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Regional Variation of Cancer Mortality Incidence and Its Relation to Selenium Levels in China

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ABSTRACT

The epidemiological relationship between selenium level and age-adjusted human cancer mortality (incidence) was studied in 24 regions located in eight provinces of China. Statistically significant inverse correlation was found between age-adjusted total cancer death rates and selenium levels in whole blood from local residents. In the areas with high selenium levels, there was significantly lower mortality in both males and females from cancer of the stomach and esophagus. In addition, an inverse correlation between regional distribution of liver cancer incidence and selenium contents in blood and grains in Qidong county, an area with high risk of hepatoma, was observed. With the intention of providing selenium supplements to residents living in low selenium regions, the selenium content in grains was raised by means of foliar spraying of crops with Na_2Se0_3 solution.

Index Entries: Selenium, cancer mortality correlation; cancer mortality, stomach, esophagus, liver, inverse associatioin with blood

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selenium level; selenium, in high risk areas for liver cancer; China, selenium and cancer distribution in; selenium supplementation, enrichment of selenium in grains; foliar spraying with selenite, of grains; stomach cancer mortality rate, and selenium in China; esophageal cancer mortality rate, and selenium in China; liver cancer mortality rate, and selenium in China.

INTRODUCTION

The essential trace element selenium (Se) appears to be a natural cancer-protecting agent. Numerous experiments have demonstrated that Se as a supplement to a normal diet can decrease tumor incidence in animals exposed to known carcinogens (*1–5*). Epidemiologic evidence has indicated that the incidence of some cancers is inversely correlated to Se levels in human blood, locally grown crops, and plants in cities of United States and other countries (*6–9*). China offers unique conditions for the study of the interrelationship between Se levels and cancer mortality: The vast populations of China are generally nonmobile and have their own local dietary pattern. In addition, the characteristic geographical distribution of cancer in China provides an ideal model for elucidating the possible role of Se in human carcinogenesis. In the present paper the correlation between human cancer mortality and whole blood Se level in 24 regions distributed in various provinces in China is reported. Furthermore, the geographic distribution of primary liver cancer (PLC) in relation to Se level in Qidong county, one of the high risk areas for liver cancer in China, is presented in detail. These studies may help elucidate the effect of Se on human liver cancer and its application to prevention.

MATERIALS AND METHODS

Sources of Data

The age-adjusted mortality rates from cancer by county and city were provided by the committee for the Atlas of Cancer Mortality in the People's Republic of China. The age-adjusted mortality and incidence rate from hepatoma by commune in Qidong were the average figures for 1972–1981.

Samples and Selenium Analysis

There were 1458 blood samples collected from healthy adult residents in 24 regions of eight provinces of China and a total of 419 samples of maize and barley corn were collected from 220 production teams in 43 communes of Qidong county. Selenium contents in samples were measured by the fluorimetric method (*10*) after wet-ashing of all organic matter with hot $HNO_3/HClO_4$.

RESULTS

Selenium Concentration in Human Whole Blood

The Se levels in whole human blood from 1458 donors at 24 locations in China ranged from 2.2 to 31.4 μg/100 mL (mean, 10.7 μg/100 mL). The variation in blood Se concentration as a function of age and sex was examined for donors from Jiashan county. There was no pronounced trend of Se concentration that was associated with age from 27 to 72 yr (rank correlation coefficient, $r_s = -0.0584$, $p > 0.05$), and no sex difference was observed (Table 1).

Correlation of Cancer Mortality with Blood Se Levels

Blood Se levels of persons from 24 regions were found inversely correlated with the age-adjusted total cancer mortality for both sexes ($r_s = -0.64$, $p < 0.01$ for males and $r_s = -0.60$, $p < 0.01$ for females) (Fig. 1). When the data on the Se levels were compared with the age-adjusted cancer rate by organ sites, statistically significant negative correlations were seen, particularly for the major types of cancer in China: stomach cancer ($r_s = -0.64$, $p < 0.01$ for both sexes) and esophageal cancer ($r_s = -0.66$, $p < 0.01$ for males; $r_s = -0.60$, $p < -0.01$ for females). A regional classification by the amount of Se in the blood of residents was employed, which places the regions with blood Se level of 5.0–8.0 μg/100 mL into a group designated as low Se areas, 8.1–11.0 μg/100 mL as medium Se areas, and > 11 μg/100 mL as high Se areas. When the areas with high Se levels were compared to those with medium and low levels, significantly lower total cancer death rates were observed in regions with high Se levels, and the mortality of cancer of the stomach, esophagus, and liver was particularly increased in the low Se areas (Fig. 2).

Geographic Distribution of Liver Cancer and Its Relation to Se Levels in Qidong County

Qidong county, Jiangsu province, one of the high risk areas for liver cancer in China, has primary liver cancer (PLC) mortality rates of 79.26 for males, and 21.57 for females (per 100,000 population). It has a popula-

TABLE 1
Blood Se Concentrations in Jiashan County

Sex	No. of donors	Se concentration, μg/100 mL (M ± SD)	P
Male	59	7.12 ± 1.15	
Female	51	7.10 ± 1.10	>0.05

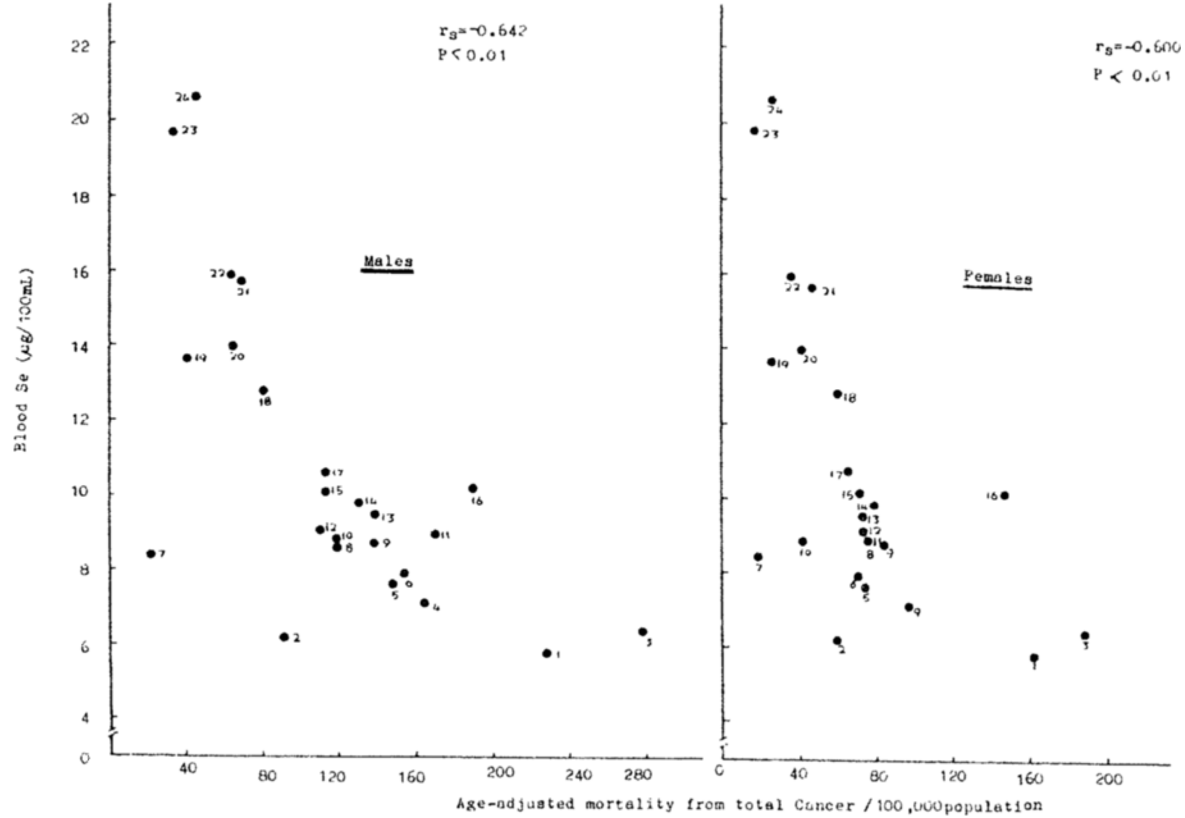

Fig. 1. Relationship between blood Se content and age-adjusted mortality from all cancer sites: 1, Linxian; 2, Puxian; 3, Yangzhong; 4, Jiashan; 5, Wujin; 6, Qidong; 7, Cangshan; 8, Jinan; 9, Jintan; 10, Gejiu; 11, Wuxixian; 12, Nanjing; 13, Wuxishi; 14, Suzhou; 15, Laoshan; 16, Anyang; 17, Hangzhou; 18, Beijing; 19, Conghua; 20, Nanning; 21, Guangzhou; 22, Foushan; 23, Dianbai; 24, Zhanjang.

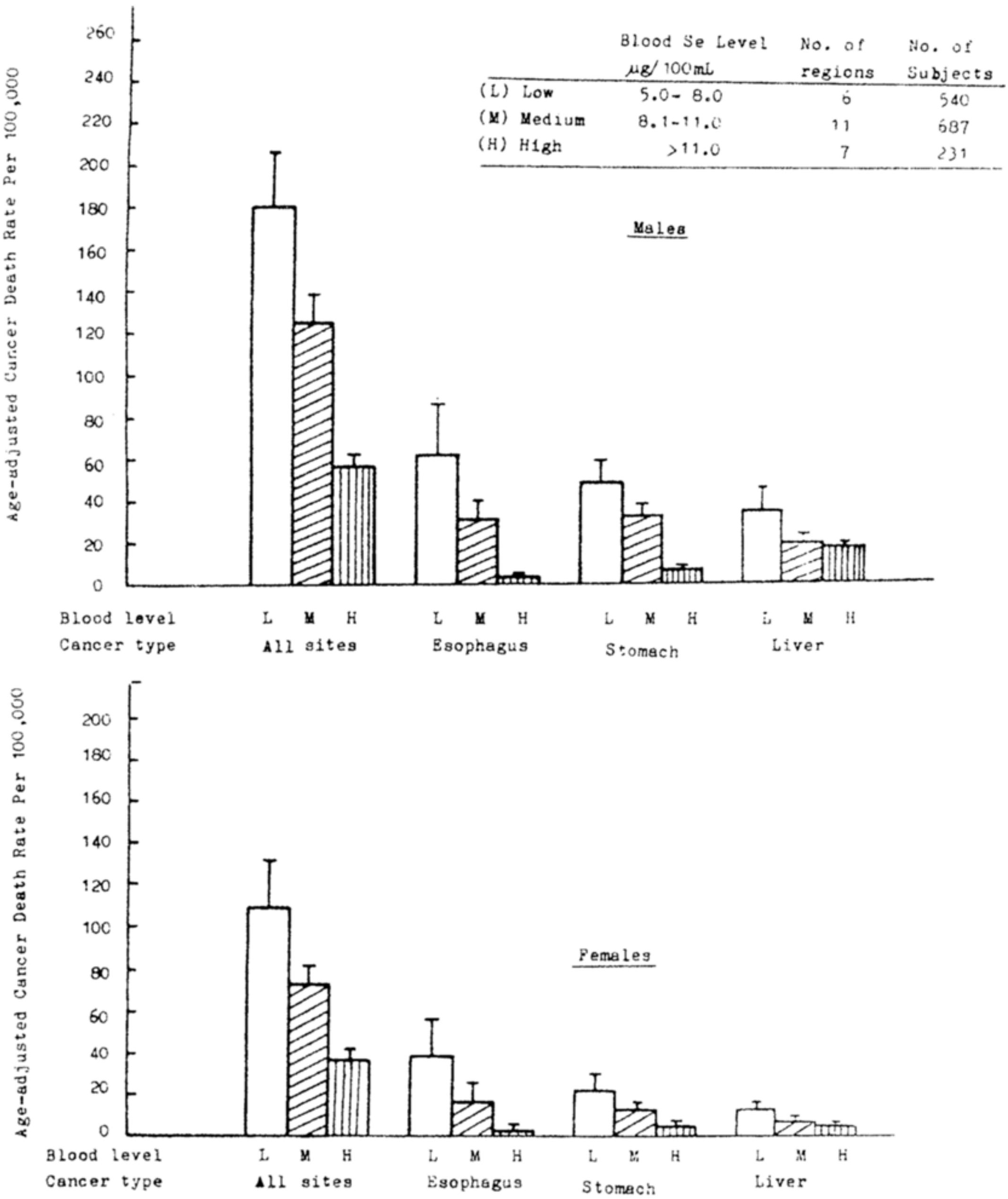

Fig. 2. Relationship between blood Se level and age-adjusted cancer mortality per 100,000 population (mean values ± SE).

lation of about 1,090,000 and covers 1140 square kilometers of land. Qidong county stirred our interest in view of the uneven distribution of PLC throughout the county. Generally, the incidence rates from PLC in the southern part of the county is higher than that in the north. There is a fourfold difference in PLC mortality (incidence) between the highest and the lowest. The Se content in maize and barley corn from 43 communes ranged from 6.9 to 48.1 ppb (mean, 13.4 ± 1.1) and from 12.9 to 113.2 ppb (mean, 25.2 ± 5.98), respectively. A statistically significant negative correlation between the PLC incidence and the Se level in the grains across the county was observed. The correlation coefficients between the age-adjusted PLC incidence by commune and the Se content in local maize and barley corn were −0.623 and −0.631, respectively, $p < 0.01$ for both. An enhanced incidence of PLC prevailed in regions where the grain Se level was low (Table 2).

The inverse correlation was also found between the age-adjusted incidence of PLC and the blood Se levels of residents in different communes. The higher the incidence from PLC, the lower the Se content in human blood (Fig. 3).

Enrichment of Se Content in Grains

The residents in Qidong county are generally nonmobile and they eat mainly what they plant on their local farmland. The cereals may be expected to provide most of the dietary Se. A change of Se content in cereals aimed at increasing the dietary Se supply is suggested as a possible means of lowering the cancer risk in the Qidong population. Thus, we tried to enrich the Se content in grains by foliar spray upon growing crops with sodium selenite solution. A preliminary trial showed that sodium selenite sprays in doses of 7.5–15 g/ha once a year led to 4–6-fold increment of Se content in maize (Table 3).

DISCUSSION

A negative correlation between the blood Se levels and the total cancer mortality in US and certain US cities has been reported by Shamberger et al. (*9*) and Schrauzer et al. (*7*). Similar results were obtained from 24 regions in China. The inverse correlation between the blood Se content and the total cancer death rate was statistically significant for both sexes ($p < 0.01$). Significant inverse correlation was also observed for cancer of the stomach, esophagus, and liver, which are the major types of cancer in China. Further detailed studies on Qidong county, a region with high incidence rate and uneven distribution of PLC, again revealed an inverse correlation between Se level and PLC incidence in people living in this area. These results indicate that Se may play an important role in the etiology of liver cancer. Though Se deficiency is not a cause of PLC, low Se intake apparently reduces the ability

TABLE 2
Grain Se Content in Regions with Different Age-Adjusted PLC Incidence in Qudong County

No. of communes	PLC incidence per 100,000	Se content (ppb) M ± SD	
		Maize[a]	Barley corn[a]
8	15–39	15.1 ± 4.4 (40)	42.3 ± 1.9 (39)
17	40–49	13.5 ± 2.2 (85)	24.7 ± 7.8 (84)
17	50–59	12.7 ± 1.6 (81)	23.5 ± 4.9 (80)
1	60.6	9.7 (5)	18.1 (5)

[a]No. of samples analyzed.

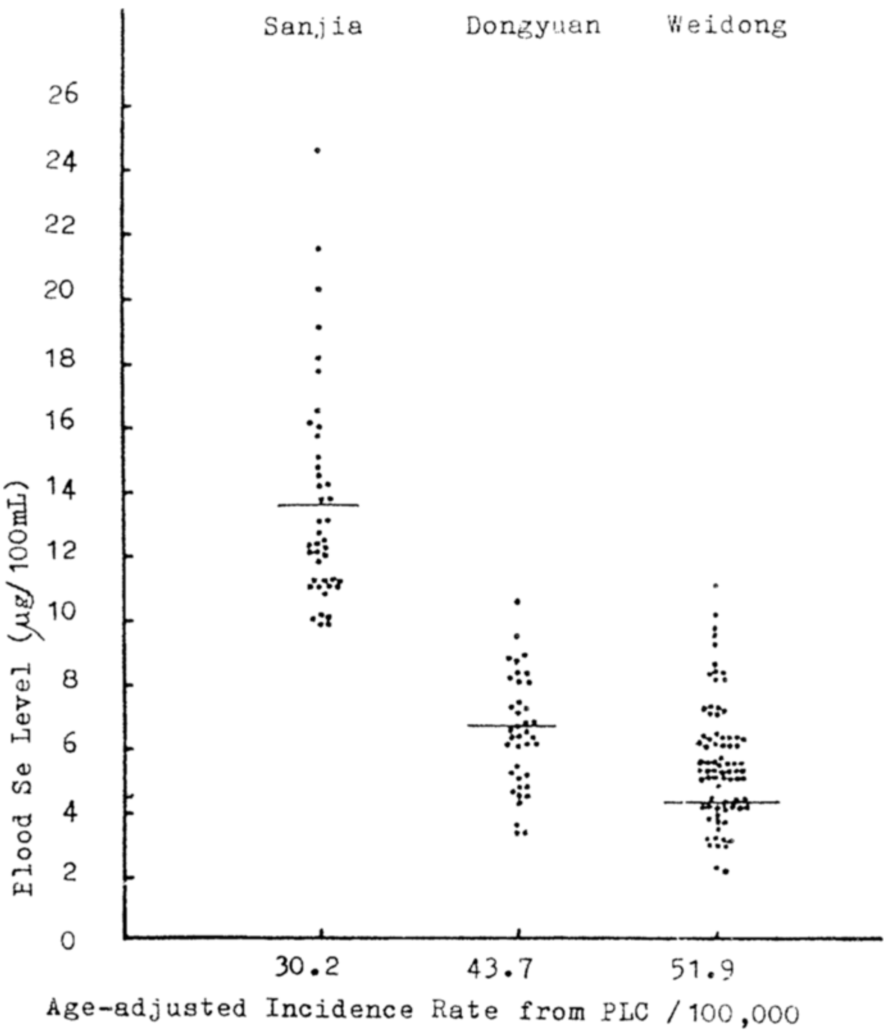

Fig. 3. Blood Se level versus PLC incidence rate.

TABLE 3
Increment of Se Content in Maize by Foliar Sprays with Sodium Selenite Solution

Dose of Na_2SeO_3 spray, g/ha	Se content in maize products, ppb
0	11.3
7.5	46.3
15.0	65.8

of the body to withstand cancer-causing stress. Moreover, numerous reports indicated that Se supplementation was capable of protecting laboratory animals against the induction of hepatoma by carcinogens (*9–11*). When the epidemiological data are taken in conjunction with the animal data, there seems little reason to doubt that Se can have an inhibitory effect of PLC. A logical corollary to this conclusion is that human liver cancer incidence and mortality could be lowered by appropriate dietary Se supplementation in low Se areas. In the present study, with the aim to increase the Se intake, spraying sodium selenite solution on the leaves of crops during their preflowering stage has been tried. Se contents in maize could be raised from 11 to 66 ppb, a level similar to those found in the low PLC incidence area in Qidong county. It has been proven in China that supplementation of Se by this method achieved a reduction in the incidence of Keshan disease, an endemic heart disease closely related with Se deficiency.

We expect that PLC incidence should decline significantly if the dietary Se intake is increased to a level that produces blood Se concentrations similar to those found in the high Se area of Qidong. This approach is convenient, easy to implement, safe, and may provide a long-term control of PLC, which has threatened the people living in low Se area. In addition, the methods succesfully used for providing Se to prevent Keshan disease (*14*), including distribution of selenite tablets, enrichment of table salt with sodium selenite, are available to supplement Se to the residents living in low Se areas to prevent cancer in high-risk areas.

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