Blood thiamin status and determinants in the population of Seychelles (Indian Ocean)

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Abstract

Study objective—Micronutrient deficiencies have become rare in industrialised countries as availability of fresh food, supplementation, and fortification have improved but a less favourable situation may still prevail in many developing countries. Blood thiamin status and determinants were therefore investigated in the Seychelles in view of the high incidence of dilated cardiomyopathy and as the staple diet is polished rice that is deficient in thiamin.

Design—This was a cross sectional population study using an age and sex stratified random sample.

Setting—Seychelles Islands (Indian Ocean).

Participants—A subsample of 206 subjects aged 25–64 years from the population of Seychelles.

Main outcome measures—Measurement of total thiamin concentration in whole blood using high performance liquid chromatography. Dietary variables measured using a face to face semi-quantitative food questionnaire.

Results—Mean (SD) whole blood thiamin concentration was 77.9 (22.4) nmol/l and low concentration (<70 nmol/l) was found in 37% of the subjects (95% CI: 31%, 44%). Blood thiamin was significantly related to education and diet but not to age, sex, smoking, and body mass index. Blood thiamin was associated positively with meat, vegetable, salad, and tea intake and negatively with alcohol and fish intake. However, no combination of the examined variables could explain more than 15% of the observed variance in blood thiamin values.

Conclusions—These data suggest that the distribution of blood thiamin in the sampled population is shifted to lower values compared with that generally accepted as normal in European populations. Further research should establish the significance of such lower values in this specific population to facilitate clinical and public health action as necessary.

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Over the past decades, beriberi heart disease and other thiamin deficient disorders have decreased in many affluent countries partly because of a larger availability of thiamin rich foods and foods artificially fortified with thiamin. Consequently, beriberi has become uncommon in Western countries and now mostly concentrates in specific population groups such as alcoholics,[1,2] institutionalised elderly patients,[3] homeless[4] or in patients receiving parenteral nutrition[5] or receiving treatment with phenytoin[6] or furosemide.[7] However, low thiamin status is still frequent and beriberi endemic in many countries in Asia—mostly resulting from the consumption of diets of unfortified polished rice lacking the vitamin rich husk—[8–10] Latin America,[11,12] Africa,[13–17] East Europe and Russia[18,19] or in the Pacific Islands.[20]

This study was prompted by the high incidence of dilated cardiomyopathy in Seychelles[21,22] and as the staple Seychellois diet is made of polished unfortified rice.[23] We therefore examined thiamin blood status in the general population of Seychelles and attempted to identify factors associated with biochemical thiamin status.

Methods

THE SEYCHELLES

The Republic of Seychelles consists of 115 islands in the Indian Ocean, about 1800 km east of Kenya and 1800 km north of Mauritius. The population has grown to 74 331 people in 1994 and is mixed urban and rural with 52% under 25 years in 1994. The ethnic distribution of the population is considered to be African in 65%, European (white) in 10%, Asiatic in 5%, and mixed in 20%.[24] The standard of living has improved considerably in the past two decades, which is concomitant with a dramatic increase in the tourism industry after the opening of the international airport in 1971. Gross domestic product (GDP) per capita increased from US$925 in 1976 to US$5850 in 1994, and the World Bank considers Seychelles to be now a middle income country.

STUDY DESIGN

The study was designed as a population based cross sectional health survey. The survey was conducted in 1994 on the island of Mahé, which is the largest island of the Seychelles and accounts for 90% of the 74 331 total population of the country. A random sex and age stratified sample of the population was drawn from the 28 695 Mahé residents aged 25–64 years, on the basis of a national census carried out in 1987 and subsequently regularly updated by the administrative authorities. A total of 1067 people (504 men and 563 women) attended the survey out of the 1226 eligible persons, a response rate of 87%. Blood thiamin concentration was determined only in a subset of the original sample by selecting every day for

Table 1   Distribution of blood thiamin (nmol/l)

				Percentiles						
	No	*Mean*	*SD*	*5*	*10*	*25*	*50*	*75*	*90*	*95*
Men	96	77.3	24.0	43	47	58	79	96	111	120
Women	110	78.5	24.8	45	51	62	76	91	116	126
Total	206	77.9	24.4	44	49	59	76	93	112	124

a two month period the five first people who had blood collected (appointment time to attend the survey was given randomly to all participants). Among the 208 subjects who had thiamin measured, two cases were excluded as thiamin concentration exceeded the mean value found for the entire subsample by more than four standard deviations and as the study focused on population parameters rather than on exceptional individual findings. Therefore this study included 206 subjects.

QUESTIONNAIRE

All participants had a face to face structured interview. Intake of fruits, vegetables, salads, and carbonated soft drinks was based on the reported consumption on the previous day. Fish and meat intakes were based on the reported weekly consumption. Participants who reported to drink at least one drink per week were specifically asked about their weekly average consumption of the three commercially marketed alcoholic beverages (beer, spirits, and wine) and three commonly home brewed beverages commonly available in the country. The average alcohol content of these home brews, which are respectively made of fermented palm sap juice, sugar cane and fruit or vegetables was previously assessed and ranged from 7 to 9 grams per litre.[21] The average daily intake of alcohol could be calculated from several questions on the reported type and amount of alcoholic beverages consumed during the previous week. Cigarette smoking was defined as regularly smoking at least one cigarette per day. Body mass index was calculated as weight in kilograms divided by height in metres squared.

BLOOD THIAMIN

Whole blood thiamin concentration was measured at the Laboratory of Vitamins, Marcel Mérieux Foundation (Lyon, France) using a straight phase high performance liquid chromatography (HPLC) technique developed in this laboratory that was previously described.[25] The method includes an extraction step using trichloroacetic acid and takadiastase (during which the phosphorylated forms are converted into free thiamin) and a pre-column derivatisation step (during which thiamin is converted into fluorescent thiochrome ester). Intra and inter assay reproducibility variation of the method were smaller than 7%. Assays were carried out less than two months after blood was collected and blood was kept frozen at −20°C in the interval, using lithium heparin as an anticoagulant. It has been previously shown that there was no loss of thiamin in blood kept frozen at −20°C.[26] Reference values (nmol/l) for whole blood total thiamin measured in the same laboratory were previously obtained from

50 French healthy volunteers (range: 70 to 128; mean (SD): 99 (15) (1 ng/l = 2.9 nmol/l)).[25]

STATISTICS

Exact binomial 95% confidence intervals were calculated for prevalence estimates. Differences in mean values between two groups and across ordered groups were tested using *t* test and non-parametric trend test, respectively. Relations between blood thiamin concentration and selected factors were estimated using univariate and multivariate linear regression models. Analyses were not weighted for age as blood thiamin did not relate to age in the considered age range. Analyses were performed using Stata Software 4.0 (Stata Corporation, College Station, Texas). All reported p values are two tailed and p values less than 0.05 considered as significant.

Results

Blood thiamin ranged from 30 to 150 nmol/l in the study sample. Table 1 shows the mean, standard deviation, and percentiles of blood thiamin across age and sex groups. Thiamin was distributed fairly normally and was similar in men and women (Kolomogorov-Smirnov test for equality of distributions: p = 0.7). Proportions of the subjects with defined blood thiamin values (nmol/l) were as follows: below 40: 2.9%; 40–50: 8.2%; 50–60: 14.1%; 70–80: 16.5%; 80–90: 16.5%; 90–100: 11.1%; 100 and above: 17.5%. Blood thiamin was low by French standards (<70 nmol/l) in 77 of 206 subjects—that is, a prevalence of 37% (95% confidence intervals: 31%, 44%). Anaemia (which has relevance when assessing thiamin concentration in whole blood) was found in only three of 96 men and four of 110 women, using packed cell volume diagnostic criteria set at 42 g/100 ml in men and 37 g/100 ml in women.

Table 2 shows the distribution of subjects and mean blood thiamin across selected groups of population. Thiamin did not substantially vary with age and sex within our sample of adults. Thiamin was lower in people who had not attended secondary school compared with those who had. Thiamin was positively associated with intake of meat, vegetable, salad, and tea and negatively with intake of alcohol and fish. Alcohol consumed by heavy drinkers originated fairly equally from homemade brews and commercially marketed beverages (data not shown). Although around 87% of the population reported to eat fish every day in average, 95% reported to almost never eat raw fish. Thiamin did not differ across categories of smoking, body mass index, fruit intake, and vitamin supplement intake not otherwise specified.

Table 3 shows results of univariate and multivariate linear regression analyses of selected factors on blood thiamin. Analyses were carried out using indicator variables. In these analyses, regression coefficients (β) indicate the predicted change in blood thiamin associated with the change of the explanatory variable (for example, thiamin is 12.8 nmol/l lower in people

Table 2 Distribution of blood thiamin across categories of selected demographic, clinical, and dietary variables

	No	Mean	SD	p value*
Age				
25–44	108	79.5	22.6	
45–64	98	76.2	26.1	NS
Sex				
Women	110	78.5	24.8	
Men	96	77.3	24.0	NS
Education after primary level				
No	169	74.9	23.2	
Yes	37	91.7	25.0	0.000
Smoking				
No	155	78.8	25.4	
Yes	51	75.3	20.9	NS
Body mass index (kg/m²)				
Less than 25	122	78.6	23.8	
25–29	44	75.1	25.4	
30 and above	40	78.9	25.2	NS
Fish servings per day				
Less than 1	26	90.6	26.4	
1 and above	180	76.1	23.6	0.004
Meat servings per week				
Less than 1	48	84.1	24.9	
1 and above	158	76.1	24.0	0.047
Number of fruits on previous day				
0	108	77.0	23.8	
1 and above	98	79.0	25.0	NS
Vegetable servings on previous day				
0	72	73.4	24.5	
1	63	74.6	23.1	
2 and above	71	85.6	23.8	0.000
Salad servings on previous day				
0	114	75.2	23.2	
1	66	77.2	22.6	
2 and above	26	91.5	29.8	0.021
Cups of tea per day on average				
0–1	51	72.3	24.1	
2–3	110	77.0	23.5	
4 and above	45	86.6	24.8	0.002
Gram of alcohol per day on average				
0	155	79.2	27.9	
1–99	25	82.1	21.7	
100 and above	26	66.4	20.7	ns
Vitamin supplement or yeast paste				
No intake within last weeks	160	76.6	23.4	
Intake within last weeks	46	82.7	27.3	ns

*Differences between categories are tested with *t* test (2 categories) or test for trend (3 categories).

Table 3 Linear regression of various demographic and dietary variables on blood thiamin

	Univariate		Multivariate (Adjusted r²=0.12)	
	β	p value	β	p value
Age (45–64 *v* 25–44)	−3.2	NS	—	—
Sex (men *v* women)	−1.1	NS	—	—
Education after primary level (yes *v* no)	16.8	0.000	—	—
Fish servings per day (≥1 *v* <1)	−14.5	0.004	−9.8	0.055
Meat servings per week (≥1 *v* <1)	8.0	0.047	4.5	NS
Fruit number on previous day (≥1 *v* 0)	2.1	NS	−1.8	NS
Vegetable servings on previous day (*v* 0)				
1	1.2	NS	−1.6	NS
2 and above	12.2	0.002	7.6	0.060
Salad servings on previous day (*v* 0)				
1	1.9	NS	2.6	NS
2 and above	16.1	0.002	12.2	0.022
Cups of tea per day on average (*v* 0–1)				
2–3	4.7	NS	2.9	NS
4 and above	14.2	0.004	11.9	0.012
Gram of alcohol per day on average (*v* 0)				
1–99	2.8	NS	2.5	NS
100 and above	−12.8	0.013	−9.6	0.057
Vitamin or yeast within last weeks (yes *v* no)	6.2	NS	1.9	NS

β=regression coefficient. The multivariate model includes all listed variables as dependent variables.

drinking more than 100 g per/day compared with people reporting not to drink regularly). The magnitude of the regression coefficients of most food items decreased in multivariate compared with univariate models indicating that these foods partly intercorrelated. A model including only the considered dietary variables could explain 12% of the variance in blood thiamin concentrations, as assessed by the adjusted *r²* of the multivariate model. Adjustment for education in addition to the dietary variables increased the explained variance to 15% but the magnitude of the regression coefficients of most dietary items slightly decreased, indicating that the effect of education on blood thiamin was partly conveyed by these dietary items (data not shown).

Discussion

This study showed that mean whole blood thiamin concentrations were substantially lower in the adult population of Seychelles compared with European populations where whole blood thiamin was similarly measured. For example, mean (SD) blood thiamin was substantially lower in the Seychelles population than in a series of 50 healthy French adults who had thiamin determined using the same technique carried out in the same laboratory (78 (24) *v* 99 (15) nmol/l; p <0.001)[25] or in a series of 56 healthy Dutch adults, using the same technique performed in another laboratory (78 *v* 117 nmol/l).[26] While blood thiamin (nmol/l) ranged from 30–150 in the sample in Seychelles, ranges were 70–128 in the French study, 71–157 in the Dutch study, and 70–185 in a first published study.[27] These findings suggest that a substantial proportion of the adult population of Seychelles has low blood thiamin compared with European populations. This proportion may amount to one third of adults if low values are considered for whole blood thiamin below 70 nmol/l, which corresponds to the cut off values suggested by all three mentioned European studies.

Direct measurement of blood thiamin by HPLC is considered to provide a reliable and accurate method for assessing long term thiamin nutritional status.[28–30] Low thiamin blood concentrations in the population may relate to clinical findings of a high incidence of dilated cardiomyopathy of unclear origin[21 22] and with findings from two Household Expenditure Surveys carried out in Seychelles in 1984 and 1993 indicating that purchased foods satisfied less than 80% of recommended thiamin requirements.[23] Major factors that probably contribute to low thiamin concentrations are the staple Seychellois diet, which is unfortified polished rice, the fact that carbohydrates account for a high proportion (around 62%, excluding alcohol) of the total energy intake of the Seychellois diet,[23] and that a substantial proportion of the population drinks large amount of alcohol (>15% of male adults drink more than 100 g of ethanol per day[31]). Thus, biochemical and dietary data provide strong evidence for low thiamin concentrations in the population.

Sex and age did not relate significantly to thiamin blood values, which is consistent with reported findings of other studies in adults[32] although higher concentrations of thiamin were also described in men compared with women.[33] Lower blood thiamin was found in people with lower education attainment, which is consistent with other studies on the effect of socioeconomic status on blood thiamin.[36 37] These relations may be partly explained by dietary factors

because education is a recognised determinant of dietary patterns.[38] Our results support the view that the effect of education on blood thiamin is partly mediated by dietary factors as the magnitude of the regression coefficients of most dietary variables relating to thiamin decreased after adjusting for education.

The negative association between alcohol and thiamin found in our study is also consistent with reports that heavy alcohol drinkers have lower thiamin values and low thiamin intake is related to decreased food intake and reduced thiamin intestinal absorption.[1 2] The associations of higher thiamin values with vegetable, salad, and meat found in this study are consistent with these foods containing substantial amounts of thiamin. The negative relation found between fish and thiamin, although fish contains fair amounts of thiamin, may be an artefact explained by the small between individuals variability of fish intake in the country—90% of the population eat fish every day—and residual confounding as fish correlated positively with alcohol (which relates negatively to thiamin) and negatively with meat and vegetables (which both relate positively to thiamin). An effect caused by anti-thiamin activity in fish is unlikely as such an anti-thiamin activity has been reported in raw or fermented fish[39–41] both of which are almost never consumed in Seychelles. Tea has also been reported to be associated with low blood thiamin caused by thiaminase, inhibition of thiamin utilisation, reduced urinary excretion of thiamin, and reduced erythrocyte transketolase activity.[42 43] In Seychelles where tea is consumed in ample amounts (2.6 (SD1.8) cups per day on average in our study) we found a positive relation instead. Although confounding by alcohol intake and other variables may not be excluded, it is unlikely that such a bias could entirely account for the observed positive association, which suggests that tea consumed in Seychelles does not contain substantial anti-thiamin activity.

Overall, dietary factors predicted blood thiamin rather poorly in our study as no combination of the considered dietary variables could explain more than 11% of the variance of blood thiamin. This does not come as a surprise as several other studies in other populations were unable to demonstrate an association between blood thiamin and thiamin intake as assessed by food questionnaire.[28 44 45] Weak or null association with thiamin intake is consistent with the fairly uniform distribution of thiamin in foods[46] and the difficulty to account for thiamin losses as a result of thiamin leaching in cooking water and thiamin cleavage by heat.[47–49]

With regard to clinical practice, our data suggest that thiamin can be given to patients with heart failure of unclear origin, in view of the high mortality of untreated cardiovascular beriberi, the dramatic efficacy of thiamin supplementation in such cases, and in view of the harmless nature of thiamin supplementation.

From a public health view, this study suggests that a substantial proportion of the adult population of Seychelles has low thiamin status compared with European adult populations. The data also indicate that thiamin deficiency cannot be accurately predicted using sociodemographic or dietary indicators. Prevention of thiamin deficiency may therefore target the entire population. Health education to change the population diet in this regard is desirable in view of various health implications. However dietary behaviours are deeply ingrained in the culture and will be slow to change at best. In addition, there are in all populations minorities with limited purchasing power (alcoholics or unemployed being examples) who may have material difficulties to adopt a fully satisfactory diet. Furthermore, a well balanced diet does not provide thiamin in excess, and thiamin cannot be stored in the body in great extent because of its short half life (1.8 days).[50] Therefore dietary fortification (the addition of micronutrients to foods in processing) may be the best long term strategy in controlling micronutrient deficiency where essential micronutrient deficiency is prevalent.[51] Fortification programmes have been implemented by many countries, mostly industrialised, and a variety of foods have been supplemented with thiamin such as rice,[52] cereals[53] or flour.[54 55] In the UK for example, breakfast cereals, most of which are fortified with thiamin and other micronutrients, was shown to account for more than 25% of dietary thiamin[44] and it is now considered that withdrawal of thiamin fortification from processed cereals would have serious negative implications for public health.[53] In developing countries, food fortification with nutrients should similarly be considered a public health priority because gradual replacement of traditional cereals with, for example, milled rice increases susceptibility to beriberi[17] and thiamin status may further be worsened by the recent tendency, particularly for teenagers, to take excessive sweet carbonated soft drinks, instant prepared carbohydrate food, which can readily induce relative thiamin deficiency.[9]

As it is well established that heavy alcohol drinkers are at particularly high risk of developing beriberi,[56–58] special prevention efforts should target this segment of population. To this end, fortification programmes of alcohol beverages have been implemented in various countries.[53 59 60] Alcohol beverage fortification does not materially affect the price of the product[61] nor the taste,[62] and bioavailability of thiamin from this source is high, for example 55 to 103% of the added vitamin in wine after 21 months of storage.[63] Homemade brews will obviously escape fortification attempts but the data in Seychelles indicate that drinkers of home brews also drink beer in large amount. A cost-benefit analysis of the fortification programme recommended in Australia by the National Health and Medical Research Council, which consists of adding thiamin to flour, wines, and beer, was shown to have, under a range of various plausible assumptions, a cost-benefit ratio as high as 6:1 to 30:1 so that the programme is also supported strongly on economic grounds.[64]

In conclusion, these data suggest that there may be a problem related to low thiamin concentrations in the adult population, which requires national attention because, if this is confirmed, it could have significant health implications. More generally, the data emphasise that thiamin deficiency, and possibly other remediable micronutrient deficiencies, may still be of considerable public health importance in various communities.

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