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Vitamin D Deficiency in High and Low Risk Populations for Esophageal Cancer in Northern Iran

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ABSTRACT

Background: Diverse relationships have been proposed between esophageal cancer (EC) and vitamin D serum levels. We aimed to assess serum levels of vitamin D in high and low-risk populations for EC in Northern Iran.

Methods: This ecological study was conducted in Golestan province, Northern Iran. Based on the incidence rates of EC, the province was divided into high-risk and low-risk populations. A stratified cluster sampling method was used. Serum vitamin D levels were assessed using the ELISA method. The proportions of vitamin D deficiency were compared between the two populations.

Results: A total of 246 persons were studied, with a mean age of 50.7 years. 96 subjects were male (39%) and 146 subjects were female (61%). 119 subjects (48.8%) were from high-risk and 127 (51.6%) were from low-risk populations. Thirty-two of 244 (13.1%) persons had vitamin D deficiency. The proportions of vitamin D deficiency were 7.9% and 18.3% in high- and low-risk populations, respectively (p=0.02).

Conclusion: We found that significantly larger numbers of people suffered from vitamin D deficiency in populations at low-risk of EC compared to high-risk populations. Regarding the ecological design of this study, causal inference could not be made from our results. Therefore, we recommend further investigation of this issue in future individual-level studies in this area, and in other high-risk populations.

Keywords: Vitamin D, Esophageal cancer, Iran

INTRODUCTION:

Esophageal cancer is the eighth most common cancer in the world, and the sixth cause of cancer death, killing more than 400,000 people in 2008[1,2]. Eighty percent of esophageal cancer cases occur in developing countries. The incidence of esophageal cancer varies in different countries and in different parts of each country. Two high risk areas for esophageal cancer have been identified. One of these, is the area between the Caspian Sea in the north of Iran and the northern part of China. The second one is located in Southeast Africa. The age-standardized incidence rates of esophageal cancer in high-risk areas were approximately 50 to 100 per 100,000 persons/year, with this number being less than 10 in the rest of the world. Even though many advances in diagnosis and treatment have recently been made, the 5-year survival rate for patients diagnosed with esophageal cancer ranges from 15% to 20%[3]. Iran is located in the western part of the Asian belt of esophageal cancer. The highest incidence of esophageal cancer in Iran has been reported in the Golestan province, located in Northeast Iran[4-5].

Numerous studies in this region have shown a significant relationship between esophageal cancer and risk factors such as opium consumption, smoking, alcohol[6], poor oral hygiene[7], consumption of hot tea[8], low socioeconomic status[9] and exposure to polycyclic aromatic hydrocarbons (PAH)[10]. A possible association was also proposed between serum vitamin D level and esophageal cancer.

Based on previous reports, there has been controversy regarding the relationship between serum vitamin D and the risk of esophageal cancer[11-15].

This topic was recently discussed in a review article by Grant. In this article, based on present evidence it was concluded that vitamin D reduces the incidence of many cancers including that of esophageal cancer[16].

Recent reports from Golestan province indicated different incidence rates for esophageal cancer in different parts of the province. The results suggested a high incidence of esophageal cancer in the east and a low incidence in the west of Golestan[17]. Given such disparity in the incidence rate of esophageal cancer in this region, as well as the proposed relationship between vitamin D and this cancer, we aimed to assess and compare serum levels of vitamin D between residents of the eastern and western parts of the Golestan province of Iran.

METHODS:

This ecological study was conducted in Golestan province, Northern Iran. Based on the incidence rates of esophageal cancer in Golestan province[17], two populations were identified, namely a high-risk population in the east and a low-risk population in the west of the province. We aimed to recruit 120 subjects from each population. Sampling was performed using a stratified cluster sampling method. Golestan cities were considered as clusters, with one of these clusters being randomly selected. Stratified sampling was carried out within the cluster. Place of residence (rural/urban) was considered as strata. After obtaining informed consent, a 5ml sample of fasting blood was collected. Samples were stored at -80 ° C prior to testing. Serum vitamin D level was assessed using the ELISA method with IDS kit, England. Vitamin D deficiency was defined based on cutoffs indicated in the manufacturer's instructions. The proportions of vitamin D deficiency were identified in high- and low-risk populations, as well as in subgroups of other variables. Chi-square test was used to assess the distribution of vitamin D deficiency in subgroups of other variables. Univariate and Multivariable regression analysis were used to assess the relationships between vitamin D deficiency and other variables. A P-value of less than 0.05 was considered significant.

This work was approved by the ethical committee of Golestan University of Medical Sciences. (Project code: 127692050624).

RESULTS:

Table 1 shows the distribution of subjects in the high-risk and low-risk population by gender, age and place of residence. A total of 246 persons were studied. The mean age of participants was 50.7 (standard deviation; 13.8). There were missing data for some variables. For example, in 4 subjects, the place of residence and gender were missing. Therefore, for each variable, subjects with missing data were removed from the analysis. Ninety six of 242 participants were male (39%). One hundred and nineteen of investigated subjects (48.8%) were from the high-risk population and 127 (51.6%) were from the low-risk population. From among 242 participants, 117 (48.3%) were from urban and 125 (51.7%) were from rural areas. Table 1 shows the distribution of subjects in high-risk and low-risk populations by gender, age and place of residence. Due to small serum sample size, vitamin D levels could not be measured in two subjects. In the remaining 244 subjects, vitamin D level was successfully measured.

The mean serum vitamin D level and standard deviation in participants were 35.9 and 30.4, respectively. Thirty-two of 244 (13.1%) subjects had vitamin D deficiency.

Table 1 shows the distribution of subjects in high-risk and low-risk populations by gender, age and place of residence.

Table 2 shows the relationship between different variables and frequency of vitamin D deficiency. Our results show that the frequency of vitamin D deficiency was higher among women (OR= 6.29; 95% CI: 2.09-18.93), urban residents (OR=2.09; 95% CI: 0.92-4.76) and in low-risk areas (OR=2.66; 95% CI: 1.13-6.26).

DISCUSSION:

In this study we investigated serum vitamin D levels in the eastern and western areas of Golestan province. We found that in the eastern area the rate of vitamin D deficiency was lower. Our results suggested significantly higher rates of vitamin D deficiency among women and in populations at low risk of esophageal cancer.

This difference may be due to environmental charac-

Table 1. The distribution of subjects in high- and low-risk populations by gender, age and place of residence.

		High-risk		Low-risk		p value
		Number	Percent	Number	Percent	
Gender	Male	42	43.8	54	56.2	0.34
	Female	73	50	73	50	
Place of Residence	City	43	36.8	74	63.2	0.001
	Rural	72	57.6	53	42.4	
Age Group	<50	57	48.7	60	51.3	0.72
	≥50	58	46.4	67	53.6	

Table 2. The relationship between different variables with frequency of vitamin D deficiency in Golestan province of Iran.

			Univariate			Multivariate		
		Number(Percent) Vit D deficiency	OR	95% CI	Pvalue	OR	95%	Pvalue
Gender	Male	4(4.2%)	-	-	-	-	-	-
	Female	28(19.4%)	5.55	1.88-16.39	0.002	6.29	2.09-18.93	0.001
Age Group	<50	17(14.5%)	1.22	0.58-2.58	0.59	1.22	0.55-2.68	0.622
	>50	15(12.2%)	-	-	-	-	-	-
Place of residence	Urban	21(18.1%)	2.27	1.04-4.95	0.04	2.09	0.92-4.76	0.077
	Rural	11(8.9%)	-	-	-	-	-	-
Incidence of esophageal cancer	High-risk	9(7.9%)	-	-	-	-	-	-
	Low-risk	23(18.3%)	2.60	1.15-5.90	0.02	2.66	1.13-6.26	0.024

teristics, lifestyle, nutritional habits, genetics and job conditions, which altogether may partly explain the lower rate. Further studies are warranted to clarify this issue in the Golestan area as well as in other similar populations.

The remarkable point of our findings is that the eastern part of Golestan province, with a lower rate of vitamin D deficiency, has been known as a high-risk area for esophageal cancer[17]. Reports from studies conducted on the relationship between vitamin D and esophageal cancer suggested conflicting results[11]. Some studies have found that vitamin D levels have been directly associated with esophageal cancer[12,13]. However, other studies suggested that vitamin D was a protective factor against esophageal cancer, and that the incidence rate of esophageal cancer was higher in people with vitamin D deficiency[11-15].

Therefore, investigation of this issue in future individual-level studies in this area and other high-risk populations is recommended. Regarding gender, there was a significant relationship between serum vitamin D level and gender. The mean serum vitamin D level in women was lower than men. McCullough et al (2010) found that men had higher 25(OH) D concentrations than women[18].

One major reason that could clarify the higher vitamin D deficiency in women compared to men could be the difference between men and women in terms of exposure to sunlight. This issue may be due to different factors. The majority of women are housewives, and are less likely to work outside, resulting in less exposure to sunlight. Another difference between men and women is in clothing that makes women less likely to be exposed to sunlight[19,20]. Therefore, women are at greater risk of vitamin D deficiency, and preventative actions such as increased physical activity are recommended. Also, a higher dietary intake of vitamin D should be considered for women. Our results showed that vitamin D deficiency was higher in urban compared to rural areas, although the difference was not significant. This may be due to different factors such as smog, dust, air pollution, cloudy air and use of sunscreens. These factors may act as a barrier preventing sunlight reaching the skin, resulting in vitamin D deficiency.

Another factor affecting the difference between serum vitamin D levels in urban and rural areas may be nutritional differences. The nutritional status of rural residents could provide their vitamin D requirements, for example their high consumption of dairy products[21,22]. Another reason could be the fact that most villagers work in an open environment, their houses have courtyards and are more exposed to sunlight. Living in apartments and working in closed environments such as offices in urban areas makes people less likely to be exposed to sunlight.

Our findings also showed that the mean serum vitamin D levels in age groups younger than 50-years was lower than age groups older than 50 years, but this difference was not statistically significant. Several studies have reported different results for vitamin D deficiency among different age groups, however, this deficiency was found to be more common among older people (23-26). Researchers found that older people due to multiple risk factors such as decreased food intake, reduced thickness of skin, reduced exposure to sunlight, diminished intestinal absorption and deteriorated hydroxylation in the kidneys and liver are more prone to vitamin D deficiency[27,28]. A periodic monitoring and vitamin D supplement to eliminate the need for vitamin D is recommended for elderly people. Low sample size and ecological design were the most important limitations of this study. It is recommended to consider this point in future studies.

CONCLUSION:

Our results showed that factors such as geographic area (east or west), gender, and place of residence (urban or rural) were related to serum vitamin D deficiency. The remarkable point of our finding is that there was a lower rate of vitamin D deficiency in the eastern area of Golestan province, which has been known as a high-risk area for esophageal cancer. Therefore, investigation of this issue in future individual-level studies in this area and other high-risk populations is recommended.

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