

*Short report*

## Urinary iodine/creatinine ratio in patients with stomach cancer in Urmia, Islamic Republic of Iran

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**SUMMARY** We carried out a case-control study to investigate the relationship between iodine deficiency and stomach cancer. We compared the ratio of urinary iodine to urinary creatinine in 100 patients diagnosed with stomach cancer and 84 people in a control group. Mean urinary iodine levels were lower in the patients with stomach cancer, 61.9 µg/g creatinine, compared to 101.7 µg/g creatinine in the control group ( $P < 0.0001$ ). More of the cancer patients (49.0%) had severe iodine deficiency ( $< 25$  µg/g creatinine) than people in the control group (19.1%) ( $P < 0.0001$ ). We found the relationship between stomach cancer and iodine deficiency to be significant.

### Introduction

Stomach cancer was reported as the leading cause of cancer-related deaths among American men in 1930. Despite the general decrease in its prevalence, it was estimated in 1989 that 20 000 new cases were diagnosed in the United States of America (USA) and that 13 900 Americans died of the disease [1]. Epidemiological studies conducted in Italy indicate that there is a relationship between increasing incidence of goitre due to iodine deficiency and incidence of gastric cancer in some regions of the country [2].

Although a review of the literature shows there have been a limited number of studies concerning the prevalence of stomach cancer in the Islamic Republic of Iran, considering the high rate of patients referred to endoscopy clinics, it may be one of the most prevalent cancers in West Azerbaijan.

The thyroid is derived both embryogenetically and phylogenetically from the

primitive gut and thyroid cells can therefore be considered to be primitive gastroenteric cells that migrated during evolution and specialized in iodine uptake, storage and utilization [3]. The stomach and thyroid share an iodine concentrating ability as well as morphological and functional features such as apical microvilli, amino acid hormones, the ability to digest and reabsorb, and to form iodotyrosines by peroxidase activity [4]. The gastric iodide pump is, however, phylogenetically more primitive than that of the thyroid, has a lower affinity for iodide and does not respond to thyroid stimulating hormone [5].

Mammary cells are also known to have a high ability to concentrate iodine and incorporate it into proteins by mammary peroxidase during pregnancy and breastfeeding, which are considered protective factors against breast cancer [6].

In the normal thyroid of rats, iodine decreases hydrogen peroxide levels [7]. This protects the cells against lipid peroxidation. It has been shown that iodine deficiency or

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excess constitute risk factors for stomach cancer and atrophic gastritis by modifying gastric response and by antagonizing the activities of inhibitors such as nitrates, thiocyanates and salt. Iodine appears to have an antioxidant role in the more ancient organs, particularly the stomach [5].

The known risk factors for stomach cancer include a high salt diet, eating roasted foods, smoking, previous surgery on the stomach, atrophic gastritis, stomach polyps, being male, pernicious anaemia and *Helicobacter pylori* infection [1].

We carried out this study to determine the ratio of urinary iodine to creatinine in people with stomach cancer in Urmia, West Azerbaijan and to compare it with the ratio in people who did not have stomach cancer.

## Methods

We carried out a case-control study over a 2-year period (1999–2001) on (1999–2001) 115 patients with stomach cancer who were referred to the endoscopy clinic of Imam Khomeini Hospital and whose diagnosis was confirmed by endoscopy and pathology. Exclusion criteria were history of previous gastric surgery, stomach polyp and medication with levothyroxine or anti-thyroid drugs. The control group was selected from the people attending the ophthalmology department of the hospital. We selected 100 people consecutively who had no symptoms or diagnosis of gastric carcinoma. They were matched for age and sex with the patient group. After elimination of confounding factors, we had 100 participants with gastric cancer, 67 males and 33 females, and 84 in the control group, 50 males and 34 females.

A morning urine sample was collected from all of the participants. The samples were sent to Urmia reference laboratory for

analysis. Urinary iodine and urinary creatinine were measured and ratios of iodine to creatinine were calculated [8]. We considered values  $< 25 \mu\text{g}$  iodine/g creatinine as severe deficiency,  $25\text{--}50 \mu\text{g}$  iodine/g creatinine moderate deficiency and  $> 50 \mu\text{g}$  iodine/g creatinine normal.

## Results

Because these were matched samples, there was no marked difference between numbers of males and females in the 2 groups ( $P = 0.82$ ). Nor was there any significant age difference ( $P = 0.12$ ). The mean age of patients was 56.6 years (median 60 years; range 22–85 years) and in the control group it was 52.8 years (median 55 years; range 15–84 years). There was no marked difference regarding the use of iodized salt, 89.6% of the patient group and 88.9% of the control group were using iodized salt ( $P = 0.1$ ).

Comparison of urinary iodine/creatinine ratios for the 2 groups indicated that the prevalence of severe iodine deficiency (iodine/creatinine  $< 25$ ) was greater in the group with stomach cancer, 49.0% (Table 1). Correspondingly, the number of people with a normal iodine/creatinine ratio ( $> 50$ ) was greater in the control group, 66.7%.

Mean urinary iodine level in patients with stomach cancer was about 40 units lower than that of people in the control group ( $61.9 \mu\text{g}$  iodine/g creatinine in patients,  $101.7 \mu\text{g}$  iodine/g creatinine in the control group) ( $P < 0.0001$ ). Mean urinary iodine levels for those using iodized salt was also lower in those with stomach cancer ( $61.4 \mu\text{g}$  iodine/g creatinine) than in the control group ( $102.7 \mu\text{g}$  iodine/g creatinine) ( $P < 0.0001$ ), but there was no significant difference between the 2 groups for those who did not use iodized salt,  $72.6 \mu\text{g}$  iodine/g creatinine in the patient

Table 1 Iodine deficiency in patients with stomach cancer and a control group

Iodine/ creatinine ratio <sup>a</sup>	Patients, n = 100		Control group, n = 84		P- value
	No.	%	No.	%	
< 25 <sup>b</sup>	49	49.0	16	19.1	0.0001
25–50 <sup>c</sup>	11	11.0	12	14.3	0.5
> 50	40	40.0	56	66.7	0.001

<sup>a</sup>µg urinary iodine/g creatinine.

<sup>b</sup>Severe deficiency.

<sup>c</sup>Moderate deficiency.

group, 95.1 µg iodine/g creatinine in the control group ( $P = 0.62$ ).

## Discussion

Venturi et al. have suggested that dietary iodine was associated with the development of some cancers of the stomach and breast as well as thyroid cancer. In Italy, gastric cancer is more frequent in iodine-deficient populations living in mountainous regions than in fishermen. The decrease in gastric cancer in Italy in the last 2 decades of the 20th century was correlated to a higher dietary consumption of iodine-rich fish over the same period [9]. Urinary iodine excretion was < 100 µg/day. The Food and Agricultural Organization recommends a level of 400 µg/day to compensate for environmental dietary goitrogens [10].

Urinary iodine excretion in Scandinavian countries now reaches 250 µg/day since introducing iodized salt, and in the USA it is 300–400 µg/day [11,12].

Urinary iodine excretion in Italian populations of the central Apennines was < 100 µg/day, lower among older people, farmers and those in poorer social classes, the people most at risk for goitre as well as gastric cancer [2,9,13,14].

It has previously been demonstrated that the frequent association between atrophic gastritis and goitre dysthyroidisms (thyrogastric syndrome) and between gastric antimucosa and antithyroid antibodies, which might be attributable to common organ specific antigens, are due to the same embryogenetic derivation [11].

Venturi et al. have shown the atrophic regulating action of iodine on gastric mucosa to be similar to the action on the thyroid. They also found a correlation between iodine deficiency, goitre and atrophic gastritis through gastric biopsy. Prevalence of atrophic gastritis was significantly correlated to the degree of iodine deficiency and goitre [15,16]

Prevalence of atrophic gastritis, which is considered a risk factor for stomach cancer in iodine deficient regions, has been very obvious in West Azerbaijan. Our findings also indicate a correlation between stomach cancer and iodine deficiency which is still valid even after the elimination of confounding factors such as age, sex and use of iodized salt.

The following questions should be considered in planning future research:

- Was iodine deficiency in patients with stomach cancer extant before or after cancer was diagnosed?
- Why was iodine absorption low in the patients with stomach cancer even though iodine intake was similar to that of the control group?
- Do the people who have stomach cancer have a genetic defect which affect iodine absorption?
- Would the prescription of iodine (other than iodized salt) prevent the development of stomach cancer?

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