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Dietary B Vitamins and Depression in Persons with Human Immunodeficiency Virus Infection: The Positive Living with HIV (POLH) Study

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Summary B vitamins have beneficial roles in mental health functional impairments; however, research on the role of B vitamins in depression among HIV-infected persons is limited. This study assessed the association between dietary B vitamin intake and depressive symptoms in a cohort of HIV-infected persons. A cross-sectional survey was conducted among 314 HIV-infected persons (180 men and 134 women) aged 18 to 60 y residing in the Kathmandu, Nepal. The Beck Depression Inventory-I was used to measure depression, with a cutoff score of 20 or higher. Dietary intake was assessed using two nonconsecutive 24-h dietary recalls. The relationships between B vitamins and depressive symptoms were assessed using multiple logistic regression analysis. Twenty-six percent participants (men: 23%; women: 29%) were depressed. More than two thirds of participants' B vitamins intake were below the estimated average requirements (EAR) level. Low intake of riboflavin was associated with an increased risk of depression in women but not in men. Multivariate OR (95% CI) for depression in the first, second, and third tertiles of riboflavin in total participants were 1 (reference), 0.87 (0.46–1.64), and 0.49 (0.24–0.98), respectively (p for trend=0.048) and in women were 1 (reference), 0.94 (0.36–2.40), and 0.23 (0.07–0.77), respectively (p for trend=0.020). No clear associations were seen between other B vitamins and depressive symptoms in either sex. Low intake of riboflavin was independently associated with an increased risk of depressive symptoms in all participants and in HIV-infected women. Further prospective studies are warranted to confirm the role of vitamin B vitamins in depressive symptoms among HIV-infected persons.

Key Words B vitamins, depression, diet, HIV, riboflavin

B vitamins have beneficial roles in mental health functional impairments due to their involvement in neurochemical pathways in which they regulate the homocysteine cycle and synthesize monoamines in the brain (*1–9*). B vitamins provide various enzymes required for the metabolism of homocysteine. For example, methylene tetrahydrofolate reductase and flavin mononucleotide (a coenzyme of riboflavin) and cystathionine-B-synthase and y-cystathionase (pyridoxal phosphate-dependent enzymes) are involved in the conversion of homocysteine to methionine and cysteine (*1*, *2*). Methionine has antidepressant properties and is involved in the synthesis of monoamines in the brain (*10*, *11*). Thus, a decreased intake of B vitamins may increase depression due to the accumulation of homocysteine (*4–9*) and decreased synthesis of monoamines in the brain (*10*, *11*).

In accordance with these biologic mechanisms, several observational (*12–16*) and clinical trials (*17–19*) have reported a potential benefit of high B vitamin status on decreasing the risk of depression. In the general population, cross-sectional and prospective studies have found that low intake of riboflavin (*16*), pyridoxine (*13*), cobalamin (*15*, *20–22*), and folate (*12*, *23*, *24*) were associated with increased risk of depression. Furthermore, in patients with depression, studies have reported low serum or plasma concentrations of pyridoxine (*25*, *26*) and folate (*14*, *27–29*) in depressive patients. High cobalamin (*30*) and folate (*17–19*, *31*) status has been associated with a better response to antidepressant treatment. Clinical studies (*32*, *33*) also reported an improved mood disturbance among women with thiamin, riboflavin, and pyridoxine supplementation. Two systematic reviews (*34*, *35*) of dietary intake and depression suggested that diet may have a role in the aetiology of depression; however, there is no strong consistency in the findings across different studies that have assessed the association between dietary variables and depression.

Although studies have shown the benefit of B vitamins against depression in the general population and patients with mental disorders, no published studies have examined the relationship between B vitamins and depression in HIV-infected persons. B vitamin deficiency is common among HIV-infected persons due to malabsorption, diarrhea, impaired storage and altered metabolism (*36–41*). Among them, depression is one of the most common co-morbid conditions (*42*, *43*) that is associated with higher mortality from both AIDS-related and non-AIDS related causes (*44*, *45*).

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Studies have shown that serum folate concentrations were independently associated with hyperhomocysteinemia in HIV-infected persons (*46*, *47*). Thus, this study aimed to assess the association between B vitamins and depressive symptoms in persons infected with HIV while accounting for important HIV-related clinical and other confounders including anti-retroviral therapy (ART). As B vitamins have a potential benefit in mental health, this study hypothesized that a low intake of B vitamins is associated with depressive symptoms, and tested this hypothesis in a sample of HIV-infected persons. This study adds information on the potential benefit of B vitamins in mental health status among the immune-deficient population, apart from previous studies that focused mainly on socio-demographic, psychological, and social risk factors of depression (*48*).

METHODS

Study design and setting. The present analysis used baseline data of a longitudinal healthy living study entitled "Positive Living with HIV" (POLH) conducted from February to March, 2010. This cross-sectional study was conducted among people living with HIV-infection in the Kathmandu, Lalitpur, and Bhaktapur districts of Kathmandu Valley, Nepal. In Nepal, the prevalence of HIV-infection was 0.3% in the general population and it was particularly high among risky groups, for example injecting drug users (IDUs) (6.3%), female sex workers (4.2%), men who have sex with men (3.8%), and male labor migrants to India (1.8%), in particular to Mumbai (*49*).

Study participants. The study procedures have been reported in detail elsewhere (*50*–*56*). In brief, HIV-infected persons were recruited through the network of five non-government organizations (NGOs) working with HIV-infected persons in the Kathmandu Valley. Five different NGOs were providing need-based care and support services to HIV-infected persons in the Kathmandu Valley during the study period. These NGOs' staffs contacted approximately 360 HIV-infected persons either through phone calls or in person during their visit to the NGO. Of them, 330 participants made a recruitment visit, but eight of them did not participate in the study. All together 322 HIV-positive people, aged between 18 and 60 y, participated in the study voluntarily with their written informed consent. None of the participants reported receiving either vitamin or mineral supplementation in previous 12 mo. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Ethics Committee of the Nepal Health Research Council, Kathmandu, Nepal; National Center for Global Health and Medicine, Japan; and Waseda University, Tokyo, Japan. The study procedures were also approved by the Institutional Review Board of the University of Massachusetts, Amherst, USA.

Outcome measure. The Nepali version of the 21-item Beck Depression Inventory (BDI)-I was used to measure depressive symptoms experienced over the prior 2 wk (*57*, *58*). A four-point Likert scale was used to score each item, with a total range between 0 and 62 for the instrument. The Nepali version scale was validated in Nepal with clinical DSM-IV diagnoses (*59*) of major depressive disorder (sensitivity 0.73, specificity 0.91; area under the curve 0.92). The symptoms of 20 and higher are consistent with moderate to severe depressive symptoms according to the validation study (*57*).

Trained interviewers were used to conduct face-to-face interviews in a private setting using a structured pre-tested Nepali version questionnaire. Each interview lasted about 45–60 min. Interviewers informed all participants about the study procedures using a prepared information sheet prior to conduct a survey. Participants were requested to sign informed consent forms prior to being interviewed. Participants were reassured about the confidentiality of their information.

Dietary assessment. The dietary intake was calculated from 2 24-h dietary recalls 1 wk apart and on different weekdays. Trained persons collected detailed information on all food and beverages consumed by participants in 24 h. The information on food preparation methods and recipes used including brand names of food products were collected by showing real food samples and pictures of commonly eaten food. The portion size of food was measured by using locally available standard spoons, glasses, bowls, food models, recording recipes, and a diet measurement scale. The daily intake of B vitamins was calculated using Indian food tables from the Wfood2 program version 1.0 (*60*). The intake of B vitamins was adjusted for energy intake using the nutrient density method calculated by dividing nutrient intake by total energy per 1,000 kilo calories (*61*) and was categorized into tertiles for analysis.

Covariates measure. A variety of information on socio-demographic, life-style, cardiovascular risk factors, and ART was collected using the instruments from previous studies conducted in Nepal (*62*–*65*). ART use was measured by participants' current use of medication at the time of the survey along with specified duration and names of medication and adherence. The past history of any disease was solicited by the question "In the past 12 months, did you suffer from any type of diseases including minor illnesses?" with response options of yes or no. If the response was yes, the signs or symptoms of disease or disease diagnosis with details of health seeking behavior and treatment of each disease were queried. The measurement of other socio-demographic and life-style variables has been described elsewhere (*66*, *67*).

Physical examination. The body weight of participant was measured in kilograms on a digital scale and the height was measured in centimeters by a stadiometer. Body mass index (BMI) was calculated as body weight in kilograms divided by the square of body height in meters. Blood pressure was measured with the Omron Automatic Blood Pressure Monitor after the participants had been seated for at least 10 min with their feet on the floor and their arms supported at heart level. All anthropometric measurements were repeated to estimate mean values for these parameters.

Table 1. Baseline characteristics of HIV-infected persons.

	Male	Female	*p*-value[1]
Subjects (*n*)	180	134	
Age (mean±SD, y)	35.60 (6.93)	32.59 (6.95)	0.0002
Smoking (never, %)	51 (28.33)	115 (85.82)	<0.0001
Alcohol consumption (never, %)	151 (83.89)	125 (93.28)	0.011
Anti-retroviral therapy (yes, %)	119 (66.11)	109 (81.34)	0.002
History of any disease in past 12 mo (yes, %)	104 (57.78)	94 (70.15)	0.024
Body mass index (mean±SD, kg/m^2)	21.49 (2.87)	21.97 (3.08)	0.157
CD4$^+$ T-cell count (median, range; cells/μL)	333 (41–962)	360 (15–1551)	0.019
Energy intake (mean±SD, kcal)	1,985.35 (600.67)	1,548.34 (443.28)	<0.0001
Thiamin (median, range; mg/1,000 kcal)	0.36 (0.24–0.79)	0.37 (0.23–0.80)	0.151
Riboflavin (median, range; mg/1,000 kcal)	0.35 (0.17–1.32)	0.34 (0.16–0.80)	0.116
Niacin (median, range; mg/1,000 kcal)	5.48 (2.56–9.94)	5.32 (2.66–9.65)	0.382
Pyridoxine (median, range; mg/1,000 kcal)	0.69 (0.40–1.40)	0.71 (0.37–1.52)	0.793
Folic acid (median, range; μg/1,000 kcal)	83.12 (37.48–257.04)	80.70 (31.75–300.73)	0.745
Cobalamin (median, range; μg/1,000 kcal)	0.56 (0.04–3.38)	0.49 (0.04–3.00)	0.519

Values for B vitamin intake are adjusted for energy intake by using the nutrient density method.
[1] *p* values were based on the Student *t* test for continuous variables and chi-square test for categorical variables.

Table 2. Correlation coefficients among energy-adjusted B vitamins in HIV-infected participants.

B vitamins	Thiamin	Riboflavin	Niacin	Pyridoxine	Folic acid	Cobalamin
Thiamin[1]	1.000	0.360*	0.719*	0.703*	0.387*	0.202*
Riboflavin[1]	0.360*	1.000	0.252*	0.343*	0.401*	0.555*
Niacin[1]	0.719*	0.252*	1.000	0.715*	0.111**	0.357*
Pyridoxine[1]	0.703*	0.343*	0.715*	1.000	0.362*	0.343*
Folic acid[2]	0.387*	0.401*	0.111**	0.362*	1.000	0.041**
Cobalamin[2]	0.202*	0.555*	0.357*	0.343*	0.041**	1.000

Unit: [1] mg/1,000 kcal, [2] μg/1,000 kcal.
* $p<0.001$, ** $p>0.05$.

Statistical analyses. Eight participants who did not have information on B vitamin intake were excluded, resulting in a final study population of 314 participants (180 men and 134 women). Student's *t* test and the chi-square test were used to assess the difference in demographic, life-style, anthropometric, B vitamin intake, and clinical parameters by depression symptoms, for continuous variables and categorical variables, respectively.

The relationships between B vitamin intake and depressive symptoms were assessed using multivariate logistic regression analysis. Odds ratios and 95% confidence intervals (CI) for depressive symptoms were calculated across tertiles of B vitamin intake. Major socio-demographic characteristics and other confounding factors having previous establishment or plausible associations with the dependent variable were included as covariates in the analyses. Age (years, continuous), sex (men or women), alcohol intake (never or ever), smoking (never or ever), body mass index (kg/m^2, continuous), history of any disease in the past 12 mo including minor illnesses (yes or no), CD4$^+$ T-cell count (cells/μL; continuous), and ART (yes or no) were adjusted for in the multivariate models. The ordinal numbers 0–2 assigned to tertile categories of B vitamin intake were used to calculate trend associations. All *p* values were two-sided and *p* values less than 0.05 were considered statistically significant. Analyses were performed with SAS statistical software version 9.1 (SAS Institute, Inc., Cary, NC).

RESULTS

In total, 26% of participants had depressive symptoms. The prevalence of depressive symptoms was higher in women (29.1%) than in men (23.3%). Table 1 shows the demographic and clinical characteristics and B vitamin intake of the 314 HIV-infected participants by sex. Men were more likely to smoke or drink and had a lower median CD4$^+$ T-cell count than women. There were no gender differences in B vitamin intake. The energy intake in men was significantly higher than that in women. Table 2 shows the correlation coefficients among B vitamins in HIV-infected participants. Overall, B vitamins were correlated among each other except between folic acid and cobalamin, and niacin and folic acid. There was no significant difference in demographic or clinical characteristics of participants by riboflavin intake except for sex and smoking. There were more men (84/106) and smokers (67/106) in the highest tertile of riboflavin intake ($p<0.05$). The mean

Table 3. Odds ratios and 95% CIs for depressive symptoms according to dietary B vitamin intake in total HIV-infected participants.

	Dietary B-vitamin			p value[1]
	T1 (Lowest)	T2	T3 (Highest)	
Thiamin (median, range; mg/1,000 kcal)	0.29 (0.23–0.33)	0.36 (0.33–0.40)	0.46 (0.40–0.80)	
No. with depression	24/104	27/105	30/105	
Univariate model OR (95% CI)	1.00 (reference)	1.15 (0.61–2.17)	1.33 (0.71–2.48)	0.364
Multivariate model[2] OR (95% CI)	1.00 (reference)	1.15 (0.59–2.24)	1.22 (0.64–2.33)	0.545
Riboflavin (median, range; mg/1,000 kcal)	0.26 (0.16–0.30)	0.35 (0.30–0.40)	0.44 (0.40–1.32)	
No. with depression	30/104	29/105	22/105	
Univariate model OR (95% CI)	1.00 (reference)	0.94 (0.51–1.71)	0.65 (0.34–1.23)	0.192
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.87 (0.46–1.64)	0.49 (0.24–0.98)	0.048
Niacin (median, range; mg/1,000 kcal)	4.11 (2.56–4.74)	5.36 (4.74–5.91)	6.89 (5.93–9.94)	
No. with depression	30/104	26/105	25/105	
Univariate model OR (95% CI)	1.00 (reference)	0.81 (0.44–1.49)	0.77 (0.41–1.43)	0.406
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.82 (0.43–1.57)	0.74 (0.39–1.42)	0.373
Pyridoxine (median, range; mg/1,000 kcal)	0.57 (0.37–0.65)	0.69 (0.65–0.75)	0.86 (0.75–1.52)	
No. with depression	27/104	29/105	25/105	
Univariate model OR (95% CI)	1.00 (reference)	1.08 (0.59–2.00)	0.89 (0.47–1.66)	0.721
Multivariate model[2] OR (95% CI)	1.00 (reference)	1.02 (0.54–1.94)	0.75 (0.39–1.46)	0.406
Folic acid (median, range; μg/1,000 kcal)	59 (31–71)	82 (71–99)	129 (99–300)	
No. with depression	25/104	28/105	28/105	
Univariate model OR (95% CI)	1.00 (reference)	1.14 (0.61–2.14)	1.14 (0.61–2.14)	0.664
Multivariate model[2] OR (95% CI)	1.00 (reference)	1.35 (0.70–2.61)	1.08 (0.56–2.09)	0.798
Cobalamin (median, range; μg/1,000 kcal)	0.22 (0.04–0.32)	0.50 (0.32–0.75)	1.16 (0.75–3.38)	
No. with depression	24/88	25/105	28/105	
Univariate model OR (95% CI)	1.00 (reference)	0.83 (0.43–1.59)	0.97 (0.51–1.83)	0.948
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.74 (0.37–1.47)	0.85 (0.43–1.67)	0.671

Values for B-vitamin intake are medians for adjusted energy intake by using the nutrient density method for each tertile.
[1] Linear trends across tertiles of B-vitamin intake were tested using ordinal numbers 0–2 assigned to tertile categories.
[2] All multivariate models were adjusted for age (years, continuous), sex (men or women), alcohol intake (never or ever), smoking (never or ever), body mass index (kg/m^2, continuous), history of any disease in past 12 mo (yes or no), CD4$^+$ T-cell count ($\leq$200 or $>$200; cells/μL), and anti-retroviral therapy (yes or no).

energy intake and all B-vitamins were significantly higher in the highest tertile of riboflavin intake than that of the lowest tertile ($p<0.05$): energy (2183.60 vs 1367.60 kcal), thiamin (0.83 vs 0.52 mg/1,000 kcal), riboflavin (0.95 vs 0.40 mg/1,000 kcal), niacin (12.40 vs 7.30 mg/1,000 kcal), pyridoxine (1.59 vs 1.00 mg/1,000 kcal), folic acid (200.60 vs 122.60 μg/1,000 kcal), and cobalamin (1.84 vs 0.60 μg/1,000 kcal) (data not shown in the table).

This study did not find any statistically significant associations between B vitamin intake and the prevalence of depressive symptoms in total participants except for the intake of riboflavin (Table 3). The multivariate adjusted OR (95% CI) for depressive symptoms was 1 (reference), 0.87 (0.46–1.64) and 0.49 (0.24–0.98), respectively, for successive tertiles of energy-adjusted riboflavin intake (p for trend=0.048). Table 4 shows the association between tertiles of B vitamin intake and depressive symptoms among men. No significant association was observed between B vitamins intake and depressive symptoms in men. But a significant inverse association between energy-adjusted riboflavin intake and depressive symptoms was found among women (Table 5). The multivariate adjusted OR (95% CI) for depressive symptoms in women was 1 (reference), 0.94 (0.36–2.40) and 0.23 (0.07–0.77), respectively, for successive tertiles of energy-adjusted riboflavin intake (p for trend=0.020).

DISCUSSION

Among six different B vitamins, only low dietary intake of riboflavin was significantly associated with increased risk of depressive symptoms in HIV-infected women. This is the first study that has assessed the role of B vitamins in depressive symptoms among HIV-infected persons adjusting for important confounding variables.

The relationship between dietary riboflavin intake and depression has received little attention although the protective role of riboflavin intake in depression is recognized (*1, 2*). This study adds the beneficial role of riboflavin against depressive symptoms among the immune-deficient population with poor nutritional status. This finding is supported by previous observational study conducted among the general population in a developed country (*16*). For example, in the Osaka Maternal and Child Health Study (*16*), a decreased risk of postpartum depression was observed among Japanese women in the third quartile of riboflavin intake as compared to the first. In a study from Calgary (*68*), riboflavin and other B vitamins were significantly correlated with Global

Table 4. Odds ratios and 95% CIs for depressive symptoms according to dietary B vitamin intake in HIV-infected men.

	Dietary B vitamins			*p* value[1]
	T1 (Lowest)	T2	T3 (Highest)	
Thiamin (median, range; mg/1,000 kcal)	0.29 (0.24–0.32)	0.36 (0.32–0.39)	0.45 (0.40–0.79)	
No. with depression	15/60	14/60	13/60	
Univariate model OR (95% CI)	1.00 (reference)	0.93 (0.39–2.10)	0.83 (0.35–1.93)	0.666
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.92 (0.37–2.28)	0.84 (0.34–2.05)	0.702
Riboflavin (median, range; mg/1,000 kcal)	0.27 (0.17–0.30)	0.35 (0.30–0.40)	0.49 (0.40–1.32)	
No. with depression	14/60	13/60	15/60	
Univariate model OR (95% CI)	1.00 (reference)	0.90 (0.38–2.14)	1.09 (0.47–2.52)	0.829
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.99 (0.39–2.49)	1.07 (0.42–2.74)	0.875
Niacin (median, range; mg/1,000 kcal)	4.12 (2.56–4.69)	5.48 (4.74–6.09)	6.96 (6.21–9.94)	
No. with depression	18/60	12/60	12/60	
Univariate model OR (95% CI)	1.00 (reference)	0.58 (0.25–1.35)	0.58 (0.25–1.35)	0.197
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.52 (0.21–1.27)	0.52 (0.21–1.28)	0.148
Pyridoxine (median, range; mg/1,000 kcal)	0.57 (0.40–0.64)	0.69 (0.65–0.75)	0.86 (0.75–1.48)	
No. with depression	16/60	14/60	12/60	
Univariate model OR (95% CI)	1.00 (reference)	0.83 (0.36–1.91)	0.68 (0.29–1.61)	0.388
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.79 (0.32–1.94)	0.62 (0.24–1.57)	0.318
Folic acid (median, range; μg/1,000 kcal)	62.42 (37.48–73.01)	83.12 (73.09–93.64)	128.77 (94.77–257.04)	
No. with depression	11/60	17/60	14/60	
Univariate model OR (95% CI)	1.00 (reference)	1.76 (0.74–4.16)	1.35 (0.55–3.28)	0.517
Multivariate model[2] OR (95% CI)	1.00 (reference)	2.52 (0.98–6.50)	1.27 (0.49–3.25)	0.656
Cobalamin (median, range; μg/1,000 kcal)	0.24 (0.04–0.36)	0.56 (0.36–0.83)	1.19 (0.84–63.38)	
No. with depression	15/56	10/60	17/60	
Univariate model OR (95% CI)	1.00 (reference)	0.54 (0.22–1.34)	1.08 (0.47–2.44)	0.819
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.60 (0.22–1.57)	1.11 (0.46–2.68)	0.761

Values for B vitamin intake are adjusted for energy intake by using the nutrient density method for each tertile.

[1] Linear trends across tertiles of B vitamins intake were tested using ordinal numbers 0–2 assigned to tertile categories.

[2] All multivariate models were adjusted for age (years, continuous), alcohol intake (never or ever), smoking (never or ever), body mass index (kg/m^2, continuous), history of any disease in past 12 mo (yes or no), CD4$^+$ T-cell count ($\leq$200 or $>$200; cells/μL), and anti-retroviral therapy (yes or no).

Assessment of Functioning (GAF) scores among 97 community-based adults with mood disorders. A clinical trial among 120 healthy adults with supplementation of 10 times the recommended daily dose of 9 vitamins, or a placebo, reported an improved mood disturbance among women with thiamin, riboflavin, and pyridoxine supplementation (*32*, *33*).

The benefit of riboflavin on mental health may be explained by the action of riboflavin coenzymes in the remethylation and trans-sulfuration of homocysteine, as discussed earlier (*1*, *2*). Jacques et al. (*8*) in the Framingham Study population and Ganji and Kafai (*9*) in the National Health and Nutrition Examination Survey population reported an inverse relationship between riboflavin and homocysteine. Thus, hyperhomocysteinemia may mediate the relationship between increased intake of riboflavin and the decreased risk of depression.

This study did not find any significant decreased risk of depressive symptoms with increased intake of thiamin, niacin, pyridoxine, cobalamin, or folate in HIV-infected persons. The findings are both consistent with (*16*, *24*, *69–71*) and contrary to some previous studies (*12–16*, *72–75*) that assessed the relationship between thiamin, niacin, pyridoxine, cobalamin, or folate and depression in the general population living in developed countries. These discrepancies may be partly ascribed to differences in the target population, dietary intake, dietary assessment methods, depressive symptoms measurement methods, and confounding variables treatment.

In this study cohort, more than two-thirds of the participants' intake of B vitamins was below the estimated average requirements (EAR) level (*76*). The majority of participants' B vitamin intakes were below the EAR level; 86.67% for thiamin ($<$1.0 mg/d), 90.0% for riboflavin ($<$1.1 mg/d), 65.0% for niacin ($<$12 mg/d), 24.44% for pyridoxine ($<$1.1 mg/d), 78.41% for cobalamin ($<$2.0 μg/d), and 97.78% for folate ($<$320 μg/d) in men and 94.03% for thiamin ($<$0.9 mg/d), 93.28% for riboflavin ($<$0.9 mg/d), 88.06% for niacin ($<$11 mg/d), 54.48% for pyridoxine ($<$1.1 mg/d), 88.52% for cobalamin ($<$2.0 μg/d), and 99.25% for folate ($<$320 μg/d) in women. Even the median intake of these B vitamins for the participants in the highest tertiles was below the EAR level. It is very likely that the ranges of B vitamin intake are not sufficient to make an association between B vitamins and depression. However, an inverse relationship between only riboflavin and depressive symptoms in this study was significant in all participants and in women. The prevalence of depressive symptoms in the highest tertile of riboflavin (20.95%) was lower than that in the highest tertiles of other B vitamins in all participants (thiamin: 28.57%; niacin: 23.80%; pyri-

Table 5. Odds ratios and 95% CIs for depressive symptoms according to dietary B vitamin intake in HIV-infected women.

	Dietary B vitamins			p value[1]
	T1 (Lowest)	T2	T3 (Highest)	
Thiamin (median, range; mg/1,000 kcal)	0.30 (0.23–0.34)	0.37 (0.34–0.40)	0.48 (0.41–0.80)	
No. with depression	12/44	11/45	16/45	
Univariate model OR (95% CI)	1.00 (reference)	0.86 (0.33–2.23)	1.47 (0.59–3.60)	0.387
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.88 (0.31–2.44)	1.47 (0.57–3.81)	0.411
Riboflavin (median, range; mg/1,000 kcal)	0.25 (0.16–0.30)	0.34 (0.30–0.39)	0.47 (0.39–0.80)	
No. with depression	15/44	16/45	8/45	
Univariate model OR (95% CI)	1.00 (reference)	1.06 (0.44–2.55)	0.41 (0.15–1.12)	0.091
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.94 (0.36–2.40)	0.23 (0.07–0.77)	0.020
Niacin (median, range; mg/1,000 kcal)	3.97 (2.66–4.74)	5.31 (4.76–5.80)	6.65 (5.82–9.65)	
No. with depression	12/44	13/45	14/45	
Univariate model OR (95% CI)	1.00 (reference)	1.08 (0.43–2.73)	1.20 (0.48–3.00)	0.690
Multivariate model[2] OR (95% CI)	1.00 (reference)	1.31 (0.49–3.48)	1.29 (0.49–3.37)	0.602
Pyridoxine (median, range; mg/1,000 kcal)	0.56 (0.37–0.65)	0.73 (0.65–0.76)	0.86 (0.76–1.52)	
No. with depression	10/44	15/45	14/45	
Univariate model OR (95% CI)	1.00 (reference)	1.70 (0.66–4.34)	1.53 (0.59–3.95)	0.387
Multivariate model[2] OR (95% CI)	1.00 (reference)	1.45 (0.54–3.86)	1.28 (0.48–3.45)	0.635
Folic acid (median, range; μg/1,000 kcal)	58.69 (31.75–68.51)	80.18 (68.56–101.52)	130.68 (101.89–300.73)	
No. with depression	13/44	12/45	14/45	
Univariate model OR (95% CI)	1.00 (reference)	0.86 (0.34–2.18)	1.07 (0.43–2.66)	0.868
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.95 (0.36–2.53)	1.08 (0.41–2.83)	0.864
Cobalamin (median, range; μg/1,000 kcal)	0.13 (0.04–0.27)	0.45 (0.27–0.67)	1.12 (0.68–3.00)	
No. with depression	10/32	13/45	12/45	
Univariate model OR (95% CI)	1.00 (reference)	0.89 (0.33–2.39)	0.80 (0.29–2.16)	0.660
Multivariate model[2] OR (95% CI)	1.00 (reference)	0.80 (0.27–2.36)	0.55 (0.17–1.71)	0.292

Values for B vitamin intake are adjusted for energy intake by using the nutrient density method for each tertile.

[1] Linear trends across tertiles of B vitamins intake were tested using ordinal numbers 0–2 assigned to tertile categories.

[2] All multivariate models were adjusted for age (years, continuous), alcohol intake (never or ever), smoking (never or ever), body mass index (kg/m^2, continuous), history of any disease in past 12 mo (yes or no), CD4$^+$ T-cell count ($\leq$200 or $>$200; cells/μL), and anti-retroviral therapy (yes or no).

doxine: 23.80%; folic acid: 26.66; cobalamin: 26.66%). Similarly, the prevalence of depressive symptoms in the highest tertile of riboflavin (17.70%) was lower than that in the highest tertiles of other B vitamins in women (thiamin: 35.55%; niacin: 31.11%; pyridoxine: 31.11%; folic acid: 31.11; cobalamin: 26.66%). Thus, the level of riboflavin in the highest tertile of riboflavin was perhaps above the threshold where riboflavin's effects on depression could be seen. Further prospective studies are needed to assess the effects of B vitamins in the risk of depression.

Regarding sources of B vitamins, significant contributors to the B vitamin intake in the Nepalese diet are rice and cereals (*77*). The common sources of B vitamins in the Nepalese diet are rice (B1, B2), wheat bread (B1, B9), pulse/lentils (B1, B6, B9), navy beans (B1), black-eyed peas (B9), green peas (B1, B3), mushrooms (B2, B3), spinach (B2, B6, B9), broccoli (B9), lettuce (B9), dried fruits (B6), bananas (B6), mango (B9), oranges (B9), tofu (B12), low-fat dairy products and cheese (B2, B12), egg (B2, B12), chicken (B3, B6), liver (B3), red meat (B2, B12), tuna fish (B6), and trout (B1) (*77*). The mean daily consumption of food averaged 458$\pm$107 g of cereals, 436$\pm$97 g of rice, 173$\pm$127 g of colored vegetables, 101$\pm$191 g of milk and dairy products, and 60$\pm$86 g of potatoes (*77*). These items constituted more than three-fourths of the total food weight, whereas the amounts and frequency of the consumption of meat (19$\pm$43 g), fish (13$\pm$32 g) and eggs (2$\pm$14 g) were very low.

The present study had some limitations. First, the cross-sectional design of the study does not rule out the possibility of reverse causality and that depressive symptoms may influence B vitamin intake. Second, depression was measured using the BDI scale in our study. Though clinical diagnosis is the gold standard, such an approach is not feasible in community-based studies. The BDI has been validated in the context of this study and has been widely used in epidemiologic studies (*78*, *79*). Third, a 24 h recall may not provide good estimates of usual dietary intake because of within-person variation. However, this would be less relevant in the present study population due to the measurement of dietary recalls twice, 1 wk apart, and to the limited variation of dietary intake, as some studies suggest that dietary habits tend to remain stable over time (*24*, *80*). Fourth, hypohomocysteinemia may mediate the relationship between increased intake of riboflavin and the decreased risk of depression as studies have reported (*8*, *9*) an inverse relationship between riboflavin and homocysteine. However, the homocysteine level of participants was not measured in this study. Fifth, the possibility of

residual confounding cannot be excluded although we adjusted for known factors that could influence both B vitamin intake and depressive symptoms. Finally, study participants were not selected using a random sampling method; thus caution should be taken in generalizing our study findings to the entire population of HIV-infected persons in the country.

In conclusion, the present study suggests that higher intake of riboflavin may be associated with low depressive symptoms in all participants and in HIV-infected women even after taking account of ART and other important confounding factors. This finding adds the importance of B vitamins in the mental health status of HIV-infected persons. Further prospective studies and/or clinical trials are needed to confirm the role of B vitamins in depression in HIV-infected persons.

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Author contribution

K.P.T. designed the main study and collected data, conceived the research question of the present study, analyzed and interpreted the data, and prepared the manuscript. K.P.T. had primary responsibility for the final content.

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