ecological Study in Northern Iran

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ABSTRACT

BACKGROUND

We assessed dietary intakes in the high- and low-risk areas for esophageal cancer (EC) in Golestan province, Northern Iran.

METHODS

Considering the EC rates, Golestan province was divided into high- and low-risk regions. Data on households' food consumption were obtained from the Statistical Center of Iran. We used multivariable logistic regression to assess the relationships between consumption of main food and EC risk. Adjusted odds ratios (aOR) were calculated. Joint point program was used for time trend analysis and average annual percent changes (AAPC) were reported.

RESULTS

Overall, 11910 households were recruited during 2006-2015. 4710 (39.5%) households were enrolled from the high-risk region. There were significant positive relationships between high consumption of sweets (aOR = 1.62; 95% CI: 1.24-2.10), oil/fat (aOR = 1.36; 95% CI: 1.04-1.79), and red meat (aOR = 1.33; 95% CI: 1.07-1.65) with EC risk. We found significant negative relationships between high consumption of dairy products (aOR = 0.62; 95% CI: 0.46-0.82), vegetables (aOR = 0.66; 95% CI: 0.50-0.87) and fruit (aOR = 0.72; 95% CI: 0.55-0.95) with the risk of EC. Time trend analysis showed a significant increasing trend in the proportions of households with low consumption of vegetables (AAPC = 4.71, $p = 0.01$) and dairy products (AAPC = 5.26, $p = 0.02$) in the low-risk region for EC.

CONCLUSION

Dietary intakes may be important etiological factors for EC in Northern Iran. Further studies are warranted to assess the role of dietary factors in this high-risk population.

KEYWORDS:
Diet, Esophageal cancer, Vegetables and Fruit, Ecological study

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INTRODUCTION

Esophageal cancer (EC) is the 11th most common cancer (3.2% of all incident cancers) and the 8th most common cause of cancer death (5.3% of all cancer deaths) worldwide. Most of the EC incidence and mortality occur in developing countries.[1]

There are diversities in the incidence rates of EC between different countries

as well as different parts of each country. A very high incidence rate of EC was reported from the northeast of Iran.[2,3] Several reports from this region showed a significant relationship between EC and some risk factors such as low socioeconomic status,[4] opium consumption, smoking, alcohol consumption,[5] poor oral hygiene,[6] drinking hot tea,[7] exposure to inappropriate polycyclic aromatic hydrocarbons (PAH),[8] and dietary intakes.[9,10] The association between EC and dietary intakes were investigated in different studies in Northern Iran. Cook-Mozaffari and colleagues reported strong associations between low socioeconomic status and low intake of fresh fruit and vegetables with the risk of EC.[11]

High consumption of vegetables, fruits, cereals, and tea had a protective association with the risk of EC. But, frequent consumptions of meat, animal fats, and salt were mildly associated with increased risk.[12] In another study on EC, Eduardo De Stefani and co-workers reported a clear protective effect for consumption of fruits and vegetables. They also reported an increased risk with daily consumption of barbecued meat.[13,14] Hormozdiari and others found a low intake of vitamins A and C, riboflavin, animal protein, fresh vegetables. and fruit as well as high consumption of sheep's and goat's milk in a high-risk area for EC.[15]

Golestan province in Northern Iran has been known as a high-risk region for EC since 1970s.[3] Recent studies showed different incidence rates for EC in different sub-divisions of Golestan province.[16,17] Accordingly, we divided the province into high and low-risk regions for EC.[18] Some studies showed differences in the levels of some risk factors between the two regions.[18-20] Investigation of dietary intakes, as an important risk factor for EC, may produce helpful evidence in identifying the etiologic factors for EC in this population. The aim of this study was to compare the consumption of main foods between high and low-risk regions for EC of Golestan province during 2006-2015.

MATERIALS AND METHODS

This was a population-based ecological study. It was conducted in Golestan province, Northern Iran. Considering previously described methods and based on the incidence rates of EC, we divided the province into high (Turkmensahra) and low-risk areas for EC.[16-18]

We collected household food consumption data from the Household Income and Expenditure Survey (HIES) of the Statistical Center of Iran (SCI) during 2006 and 2015.[21] The methodological issues of the HIES including sample size calculation and sampling methods were designed according to the Standard Protocols of the National Household Survey Capability Program (NHSCP),[22] and System of National Accounts (SNA).[23] Briefly, using a multi-stage stratified sampling method, 387250 households were recruited in HIES during 2006-2015. At the main national level, each province was considered as a stratum. The sample size (number of households) of each stratum was calculated using a proportional to size method. In each province, villages (in rural areas) and city blocks (in urban areas) were identified as provincial-level strata. Finally, a simple randomization method (using household code) was considered to select the study units (households) according to the previously identified sample size in each stratum.

The present study was designed in Golestan province. Regarding the findings of the HIES project in previous years (unpublished data), the proportions of households with high consumption of sweet, oil and fat, and red meat in high versus low-risk areas of Golestan province were 40% versus 32%, 37% versus 27%, and 36% versus 30%, respectively. The results of previous HIES projects in this region also suggested that the proportions of low consumption of vegetables, fruits, dairy products, spices, and grain/beans in low versus high-risk areas were 31% versus 37%, 33% versus 39%, 29% versus 34%, 39% versus 30%, and 30% versus 27%, respectively. Considering a confidence level of 0.95 and a study power of 80%, the highest sample size was calculated for grain/bean (7108 households). Considering a design effect of 1.5 and a response rate of about 90% (based on the results of a previous survey), the final sample size of this study was calculated as 11500 households.

The process of data collection in HIES was done using a standard questionnaire. The questionnaire was developed according to the United Nations (UN) recommendations and considering the National Household Survey Capability Program (NHSCP)[22] and SNA publications.[23] It consisted of two main parts including income and expenditure, and the section of expenditure was further categorized into dietary and non-dietary parts. The

dietary section of HIES questionnaire included information about the amount of foods (in gram) consumed by households during the last month.[24] Time of interview (in each year) and the structure of the questionnaire were not changed during the study period.

For the present study, amounts (in gram) of households' consumption of nine commonly used major food groups including red meats, fish, dairy products, oils, fruits, vegetables, cereals and legumes, sweet, and spices during 2006-2015 were extracted from the HIES dataset and entered into the analysis. Considering the tertile distribution of food consumption, households were categorized into three groups including the 1st tertile (low consumption), the 2nd tertile (intermediate consumption), and the 3rd tertile (high consumption). We calculated the proportions of households in each group of food consumption.

The proportions of households in the subgroups of food consumption were compared between the low and high-risk areas for EC. Crude odds ratios and 95% confidence intervals (CI) were calculated. Multivariable logistic regression analysis was performed to assess the strongest variables (food groups) related to the risk of EC. Variables with P values less than 0.2 in univariable analysis were entered into the multivariable model. Adjusted odds ratio (aOR) and 95% CI were calculated. Regarding the possible differences in dietary intakes between rural and urban areas, households' place of residence was also entered into the analysis. Finally, the results were adjusted for the place of residence as well as for selected food groups including red fruits, vegetables, meats, fish, dairy products, oils, cereals and legumes, sweet, and spices.

We also performed a time trend analysis using a Joint point software version 4.0.4.[25] The proportions of households with low consumption of vegetables, fruits, and dairy products as well as those with high consumption of sweets, oil and fat, and red meats were entered into the trend analysis. Assuming a Poisson distribution, the average annual percent changes (AAPCs) in proportions were calculated by generalized linear models. A weighted least-square regression was performed, considering the year and the neutral logarithm of proportions as independent and dependent variables, respectively. Finally, 95% CI of AAPCs was calculated using heteroscedastic errors. The trend was considered as significant if 95% CI of AAPC did not include zero. p values of less than 0.05 were considered significant. Ethical issues of this project were reviewed and approved by the Ethics Committee of Golestan University of Medical Sciences.

RESULTS

In total, 11910 households were recruited in this study. 4710 (39.5%) households were selected from high-risk region for EC and 5680 (47.7%) households were recruited from cities (table 1).

The proportions of households with high consumption of red meat (34.1% vs 31.5%), oil and fat (36.0% vs 31.9%), sweets (37.5% vs 30.3%), fish (30.2% vs 24.7%), grain and bean (35.9% vs 31.7%), and spices (34.3% vs 30.5%) were higher in high risk region compared with low risk region (table 1).

Households from high risk region showed lower consumption of vegetable (28.4% vs 36.3%), fruits (31.5% vs 34.3%), and dairy products (29.2% vs 35.2%) compared with those from low risk region (table 1).

Results of multivariable logistic regression suggested significant positive relationships between high consumption of sweets (aOR = 1.62; 95% CI: 1.24-2.10), oil and fat (aOR = 1.36; 95% CI: 1.04-1.79), and red meat (aOR = 1.33; 95% CI: 1.07-1.65) with the risk of EC (table 2). Our findings also showed significant negative relationships between high consumption of vegetables (aOR = 0.66; 95% CI: 0.50-0.87), fruits (aOR = 0.72; 95% CI: 0.55-0.95), and dairy products (aOR = 0.62; 95% CI: 0.46-0.82) with the risk of EC (table 2).

The results of trend analysis showed a significant increasing trend in proportions of households with low consumption of vegetables (AAPC = 4.71; $p = 0.01$) and dairy products (AAPC = 5.26; $p = 0.02$) in the low-risk region (figure 1). There was a significant decrease in the proportion of households with high consumption of sweets both in high-risk (AAPC = -1.79; $p = 0.02$) and low-risk regions (AAPC = -6.03; $p < 0.01$) (figure 2). Similar decreasing trends were also found in oil and fat consumption but the trend was significant only in high-risk region (AAPC = -2.98; $p = 0.01$) (figure 2). There was no significant change in fruits (figure 1) and red meats (figure 2) consumption during the study period.

DISCUSSION

Our findings suggested a significant inverse relationship

Table 1: Numbers and proportions (%) of households with low, intermediate, and high consumption of foods in low and high risk regions for esophageal squamous cell carcinoma in Golestan province, Iran, 2006-2015

		Low risk region		High risk region		Total
		N*	%	N*	%	
Place of residence	Urban	3565	49.5	2115	44.9	5680
	Rural	3635	50.5	2595	55.1	6230
Red meat	Low	1883	50.6	1078	47.9	2961
	Intermediate	666	17.9	406	18.4	1072
	High	1173	31.5	767	34.1	1940
Oil and fat	Low	2054	30.9	1128	25.8	3182
	Intermediate	2473	37.2	1672	38.2	4145
	High	2117	31.9	1575	36.0	3692
Vegetables	Low	2361	33.1	1771	38.0	4132
	Intermediate	2177	30.5	1568	33.6	3745
	High	2589	36.3	1322	28.4	3911
Fruits	Low	2530	35.4	1703	36.4	4233
	Intermediate	2166	30.3	1501	32.1	3667
	High	2457	34.3	1475	31.5	3932
Sweets	Low	2425	36.4	1300	29.1	3725
	Intermediate	2212	33.2	1488	33.3	3700
	High	2017	30.3	1674	37.5	3691
Fish	Low	2195	45.4	1712	40.0	3907
	Intermediate	2328	29.9	1501	29.7	3829
	High	2456	24.7	1325	30.2	3781
Dairy Products	Low	2195	31.4	1712	37.7	3907
	Intermediate	2328	33.4	1501	33.1	3829
	High	2456	35.2	1325	29.2	3781
Grain and bean	Low	2453	35.0	1466	31.9	3919
	Intermediate	2330	33.3	1476	32.2	3806
	High	2221	31.7	1648	35.9	3869
Spices	Low	2361	37.0	1227	28.1	3588
	Intermediate	2067	32.4	1636	37.5	3703
	High	1947	30.5	1497	34.3	3444

*Missing values were excluded

between vegetable and fruit consumption with the risk of EC. Higher consumption of fruit and vegetables was associated with significant decreases in the risks of different malignancies including malignancies of the esophagus, lung, stomach, and colorectal.[26-28] According to the previous reports from different populations, higher consumption

Table 2: Multivariable logistic regression analysis for assessing the relationship between dietary intakes with the risk of esophageal squamous cell carcinoma in Golestan province of Iran

		Univariate analysis				Multivariable analysis*			
		Crude OR	95% CI		*p*	Adjusted OR	95% CI		*p*
Place of residence	Urban	-	-	-	-	-	-	-	-
	Rural	1.20	1.12	1.30	< 0.001	1.05	0.86	1.28	0.629
Red meat	Low	-	-	-	-	-	-	-	-
	Intermediate	1.06	0.92	1.23	0.394	1.44	1.12	1.85	0.004
	High	1.14	1.02	1.29	0.027	1.33	1.07	1.65	0.010
Oil and fat	Low	-	-	-	-	-	-	-	-
	Intermediate	1.23	1.12	1.35	< 0.001	1.08	0.84	1.39	0.560
	High	1.35	1.23	1.49	< 0.001	1.36	1.04	1.79	0.027
Vegetables	Low	-	-	-	-	-	-	-	-
	Intermediate	0.96	0.88	1.05	0.374	0.92	0.71	1.20	0.562
	High	0.68	0.62	0.75	< 0.001	0.66	0.50	0.87	0.003
Fruits	Low	-	-	-	-	-	-	-	-
	Intermediate	1.03	0.94	1.13	0.527	0.94	0.72	1.22	0.639
	High	0.89	0.82	0.97	0.012	0.72	0.55	0.95	0.019
Sweets	Low	-	-	-	-	-	-	-	-
	Intermediate	1.25	1.14	1.38	< 0.001	1.22	0.96	1.57	0.111
	High	1.55	1.41	1.70	< 0.001	1.62	1.24	2.10	< 0.001
Fish	Low	-	-	-	-	-	-	-	-
	Intermediate	1.13	0.97	1.32	0.121	1.21	0.97	1.51	0.085
	High	1.39	1.19	1.63	< 0.001	1.15	0.91	1.46	0.229
Dairy products	Low	-	-	-	-	-	-	-	-
	Intermediate	0.83	0.76	0.91	< 0.001	1.02	0.78	1.35	0.868
	High	0.69	0.63	0.76	< 0.001	0.62	0.46	0.82	0.001
Grain and bean	Low	-	-	-	-	-	-	-	-
	Intermediate	1.06	0.97	1.16	0.214	0.97	0.77	1.22	0.812
	High	1.24	1.13	1.36	< 0.001	1.18	0.92	1.51	0.184
Spices	Low	-	-	-	-	-	-	-	-
	Intermediate	1.52	1.39	1.67	< 0.001	1.24	0.98	1.51	0.092
	High	1.48	1.34	1.63	< 0.001	1.21	0.95	1.55	0.128

*The results were adjusted for place of residence as well as for selected food groups including red meats, fish, dairy products, oils, fruits, vegetables, cereals and legumes, sweet, and spices.

of fruit and vegetables may decrease the risk of EC.[3,29-33] Fruits and vegetables are the main sources of antioxidants, phytoestrogens, and flavonoids especially flavanones, which can prevent the development of cancer by anti-in-

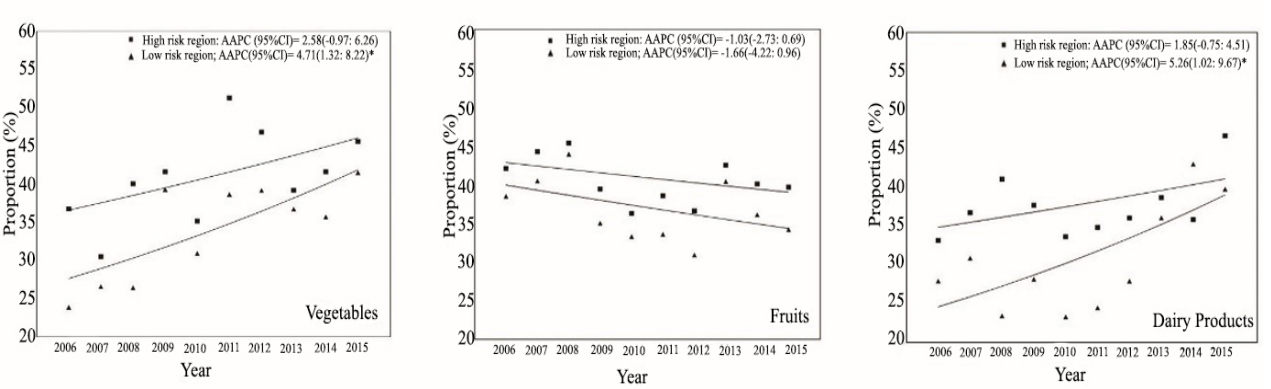

Fig.1: Proportions (%) of households with low consumption of vegetables, fruits, and dairy products in high- and low-risk regions for EC of Golestan province, Iran, 2006-2015. (AAPC indicates average annual percent change; * indicates that AAPC is significantly different from zero at alpha = 0.05; Dots indicate observed values; Solid lines indicate fitted lines; EC indicates esophageal cancer)

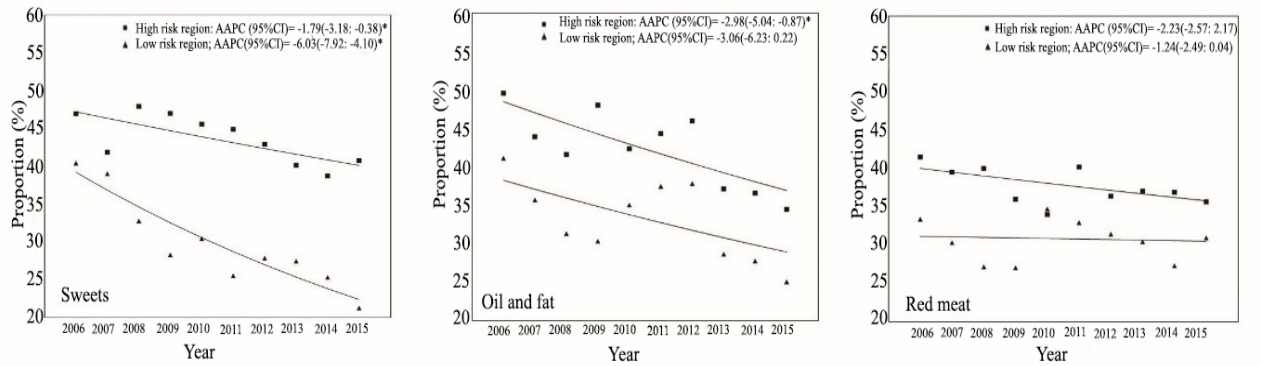

Fig.2: Proportions (%) of households with high consumption of sweets, oil and fat, and red meat in high- and low-risk regions for EC of Golestan province, Iran, 2006-2015. (AAPC indicates average annual percent change; * indicates that AAPC is significantly different from zero at alpha = 0.05; Dots indicate observed values; Solid lines indicate fitted lines; EC indicates esophageal cancer)

flammatory effects, free-radical scavenging, or blocking the formation of N-nitroso compounds. Other components of these foods including fiber, folate, vitamin C, vitamin A, and beta-carotene equivalents may also have anti-cancer effects.[34-36]

Our results also showed an increase in the proportion of households with low vegetable consumption. The trend was statistically significant in low EC risk area. Therefore, considering the relationship between low consumption of vegetables and fruits and EC as well as the decreasing trend in vegetable consumption, a priority in health policy making especially for cancer controlling programs in this population should be considered. Appropriate interventions should be designed and implemented to increase vegetables and fruits consumption in both high and low-risk regions for EC of Golestan province.

We found a significant positive relationship between high red meat consumption and EC risk. Other studies also showed that high red meat consumption may be related to increased risk of EC.[14,34,35,37-42] The carcinogenic effects of red meat may be due to its compounds including N-nitroso compounds, heterocyclic amines (HCA), or polycyclic aromatic hydrocarbons (PAH). Heme iron that is seen especially in high amounts in red meat causes the formation of N-nitroso compounds.[42,43] When muscle meat, such as beef is cooked using high-temperature cooking methods for example in pan-frying or grilling directly over an open flame or smoking of meats, HCAs and PAHs are formed.[44] These compounds may increase DNA synthesis and cell proliferation, affect hormone metabolism, increase insulin-like growth factors, promote free radical damage, and produce carcinogenic heterocyclic amines, all of which may progress into the development of cancer.[41] The results of a recent study from Northern Iran,

showed a considerable dose-response relationship between PAH and risk of EC, suggesting a causal role for exposure to PAH in the pathogenesis of EC.[45] HCAs and PAHs may cause changes in DNA by specific enzymes in the body, the "bioactivation" process that may increase the risk of cancer. Diversities in the activity of these enzymes in different individuals may be related to the risk of developing cancers in those exposed to HCAs and PAHs.[46-48] Interventions reducing red meat consumption will decrease exposure to these carcinogenic compounds. Therefore, red meat consumption reducing interventions may be considered as an important activity in EC controlling program. Our results showed no significant change in the proportion of households with high red meat consumption in Golestan province during 2006-2015. Therefore, reducing red meat consumption may be noted as a priority in health policy making in our population as well as other high-risk regions.

Our findings showed that households in the high-risk region had significantly higher consumption of oil and fat. The relationship between high fat consumption and different cancers including colorectal cancers [49] and EC [34,50-52] were suggested in previous studies. High consumption of oil and fat have been known as risk factors for EC, and controlling this risk factor will result in reducing the burden of EC in high-risk populations. The observed decreasing trend in oil and fat consumption in our population (figure 2) may possibly be occurred due to the implementation of oil and fat reducing policies during the last decade in Iran. But, despite this decreasing trend, the proportion of households with high consumption of oil and fat remained higher in high-risk regions. So, additional and more effective interventions are needed in this high-risk region.

Households in the high-risk region for EC showed significantly higher consumption of sweets. High intake of sweet foods was associated with different cancers including colorectal cancer, [49] breast cancer, [53] and pancreatic cancer.[54] High sweet consumption may increase the glycemic index (GI) and glycemic load (GL). Increasing in GI is often associated with obesity and underlies the increased risk of EC.[55] The increase in GI and GL may also change the regulation of insulin-like growth factors and apoptosis in cancer cells in the esophagus, resulting in a higher risk of EC.[56] We also found a significant decreasing trend in the consumption of sweet foods in our population, most probably resulted from the implementation of administrative policies and educational programs. But, the AAPC was considerably lower (-1.79) in high risk than low risk (-6.03) regions, suggesting the need for more serious interventions in high-risk regions.

Our results suggested a significantly lower consumption of dairy products in the high-risk area. Previous studies also showed inverse relationships between consumption of dairy products and the risk of different cancers including colorectal, [57] breast, [58,59] and EC. [13,38] The results of a recent study from Golestan province suggested a negative association between dairy product intake and all-cause mortality as well as cardiovascular mortality. The findings did not show a significant relationship between dairy product intake and cancer mortality.[60] Further investigations should be conducted to clarify this point in our population.

In this study, we considered an ecological design and data collection was performed at the household level. Therefore, the issue of ecological fallacy should be considered in the interpretation of the results especially for findings with discrepancies with the results of previous studies. In addition, we have used previously collected data from the HIES project and we did not have access to information regarding the response rate and therefore, we could not adjust the results for selection bias due to non-response. Lack of data on types of fats (saturated, monounsaturated, trans, and polyunsaturated) was another limitation of this study.

The relationship between fat consumption and the risk of EC may depend on the types of fat. Therefore, this point should be notified in future studies. These limitations should be mentioned in the interpretation of our findings. However, our findings were in line with the results of previous individual-level studies on different populations. Therefore, the results of the present study may be useful in designing EC controlling programs.

In conclusion, we found a significant inverse relationship between EC risk and consumption of vegetables, fruits, and dairy products. Our results also suggested significant positive relationships between meat, sweet, and oil and fat consumption with the risk of EC. We also found an increase in the proportions of households with low consumption of vegetables and dairy products, and the trends were statistically significant in low-risk regions. Dietary intakes may be considered as important etiological factors for EC in Northern Iran. Therefore, further individual-level studies

are warranted to clarify the role of dietary factors on the risk of EC in this high-risk population.

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ETHICAL APPROVAL

There is nothing to be declared.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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