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The Prevalence of Thiamine Deficiency and Associated Factors among Adult Population in Shiraz, Southern Iran

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ABSTRACT

Background: Thiamine is an essential nutrient, and its deficiency is accompanied by nervous and cardiovascular disorders. This study aimed to assess the prevalence of thiamine deficiency and associated factors among adults in Shiraz, southern Iran.

Methods: In a cross-sectional study using random multistage sampling method, 180 men and women who were 20-60 years old were enrolled. Demographic data were collected and a food frequency questionnaire was used to assess dietary intakes. Serum transketolase level was measured to estimate thiamine deficiency.

Results: Mean serum transketolase level was 2.19±2.71 ng/dL, and the mean intake of thiamine was 1.39±0.58 mg/day. Overall serum transketolase level was in the normal range of 0.05-9 ng/dL; however, it was lower than 0.88 ng/dL among 50% of the subjects. No significant association was found between serum transketolase level and either dietary intake of thiamine and weekly intake of whole bread.

Conclusion: Despite the normal serum transketolase level and dietary intake of thiamine, half of the participants were at lower levels of serum transketolase. Therefore, increasing the knowledge of the community about dietary sources of thiamine could prevent thiamine deficiency and enhance their health status.

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Introduction

Thiamine or vitamin B1 is a water-soluble vitamin. Mammals, including humans, do not have the main pathway of thiamine synthesis, so they are dependent on receiving adequate amounts of thiamine from diet (1-3). Thiamine and its phosphate ester are coenzyme in carbohydrate metabolism and the nervous system. Thiamine is a coenzyme required for several mitochondrial enzymes, which are involved in carbohydrate and lipid metabolism and works in three enzyme complexes including pyruvate dehydrogenase, alpha-glutarate dehydrogenase, and transketolase (2, 4).

Thiamine deficiency leads to decreased transketolase activity. Therefore, the production of mediators of the glycolysis pathway is disrupted and carbohydrate metabolism is impaired (5). Thiamine is also involved in other important metabolic pathways in energy production. Free thiamine mediates the activity of the parasympathetic nervous system so

that a deficiency of this vitamin leads to impaired nervous conduction, peripheral neuropathy, and irreversible brain damage (1-4). Moreover, thiamine deficiency leads to lactate and pyruvate accumulation and decreased levels of alpha-ketoglutarate, acetate, citrate, and acetylcholine. If this deficiency is not detected in time, changes in the levels of each of these metabolites can lead to abnormalities such as metabolic diseases, cardiovascular and neurological disorders (6).

Thiamine is essential in the aerobic oxidation of glucose. Thus, brain is the first organ that is affected by thiamine deficiency, because it usually receives all its energy from aerobic oxidation of glucose (1, 7, 8). Thiamine deficiency has been reported in different populations as well as different groups of patients. A study conducted on students in Taiwan reported that 7.5% were thiamine deficient and more than 10% were marginally thiamine deficient (9). The prevalence of thiamine deficiency among patients on emergency admission to a hospital in London was 21%, although they had poor clinical symptoms (10). A retrospective study in the UK investigated the association of thiamine status with disease prognosis on adults admitted to intensive care unit. They found that thiamine levels were lower in the expired patients than in the living patients; however, none of the studied patients showed symptoms of deficiency (11).

Thiamine is found in various herbal and animal products in limited amounts and is abundant just in a small number of foods. Food sources of thiamine are yeast, whole grains, legumes, as well as animal sources such as beef and pork (2, 12). Thiamine deficiency is common in areas where refined rice is one of the main dishes and other major sources of thiamine, such as red meat, fish, and legumes are low. Besides, thiamine deficiency is exacerbated when diet contains anti-thiamine compounds such as fermented fish, tea, and betel nut (13). Furthermore, Thiamine is often degraded during food processing.

Considering the main role of thiamine in the activation of transketolase enzyme, and due to impairment of transketolase activity in thiamine deficiency, the measurement of the transketolase enzyme can be a good marker to assess thiamine status. According to the mentioned contents, thiamine deficiency is a disorder that affects various systems of the body. However, so far no study in Iran has estimated the prevalence of thiamine deficiency in healthy populations and other groups. There is a risk of marginal deficiency of this vitamin due to the low intake of rich sources of thiamine (whole grains) in Iranian diet, limited body reserves of thiamine, and somewhat inaccurate diagnosis of thiamine deficiency with clinical signs and symptoms. Therefore, it is necessary to determine the prevalence of thiamine deficiency to implement corrective interventions. In this regard, this study aimed to assess the prevalence of thiamine deficiency and associated factors among adults in Shiraz, southern Iran.

Materials and Methods

This cross-sectional study was conducted in health centers affiliated to Shiraz University of Medical Sciences, Shiraz, Iran in 2017. The study was approved by the Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran (No. 12873-87-01-95). All the study steps were performed in accordance with the Helsinki Declaration. According to a previous study (14) and considering α=0.05 and power of 90%, the sample size was estimated as 168. Then, this was increased to 180 to compensate the probable dropout and ensure the accuracy of the study.

A multi-stage random sampling method was used in this study. First, according to the geographical areas covered by health centers, Shiraz was divided into 2 areas and from each area, 3 clinics with different geographical locations were selected. Finally, sampling in each clinic was done randomly among the clients. Adult men and women aged 20 to 60 years who had referred to health centers in Shiraz, Iran were included in the study. Exclusion criteria were subjects with chronic disease, malabsorption syndromes, experiencing cholecystectomy or pancreatectomy, taking diuretics, multivitamin and mineral supplements, and alcohol.

After explaining the objective of the study to the participants, with an emphasis on confidentiality, written informed consent was obtained and human rights were respected in accordance with the Helsinki Declaration. Then, the data of age, gender, education, occupation, history of disease, medications, and the frequency of whole bread consumption per week were collected, using a data gathering sheet. Dietary intake was evaluated using a 147-item food frequency questionnaire, by trained experts. Then, NUTRITIONIST IV software, modified for Iranian foods, was used to estimate energy and nutrients intakes. The recommended daily allowance (RDA) was used to determine the adequacy of thiamine intake, which was 1.2 and 1.1 mg, for adult men and women, respectively. Moreover, 5 mL of fasting blood samples were taken from each participant and serums were separated and stored at -70°C.

Serum transketolase was measured using Enzyme Linked Immunosorbent Assay (ELISA) kit (Bioassay Technology Laboratory, BT lab, China).

A wall mountable height rod with an accuracy of 0.1 cm was used to measure the height and a scale (Seca, Germany) with an accuracy of 100 g was used to measure the weight. Then, body mass index (BMI) was calculated as weight in kg/height in m^2 and subjects were classified as obese (BMI more than 30), overweight (BMI between 25 and 29.9), normal-weight (BMI between 18.5 to 24.9), and under-weigh (BMI lower than 18.5). The frequency of whole bread consumption was categorized once or less per week, 2 to 3 times a week, more than 3 times per week, and during all meals and every day.

Data were analyzed using SPSS software (version 20.0, Chicago, IL, USA). Kolmogorov-Smirnov test was used to assess the normality of the data. Quantitative and qualitative variables were expressed as mean±SD and number (%), respectively. Multiple linear regression analysis was used to explore the factors affecting serum transketolase enzyme. The association between categorical variables was assessed using Chi-Square test. A P value less than 0.05 was considered at significant level.

Results

Out of 180 participants in the study, 2 were excluded due to errors in biochemical measurements and 4 due to incomplete completion of the questionnaires. Finally, 174 patients remained in the study. The mean age of the participants was 34.86±11.89 years old and 125 (71.8%) were women. Demographic data, anthropometric measurement, dietary intake, and serum transketolase level were reported in Table 1. The mean serum transketolase level was 2.19±2.71 ng/dL. As shown in Table 2, serum transketolase was lower than 0.88 ng/dL, among 50% of the participants. Regression analysis showed no significant association between serum transketolase level and thiamine intake. Non-significant association was also observed between serum transketolase and energy, carbohydrate, age, sex, and BMI. However, serum transketolase

Table 1: Demographic data and dietary intake of the participants (n=174).

Variables	Numerical values
Age (year)	34.86±11.89*
Sex	
Male	49 (28.2%)**
Female	125 (71.8%)
Occupation	
Jobless or housekeeper	105 (60.3%)
Employee	58 (33.3%)
Self-employed	8 (4.6%)
Retired	3 (1.7%)
Education	
Illiterate	3 (1.7%)
High school	29 (16.7%)
Diploma	39 (22.4%)
Bachelor	84 (48.3%)
Higher education	19 (10.9%)
Weight (Kg)	67.94±12.3
BMI (kg/m2)	24.78±4.01
Serum transketolase (ng/dL)	2.19±2.71
Dietary thiamine (mg/day)	1.39±0.58

* Mean and standard deviation (Mean±SD). ** Number and percentage.

Table 2: Serum transketolase level among the participants (n=174).

Quartile	Sample size	Serum transketolase level per quartile
First (25%)	43	0.47 (0.25, 0.54)*
Second (50%)	44	0.71 (0.56, 0.88)
Third (75%)	44	1.19 (0.89, 2.67)
Fourth (100%)	43	6.16 (2.80, 10.97)

* Median (minimum and maximum).

Table 3: Association between serum transketolase level and demographic variables and dietary intake among the participants (n=174).

Variable	β	95% CI
Age	-0.02	(-0.07)–0.01
Sex	-0.07	(-1.05)–0.90
BMI	0.06	(-0.05)–0.18
Daily thiamine intake	0.10	(-1.08)–1.30
Daily energy intake	-0.00001	(<-0.0001)–(>0.0001)
Daily carbohydrate intake	0.004	(-0.01)–(0.003)
Occupation		
Worker (reference)		
Employee	1.88	1.01–2.75
Self-employed	0.89	(-1.21)–3.01
Retired	0.73	(-2.50)–3.97

The results were obtained from multiple linear regression model.

Table 4: Association between serum transketolase and BMI (n=169).

Serum transketolase (ng/mL)	BMI lower than 18.5 (underweight)	BMI of 18.5-24.9 (normal weight)	BMI of 25-29.9 (overweight)	BMI higher than 30 (obese)
The first quartile	1 (16.7)*	23 (25.6)	9 (18.0)	10 (43.5)
The second quartile	2 (33.3)	22 (24.4)	12 (24.0)	5 (21.7)
The third quartile	1 (16.7)	22 (24.4)	15 (30.0)	4 (17.4)
The fourth quartile	2 (33.3)	23 (25.6)	14 (28.0)	4 (17.4)

*Number and percentage. The *p* value was estimated using Chi-Square test (p=0.68). BMI: body mass index.

Table 5: Association of serum transketolase and the frequency of whole bread consumption per week (n=148).

Serum transketolase (ng/mL)	Once a week or less	More than 2 times a week	All meals and every day
The first quartile	24 (22.0)*	7 (26.9)	4 (30.8)
The second quartile	28 (25.7)	2 (7.7)	6 (46.2)
The third quartile	32 (29.4)	8 (30.8)	2 (15.4)
The fourth quartile	25 (22.9)	9 (34.6)	1 (7.7)

* Number and percentage. The *p* value was estimated using Chi-Square test (p=0.13).

was higher among employees than workers (Table 3).

Table 4 shows that serum transketolase quartiles were not associated with BMI categories including underweight, normal weight, overweight, and obesity (p=0.68). Furthermore, as reported in Table 5, no significant association was seen between serum transketolase quartiles and the frequency of whole bread consumption per week (p=0.13). We merged "2 to 3 times a week" and "more than 3 times per week" categories because the frequency of more than 25% of the cells was less than 5 (Table 5).

Discussion

This study showed that serum transketolase level was at lower levels of normal range, among half of the participants. Moreover, we found no association between serum transketolase and thiamine intake. Serum transketolase in all participants was within normal range of 0.05 and 9 ng/mL. However, it was lower than 0.88 ng/mL among 50% of the subjects as first and second quartiles. Therefore, they may be at risk of thiamine deficiency. Thiamine exists in low content in almost all herbal and animal sources, however good sources of this vitamin are very few and its rich sources are whole grains and whole bread (2). Therefore, there is a risk of marginal thiamine deficiency in healthy population, when consuming white bread, although severe deficiency do not occur and clinical symptoms do not appear, because symptoms of thiamine deficiency have been reported to manifest following thiamine-free diet for 2 to 3 weeks, and worsen if continue 2 to 3 months (15).

Given the available findings, no study has been conducted in Iran to investigate thiamine deficiency. Worldwide studies have also evaluated specific groups such as the elderly, pregnant women, candidates for laparoscopic bariatric surgery, alcoholics, and smokers. Hence, there are no reports of a healthy adult population, up to our knowledge. Only a study in Cambodia measured blood thiamine levels in women of childbearing age. This study reported that 39% of urban women and 59% of rural women had marginal thiamine deficiency (16).

On the other hand, two studies assessed thiamine deficiency in subjects with morbid obesity and candidates for a laparoscopic bariatric surgery. They have reported that 15.5 and 29% of subjects were thiamine deficient in Florida and Louisiana, respectively (12, 17). Another study in Spain found that 7.2% of obese subjects were thiamine deficient, while thiamine deficiency was not seen in normal-weight people. However, no significant difference was reported between obese and normal-weight groups (18).

A study of the elderly in Malaysia found that 36.6% of the elderly had thiamine deficiency (14). Furthermore, pregnant women were monitored from the 30th week of pregnancy until 3 months after delivery. Thiamine deficiency was observed in 57.7% of mothers 3 months after delivery, of which 26.9% were severe deficient (13). Although, the present study could not find a significant association between serum transketolase and thiamine intake, there were a direct association between transketolase activity and thiamine intake in elderly subjects in Indonesia, where the prevalence of thiamine deficiency was reported as 36.6% (14).

The absence of any significant association in our study could be due to a probable similar dietary pattern among participants. Besides, the bacterial

production of thiamine by the intestinal microbial flora can change the need for this vitamin among different people. The amount of bacterial production of thiamine is dependent on the amount and type of intestinal microbial flora, which is varied by subjects, diets, and even the dietary composition of macronutrients (14). On the other hand, the presence of anti-thiamine compounds in some foods such as tea, coffee, etc. can cause thiamine degradation in the diet. Moreover, thiamine is sensitive to alkali, heat, reducing and oxidizing agents and ionizing radiation, thereby, cooking or food processing may adversely affect the bioavailability of this vitamin. Oppositely, food fermentation can increase thiamine content. Therefore, each of these factors can change the functional role of thiamine and affect the association between dietary thiamine and its clinical status (14).

In the present study, while the mean dietary intake of thiamine was followed, the RDA, the most subjects were at the lower level of serum transketolase. Therefore, it may be needed to update the thiamine content of available local breads, as a main source of thiamine, in food composition tables.

High intake of simple sugars or starch could cause thiamine deficiency, especially when it is accompanied by low thiamine intake. High glucose intake and activation of glucose metabolism increase the thiamine requirement, which is called high-calorie malnutrition. Thiamine deficiency could also cause hyperglycemia due to inhibition of the pentose phosphate pathway (5). However, the regression analysis in the present study showed that the association between dietary thiamine and serum transketolase levels was not statistically significant, after adjusting carbohydrate intake as well as energy intake as confounding factors. Therefore, carbohydrate intake in our study population did not show a negative effect on serum transketolase level.

This study was limited to measure thiamine in whole blood. However, we measured transketolase, as an alternative and accurate method. The most common method of measuring this enzyme is to measure transketolase activity in erythrocytes, which is a complex method in laboratory centers (19). Therefore, in this study, an alternative method was used to evaluate serum transketolase. One of the strengths of this study was the geographical extent of sampling that was done from the most regions of Shiraz city and it is expected that people with different socioeconomic status participated in the study.

Conclusion

Serum transketolase level in this study was in the normal range and dietary intake of thiamine was also at a desirable level, however half of the participants were at lower levels of serum transketolase. Therefore, increasing the knowledge of people about food sources of thiamine could prevent thiamine deficiency and promote the community health status. However, more studies are needed to be undertaken to assess the thiamine deficiency at community level. It is also necessary to implement national and local plans to measure thiamine in local foods, especially bread, as the most important source of this vitamin, which will be a reliable guide for dietary recommendations of thiamine.

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Conflict of Interest

None declared.

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