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Soils selenium level and esophageal cancer: An ecological study in a high risk area for esophageal cancer

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ABSTRACT

Project: Golestan province, located in northeast of Iran, has been known as a high risk area for esophageal cancer (EC). This study was conducted to assess the relationship between soils selenium (Se) level and development of EC in this region.
Procedures: In this ecological study, 135 blocks were identified in Golestan province based on geographical altitude and longitude on the map. One soil sample was collected from the center of each block. Then we investigated Se concentration in soil samples by flame atomic absorption spectrometry. Statistical analysis was performed by the Pearson correlation test and Student *t*-tests. *P*-values of less than 0.05 were considered as significant.
Results: The mean $\pm$ SD of soils Se level in Golestan province was 3.7 $\pm$ 1.61 mg/kg. There was a positive correlation between soils Se level and EC rates in this area ($P=0.03$) (Pearson correlation coefficient=0.19). Soils Se concentration was significantly higher in high (4.13 mg/kg) than in the low (3.39 mg/kg) EC rate areas ($P=0.01$).
Conclusions: We found high soils Se concentration and a significant positive relationship between soils Se level and EC rate in Golestan province of Iran. So, high soils Se level may play a possible role in developing EC in this area, specifically in Turkmensahra (very high EC rates).

Introduction

Gastrointestinal (GI) cancers are common malignancies throughout the world [1]. With approximately 386000 deaths per year, esophageal cancer (EC) is the 6th most common cause of cancer death in the world [2], with higher prevalence in Far East and Middle East [3]. Upper GI cancers are leading malignancies in a geographical belt extending from China to Iran [4]. Golestan province in northeast of Iran, located on this belt, has been known as a high risk area for EC since 1972. Kmet et al. [5] reported 108.8 and 174.1 EC cases per 100 000 population of this area for males and females, respectively. Despite the declining rates of EC reported in recent studies (43.4 and 36.3 EC cases per 100 000 population for males and females, respectively) [6], the incidence of EC in this area is still higher than that of the world (11.5 and 4.7 EC cases per 100 000 population for males and females, respectively) [7,8].

EC is a multi-factorial disease. Socioeconomic status [2], Opium consumption [9], alcohol consumption [2], drinking hot tea [10], silis contamination of flour [11], dietary intake of benzopyrene [12], germline BRCA2 mutations [13] and high serum selenium (Se) concentration [14] have been suggested as possible risk factors for EC in Golestan province of Iran. The reason for the declining trend of EC in our area has not yet been known. But improving socioeconomic status has been proposed as the most possible explanation.

Se is a trace element essential to human health [15]. Food is the most important source of Se for the human beings, with meats and cereals being the main sources. In most cases, Se in drinking water is a minor source for humans [16]. Protein-bound seleno-methionine is the dominant form in most plants [17].

The presence or absence of Se in soils depends on the composition of parent material, and is also affected by leaching or processes subsequent to soil formation [18].

Se appears to have a protective effect at various stages of carcinogenesis including both the early and late stages of cancer

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progression [19]. Mechanisms for Se anti-cancer effect have not been fully understood; however, possible explanations include antioxidant protection, enhanced carcinogen detoxification, enhanced immune surveillance, modulation of cell proliferation (cell cycle and apoptosis), inhibition of tumor cell invasion and inhibition of angiogenesis [20]. Both observational and experimental studies have shown that Se supplementation reduces the risk of upper GI cancers in Se-deficient populations [1,21–23]. Ecological relationship between cancer mortality rates and forage crop Se contents in the United States indicated that Se may have anti-cancer effects [24]. Wei et al. [25] in China reported significant inverse association between baseline serum Se and death from EC (RR: 0.83; 95% CI: 0.71, 0.98).

But Se may not have anti-cancer effect in all conditions. Laboratory studies indicated that high doses of Se can be toxic and could even promote cancer [26]. Nouraie et al. [14] reported that serum Se may be a risk factor for EC in Golestan province of Iran.

We conducted this ecological study to assess the relationship between soils Se level and development of EC in Golestan province of Iran.

Material and methods

This was an ecological cross-sectional study conducted in Golestan province of Iran in 2007. About 50.46% of the total population of the province (1 625 003 persons) in 2007 resided in villages. The total area of cultivated soils in this region was about 5600 km^2. Considering the estimation power of 80%, 135 blocks were identified in this area based on geographical information on map. One soil sample was obtained from 30 cm depth in the center of each block.

Fig. 1. Golestan province of Iran.

Then Se concentration was measured in soil samples by flame atomic absorption spectrometry.

Age standardized incidence rates (ASRs) for EC were obtained from Golestan population based cancer registry (GPCR) [27]. GPCR is a voting member of the international association of cancer registries (IACR). Two types of analysis were used for assessing the relationship between EC rates and soils Se level.

At first, we considered both variables as quantitative ones and used the Pearson correlation coefficient to determine the relationship.

Then for further analysis, Golestan province was divided into two areas, based on the ASR of EC. The first area was "Turkmensahra", a region in the northeast of Iran near the Caspian Sea, bordering Turkmenistan, the majority of whose inhabitants are from Turkmen ethnicity [28]. It has been known as high risk area for EC (ASR of EC=44 per 10^5 person years) [27] (Fig. 1). The second was "other parts of the province" (ASR of EC=19.62 per 10^5 person years) (low risk area) [27]. Genetic susceptibility [13], drinking hot tea [10], diet [12] and environmental factors [2] have been suggested as possible explanation for the difference of EC rates between the two areas, but the exact reason has not been known.

Soils PH may affect the characteristics of its minerals (water-solubility, absorption, etc.) and, consequently, may alter its mineral composition. So, we measured soils PH to assess its effects on soils Se concentration. Student *t*-test was used to compare soils Se level between the two areas. *P*-values of less than 0.05 were considered as significant.

Results

Totally, 135 soil samples were collected with mean ($\pm$ SD) PH of 8.03 ($\pm$0.32). The mean$\pm$SD of soils Se level was 3.7$\pm$1.61 mg/kg. There was a significant positive correlation between soils Se level and EC rates (Fig. 2). Table 1 shows the distribution of PH and Se level in soils of high and low EC rate areas. High EC rate area included about 60% of cultivated soils across the province. About 42% (678369 persons) of Golestan

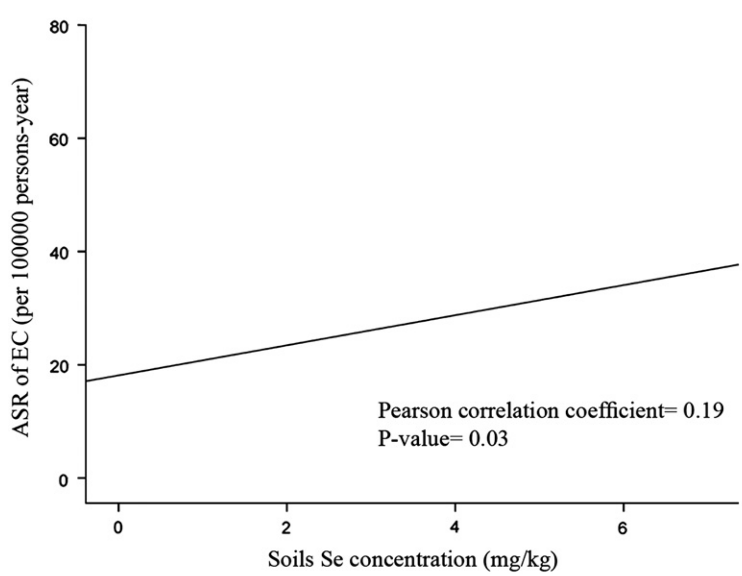

Fig. 2. Correlation between soils selenium level and aged standardized incidence rates (ASR) of esophageal cancer (EC) in Golestan province of Iran.

Table 1
Soils selenium level (mg/kg) and pH in different areas of Golestan province of Iran.

	Area	Range	Mean	SD	*P*-Value
Selenium					
	High EC* rate	3.66–4.59	4.13	1.77	0.01**
	Low EC rate	3.06–3.71	3.39	1.41	
pH					
	High EC rate	8.01–8.13	8.07	0.24	0.17**
	Low EC rate	7.91–8.08	7.99	0.37	

* Esophageal cancer.
** Student *t*-test.

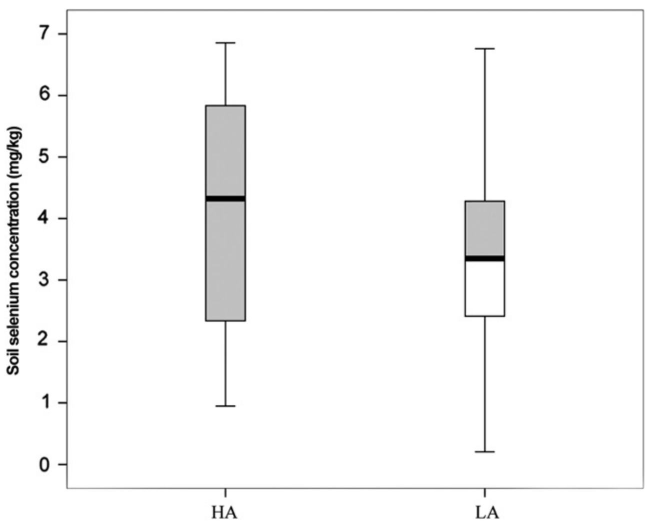

Fig. 3. Soils selenium level by areas (HA and LA=high risk and low risk for esophageal cancer) in Golestan, Iran.

population resided in high EC rate area. The percentages of villager population in high and low EC rate areas were 59% and 44%, respectively. Soil Se concentration in high EC rate area was significantly higher than the other one ($P=0.01$) (Table 1, Fig. 3).

Discussion and conclusion

Golestan province, located in northeast of Iran, has been known as a high risk area for EC. We assessed the relationship between soils Se level and EC rate in this area.

Soils Se concentration in our area was higher than its ranges in most other soils (0.01–2 mg/kg) [29]. It was also higher than the results of similar studies from other parts of the world (0.14–0.37 mg/kg) [16].

In addition to this high soils Se level, there was an underlying factor in this region that may affect the relationship between soils Se level and Se concentration in residents' bodies. The mean of soils PH was 8.03 (alkaline type). It has been known that Se water-solubility and, consequently, its uptake by plants is higher in alkaline soils than in acidic ones [30,31]. As reported in some previous studies [32–34], overuse of agricultural fertilizers (manure or chemical types) may be considered as possible explanation for high soil pH in our region.

So, it can be concluded that high soils Se concentration and its alkaline type in our area may increase Se concentration in agricultural products and this in turn may raise Se concentration in Golestan residents' body organs to high figures [16]. Appleton et al. [16], similarly, found a positive correlation between soils Se concentration, Se level in grain and Se concentration in human organs such as hair.

Our finding was in line with the results of a previous study from this region [14]. Nouraie et al. [14] reported that serum Se level in Golestan province (155 μg/L) was higher than other (low EC rate) provinces of Iran (82, 119 and 123 μg/L in Ardabil, Kerman and Mazandaran provinces, respectively). They found that serum Se concentration in Golestan province was higher than other parts of the world (80–120 μg/L) [35,36].

We found that soils Se concentration had weak significant positive correlation with EC rates in Golestan province. Our results also showed that soils Se level in high EC rate area (Turkmensahra) was significantly higher than the other one. We found no significant difference in soil pH between high and low EC rate areas. So, it could not have considerable effect on soil Se concentration in the two areas. Consequently, we can conclude that the observed significant difference in soils Se level between high and low EC rate areas could not be confounded by soil pH [31,37]. A study from China also showed a higher soil Se concentration in high (0.37 mg/kg) compared to low (0.14 mg/kg) EC rate areas [16].

Although some previous studies reported that Se deficiency plays a major role in development of EC [1,11–13], others suggested that the effects of this trace element may vary in different conditions [26]. A study by Koriyama et al. [38] in Colombia indicated that an inverse association between serum Se level and development of gastric cancer may exist only among populations with low Se level. . The results of a study from Iran did not show any significant difference in hair Se concentration between EC cases and healthy controls [39]. Appleton et al. [16] reported that serum Se deficiency did not play a significant role in the etiology of EC. Finally it should be noted that Se is a trace element essential to human and other animals' health in small doses but is harmful and toxic in excess [16]. Laboratory studies indicated that high doses of Se can be toxic and could even promote cancer [26].

So, as our findings showed, high soil Se concentration may lead to high Se concentration in Golestan residents' body organs and consequently play a possible role in developing EC in this region, specifically in Turkmensahra (very high EC rates).

This was an ecological study and, like other ones, had some limitations. Causal inference cannot be made based on the result of this study. In other words, it should be considered that all relationships in the present study were in population or group level and could not be inferred in individual level. So, complementary studies are needed to determine the actual relationship between soil Se level and development of EC in our area.

In conclusion, we found high soil Se concentration and a significant positive relationship between soil Se level and EC rate in Golestan province of Iran. High soil Se level may play a possible role in developing EC in this area, specifically in Turkmensahra (very high EC rates). So, soil Se level may be considered as a participating factor in future plans for controlling EC (e.g. improving agricultural interventions) in this region as well as in other similar parts of the world.

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