A STUDY OF THE ASSOCIATION BETWEEN SELENIUM AND CARDIOVASCULAR DISEASE IN LAMPUNG, INDONESIA

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Abstract. Selenium deficient areas have been associated with a higher prevalence of cardiovascular disease in some countries. In this study, we investigated the correlation between cardiovascular disease prevalence and selenium concentration in paddy soil and rice grains, the main staple food in Lampung, Indonesia. Paddy soil and rice samples ($n_s = 35$) from eight regencies ($n_d = 8$) in Lampung were analyzed for selenium content. The prevalences of heart disease, stroke, and hypertension in those regencies were obtained from the Ministry of Health of Indonesia. The Shapiro-Wilk's test was used to examine the data distribution. The Pearson's correlation was used to examine the correlation between cardiovascular disease prevalence and selenium concentration in the paddy soil and rice grains. Heart disease prevalence was negatively correlated with the selenium concentration in the paddy soil (r = -0.77, p = 0.02) and rice grain (r = -0.71, p = 0.05). A negative correlation was seen for stroke prevalence and selenium concentration in paddy soil (r = -0.76, p = 0.02). Hypertension prevalence was negatively correlated with the selenium concentration in the rice grains (r = -0.83, p = 0.01). These findings suggest that the selenium concentration in paddy soil and rice grains in the Lampung area may play a role in the fact the area has the lowest cardiovascular disease prevalence in Indonesia.

Keywords: selenium, cardiovascular diseases, paddy soil, rice grain, Indonesia

INTRODUCTION

Cardiovascular disease (CVD), a non-communicable disease (NCD) is a leading cause of death among humans. NCDs have been prioritized as an urgent public health problem by the United Nations (UN) (WHO, 2015). CVD is comprised of diseases of the circulatory system (WHO, 1990). The major risk factors for cardiovascular disease are tobacco use, physical inactivity, and an unhealthy diet (WHO, 2015). By 2030, CVD is projected to be the number one cause of death in Indonesia, with a projected 23.6 million deaths by that year, primarily due to heart disease

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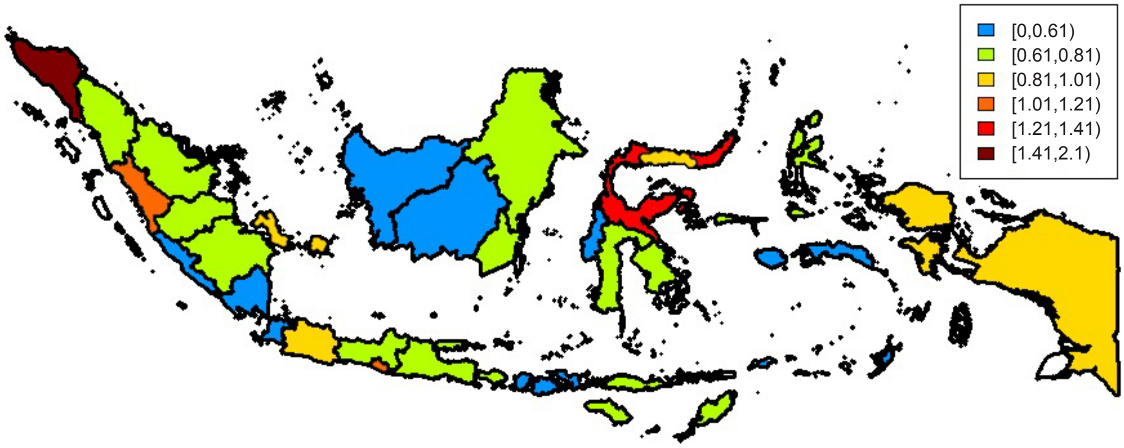

Fig 1–Map of Indonesia with prevalences of cardiovascular disease (Indonesian Ministry of Health, 2008).

and stroke. The largest increase in cardiovascular deaths world-wide is projected to occur in Southeast Asia. CVD is the leading cause of mortality, in Indonesia, comprising 31% of deaths (Indonesian Ministry of Health, 2008).

The Indonesian Ministry of Health (2008) in a study conducted in 33 provinces and 440 regencies estimated 7% of the Indonesian population has CVD, 0.9% was diagnosed by medical practitioners and the rest were diagnosed by symptoms. The same study found no relationship between either social economic status or education and the prevalence of CVD. That study also reported the highest prevalence of CVD to be in Aceh Province and the lowest prevalence to be in Lampung Province (Fig 1). The same study found the prevalence of CVD to be more common among women than men and more common in rural than urban areas. The study found the factors associated with those aged ≥15 years, were diabetes mellitus (39%), hypertension (13.1%), obesity (11.4%) and smoking (9.7%). Lifestyle factors associated with CVD in that study were low physical activity, smoking, a high fat diet and alcohol consumption.

Two previous ecological studies reported finding a negative association between selenium (Se) in the environment and CVD mortality (Shamberger *et al*, 1979; Sun *et al*, 1985). Shamberger *et al* (1979) found age-specific death rates for a number of heart diseases were significantly lower in the US regions with higher Se levels. Sun *et al* (1985) reported the average Se soil content of 6 areas in China with a high prevalence of Keshan disease was significantly lower than the Se content of 5 areas in China with a low prevalence of Keshan disease. Table 1 shows the Se concentration in the soil and the corresponding prevalence of heart disease in several countries. In countries where the Se concentration was low, such as in Turkey, a higher prevalence of heart disease was observed. The aim of the current study was to evaluate the concentration of Se in the soil and in rice grains and its correlation with cardiovascular disease prevalence in Lampung Province, Indonesia.

Table 1
Selenium concentration in the soil and prevalence of heart disease by country.

Country	Selenium concentration (mg/kg)		Reference	Heart disease prevalence (%)	Reference
	Min	Max			
Bangladesh	0.57	1.37	(Ahsan *et al*, 2009)	1.85	(Sayeed *et al*, 2010)
Brazil	1.0	9.4	(Pacheco and Scussel, 2007)	3.61	(Neto and da Silva, 2008)
Chile	0.1	0.49	(Pinochet *et al*, 1999)	1.85	(Icaza *et al*, 2009)
China	0.022	3.806	(Tan *et al*, 2002)	0.46	(Zhang *et al*, 2008)
Greece	0.7	0.7	(Chrysikou *et al*, 2008)	3.90	(Panagiotakos *et al*, 2009)
India	0.207	0.552	(Yadav *et al*, 2005)	3.00	(Ahmad and Bhopal, 2005)
Italy	0.02	1.4	(Spadoni *et al*, 2007)	9.90	(DAI Study Group, 2004)
Libya	0.09	0.62	(El-Ghawi *et al*, 2007)	1.50	(Hassadi *et al*, 1989)
Saudi Arabia	0.024	0.176	(Al-Saleh *et al*, 1999)	6.30	(Hakim *et al*, 2003)
Turkey	0.01	0.08	(Beytut and Karatas, 2002)	5.40	(Aygul *et al*, 2009)
Cameroon	0.1	3.0	(Njofang *et al*, 2009)	1.53	(Kengne *et al*, 2005)
Indonesia	0.24	1.31	Current study	7.20	(Indonesian Ministry of Health, 2008)

MATERIALS AND METHODS

This study was conducted in Lampung Province, Indonesia, in 2010. The province covers an area of 35,288.35 km², is located between 6°45'S 103°40'E and 3°45'S 105°50'E, and has a tropical climate. The area is 21.24% urban and 78.76% rural (Indonesian Central Bureau of Statistic, 2007). District levels were used for unit analysis. Using a power estimation of 80%, eight blocks were identified in this area based on geographical information. The total rice paddy area in this region is approximately 2,233 km² (Barus and Andarias, 2007). The people consume locally grown rice as their staple food.

Se concentrations in the soil and rice

Fig 1 shows a map of Indonesia with the sampling sites and the distribution of heart disease. Samples from 6 other islands in Indonesia were also collected: Papua (Jayapura), Sulawesi (Kendari), Kalimantan (Pontianak and Samarinda), Java (Subang), and Bali (Tabanan). The Se concentration was measured in the rice paddy soil and rice samples using the fluorescence method (Abdulah *et al*, 2005). Briefly, after acid digestion, the amount of Se (IV) was adjusted to a pH of 2, reacted with 1, 2-diaminonaphthalene (DAN), extracted with cyclohexane, and measured by fluorometry at 360 and 520 nm (excitation and emission wavelengths, respectively).

For this study, each soil sample was obtained from a depth of 20 cm. The paddy soil (n=34) and rice samples (n=34) were collected from: West Lampung (4°55'25.98"S, 103°57'37.25"E), South Lampung (5°44'29.06"S, 105°40'30.00"E and 5°47'27.09"S, 105°42'56.72"E), East Lampung (5°17'47.65"S, 105°49'22.31"E; 5°08'52.23"S, 105°40'53.60"E; 5°09'25.82"S, 105°42'57.01"E, and 5°09'52.01"S, 105°40'12.07"E), Central Lampung (4°54' 13.62"S, 105°20'37.45"E), North Lampung (4°46'24.72"S, 104°55'40.90"E), Way Kanan

Table 2
Se concentration in the soil and rice and prevalences of schemic heart disease, hypertension and stoke by location in Indonesia.

Area	Selenium (mg/kg)[a]		Prevalence (%)		
	Soil	Rice	Heart disease	Hypertension	Stroke
Papua	1.31±0.07	0.068±0.0015	4.3	22.0	0.38
Lampung	1.25±0.08	0.101±0.0059	2.6	24.1	0.64
Kalimantan	0.18±0.03	0.007±0.0012	4.4	29.8	0.55
Java	0.44±0.11	0.022±0.0040	8.2	29.4	0.93
Bali	0.24±0.03	0.007±0.0040	5.4	29.1	0.68
Sulawesi	0.24±0.03	0.024±0.0006	8.6	31.6	0.76

[a]Mean ± standard deviation (n=3).

(4°48'26.27"S, 104°26'16.28"E), Tulang Bawang (4°32'19.99"S, 105°15'20.01"E), and Metro (5°08'13.35"S, 105°18'34.14"E and 5°08'59.21"S, 105°18'18.14"E).

Database collection of outcomes

The prevalence of CVD (ICD/10 code I0-I99) was obtained from the database of the National Basic Health Survey conducted by the Ministry of Health of Indonesia, including coronary heart disease (ICD/10 codes I20-I25), stroke (ICD/10 codes I60-I69), and hypertensive disease (ICD/10 codes I10-I15). In Lampung Province, this survey covered 10 districts: West Lampung, Tanggamus, South Lampung, East Lampung, Central Lampung, North Lampung, Way Kanan, Tulang Bawang, Bandar Lampung, and Metro. A total of 424 census blocks, 6,490 households, and 23,833 household members were covered by 36 teams (144 field officers). Information abtained included: nutrition, maternal and child health, communicable diseases, non-communicable diseases, utilization of health services, and environmental health (Indonesian Ministry of Health, 2008).

Statistical analyses

The prevalences of coronary heart disease, stroke and hypertension were calculated as percentages. The Se concentrations in the samples were recorded as mg/kg. The Shapiro-Wilk and Kolmogorov-Smirnov tests were used to check the normality of the data distribution. Bartlett's test was used to check the homogeneity of variances. The data were presented as correlation coefficients (r) and probabilities (p). A one-way analysis of variance (ANOVA) followed by the post-hoc Tukey test was used to determine the differences and statistical significance of normally distributed variables among the groups. The Kruskal-Wallis analysis, followed by a post-hoc test using Mann-Whitney tests with the Bonferroni correction, was used for non-parametric data. The Pearson's product moment and Spearman's rank test were performed for correlation analysis. All statistical analyses were performed using R commander software, version 2.11.1 (R Development Core Team, 2008). A p-value <0.05 was considered as significant.

RESULTS

Table 2 shows the Se concentrations and prevalences of CVD in several provinces of Indonesia. The Shapiro-Wilk test showed a significant association between

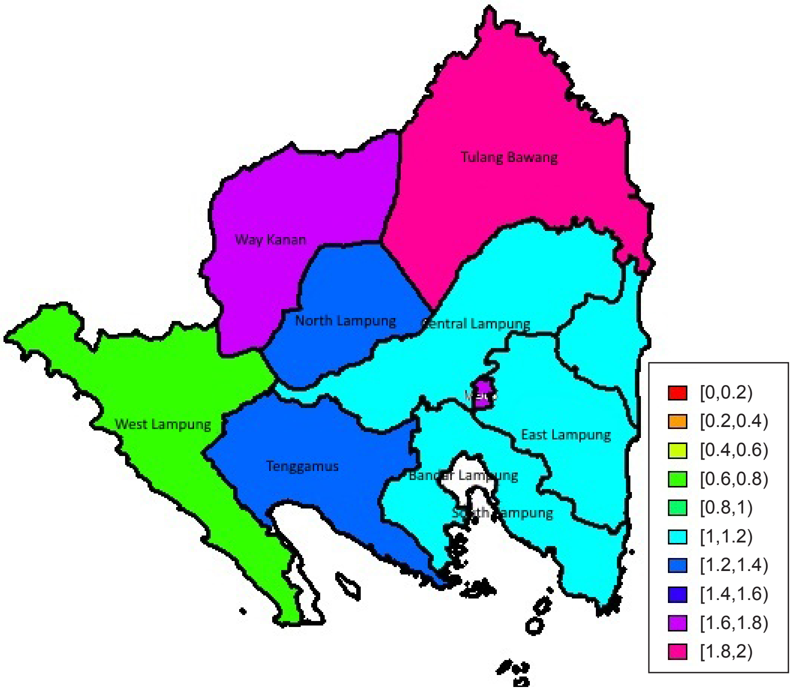

Fig 2–Concentrations of selenium in paddy soil (mg/kg), Lampung-Indonesia.

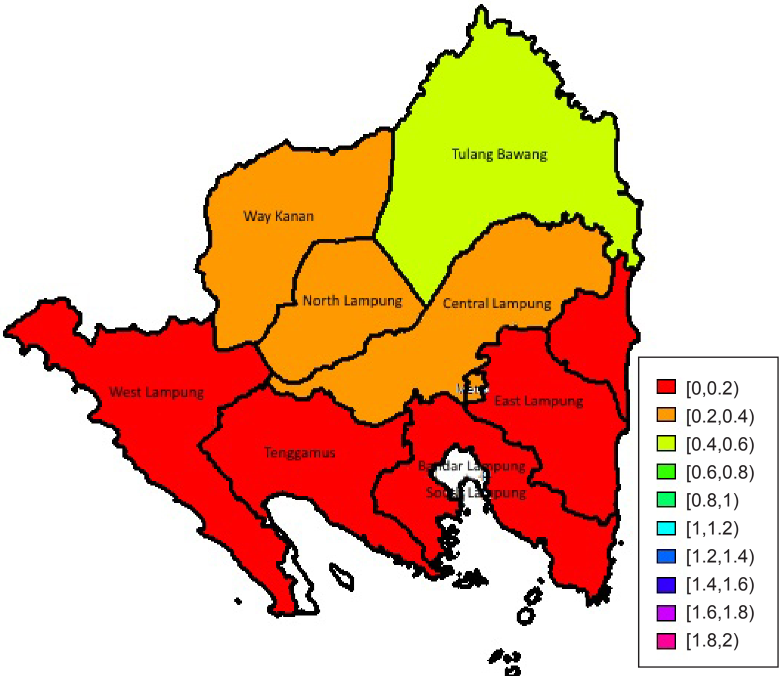

Fig 3–Concentrations of selenium in rice (mg/kg), Lampung-Indonesia.

CVD and paddy soil (W=0.7726, p=0.032) and rice (W=0.788, p=0.04570). A Kruskal-Wallis test revealed significant differences in Se concentration in the soil by province (χ^2=15.8, p<0.01). The prevalences of heart disease were significantly lower in areas where the selenium concentration was higher, such as in Lampung and Papua.

The correlation between Se concentration in the paddy soil and the rice is shown in Fig 4. A positive correlation was seen between the Se concentration in the paddy soil and the rice (Spearman's r =0.86, p=0.025).

Fig 2 shows the Se concentration in the soil of Lampung and Fig 3 shows the Se concentration in the rice of Lampung. The Shapiro-Wilk and Kolmogorov-Smirnov tests revealed the Se concentration in the paddy soil were normally distributed (W=0.94, p=0.6115 and D=0.2209, p=0.7551, respectively); the Se concentration in the rice was also normally distributed (W=0.9655, p=0.8608 and D=0.1365, p=0.9928, respectively).

The correlation between the Se concentration in the soil and the

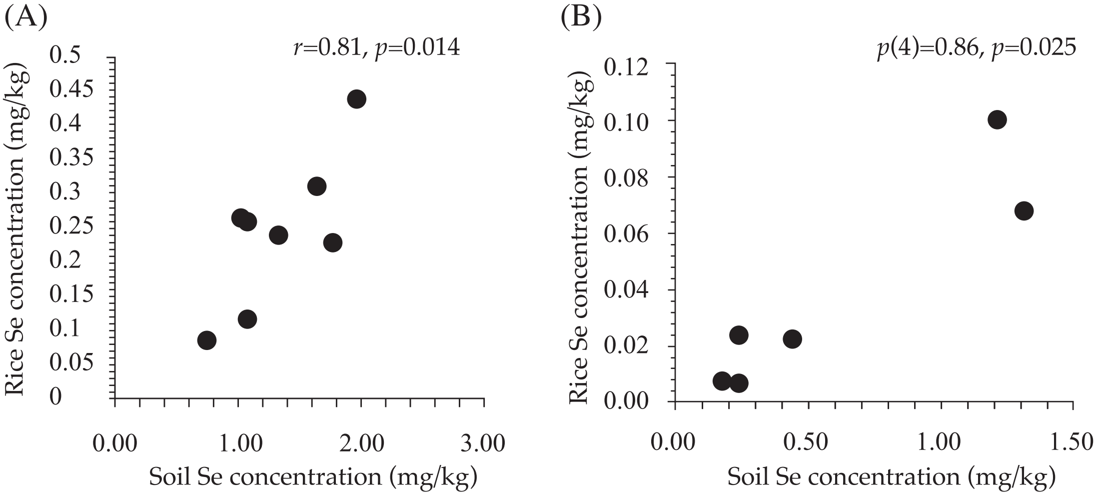

Fig 4–Correlation between selenium (Se) concentration in paddy soil and rice. (A) sample from Lampung, (B) sample from other areas.

rice from Lampung is shown in Fig 4. A positive correlation was found between Se concentration in the paddy soil and in the rice (r= 0.81, p= 0.014).

The correlation between Se concentration and cardiovascular disease in Lampung is shown in Fig 5. Heart disease prevalence was negatively correlated with Se concentration in the paddy soil (r=-0.77, p=0.02) and rice (r= -0.71, p=0.05). Negative correlations were also seen for stroke prevalence and Se concentration in the paddy soil (r=-0.59, p=0.12) and rice (r= -0.46, p=0.25). Hypertension prevalence was negatively correlated with the Se concentration in the paddy soil (r=-0.76, p=0.027) and rice (r=-0.83, p=0.01).

DISCUSSION

Problems associated with an excess or deficiency of Se are found world-wide. Keshan disease and Kashin-Beck disease, have been endemic in parts of China. Keshan disease in an endemic cardiomyoparthy and Kashin-Beck disease is an endemic osteoarthropathy; these diseases are associated with Se deficiency in the soil (Ge and Yang, 1993; Tan *et al*, 2002). A low Se concentration in the soil has been shown to contribute to increased incidence of Kashin-Beck disease in the former Soviet Union (Ermakov, 1992). In areas where the soil Se concentration is highly variable, such as in the USA, ischemic heart disease deaths were inversely correlated with blood Se concentrations in 25 cities from 22 states (Jackson, 1988). Our results showed a broad variation in Se concentration in paddy soil and rice from different islands in Indonesia.

When considering the relationship between disease and Se concentration in the soil, Tan *et al* (2002) proposed a reference values of 0.123-0.175 mg/kg and >3 mg/kg as Se-deficiency and Se-excess, respectively. Using these threshold values, the Se concentration of the paddy soil from Lampung is neither Se-deficient nor Se-excessive. The Se concentrations

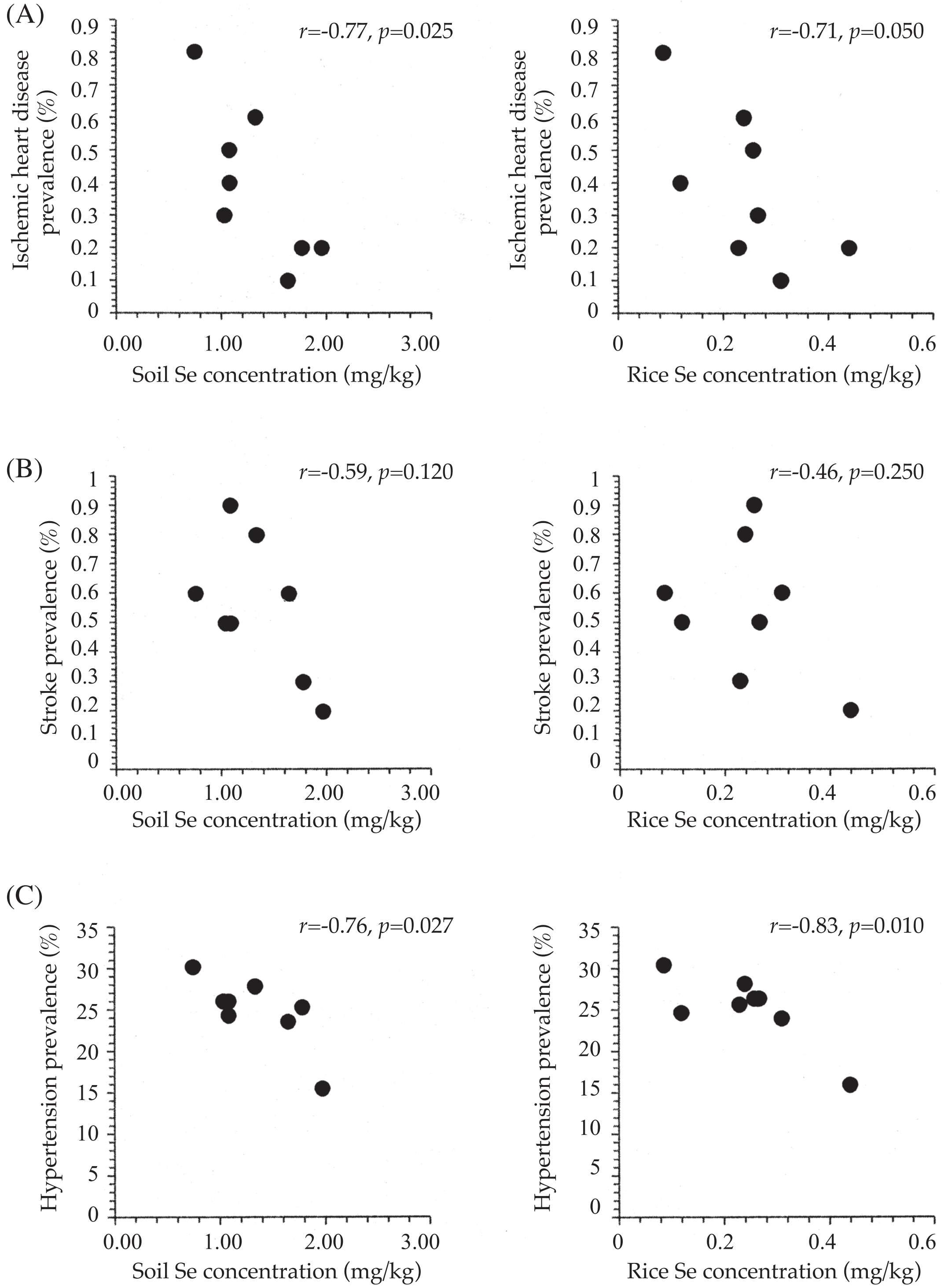

Fig 5–Correlation between Se concentration in paddy soil and rice with the prevalences of (A) heart disease, (B) stroke, and (C) hypertension in Lampung.

of the paddy soil and rice samples from Lampung were higher than the samples from the other islands. The mean Se concentration from Lampung was 1.2 mg/kg with a range of 0.41-2.38 mg/kg and 0.23 mg/kg, with a range of 0.08-0.62 mg/kg in the paddy soil and the rice, respectively.

Along with having higher Se concentrations in the paddy soil and rice in Lampung, residents had a lower prevalence of CVD than other provinces of Indonesia. The national prevalence of diagnosed heart disease is 0.9% with a range of 0.4-2.0%, while in Lampung, the prevalence of diagnosed heart disease was 0.5%. Similarly, the national prevalence of hypertension is 31.7% with a range of 20.1-39.6%, while in Lampung, the prevalence of hypertension is 24.1% (Indonesian Ministry of Health, 2008).

Rice is thought to concentrate Se more efficiently from the soil than from other food crops (Steinnes, 2009). In Enshi County, China, Se-rich soil is present. In this seleniferous area, the rice contains up to 2.5 μg/g Se (Yang *et al*, 1989). However, in West Kalimantan, where the Se concentration is 0.18 mg/kg in the soil, we found a rice Se concentration of 0.007 mg/kg. Therefore, the Se content of staple foods depends on the amount of Se present in the soil (Raghunath *et al*, 2002).

The Se intake by humans is determined mainly by the level of available Se in the soil in which their food is grown as well as their diet. The Se concentration in the human body depends mainly on the amount of Se in the diet (Dodig and Cepelak, 2004). People who consume Se-rich rice would be expected to have fewer Se deficiency symptoms than those who consume Se-poor rice. Study by Karita *et al* (2001), the serum Se concentration of Japanese living in Sao Paulo was lower than Japanese living in Tokyo and the rice grown in Japan had a higher concentration of Se than rice grown in Brazil.

In our study we found a negative association between CVD prevalence and Se concentration; however a study from New Zealand (Robinson, 1989) found no association. In that study, the Se concentration in the soil of New Zealand was lower, but the prevalence of hypertension and cancer were similar to those Western countries with higher Se intakes (Robinson, 1989). The wheat used in making bread in New Zealand is primarily imported and is Se-rich (Lyons *et al*, 2003). The negative correlation between CVD prevalence and Se concentration in our study suggests the local people primarily eat food grown locally, where there is a low soil Se concentration.

Our study had some limitations. Causal inference cannot be made based on the results of this study. Other CVD factors, such as genetics, smoking and obesity, were not controlled for in this study.

Our study gives evidence of a significant negative association between CVD prevalence and Se in the environment. These results show the importance of Se for human health, in particular, cardiovascular health. The Se concentration in the soil should be considered as associated with CVD. Further studies of providing Se supplementation as primary prophylaxis of CVD need to be conducted.

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