Nutritional intakes and associated factors among tuberculosis patients: A cross-sectional study in China

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Abstract

Abstract Background: The objectives of this study were to examine nutrient intakes of tuberculosis (TB) patients and to identify their associated factors. Methods: In this cross-sectional study, 300 adult TB patients were surveyed in two impoverished counties in China. Nutrient intakes were evaluated through two consecutive 24-h dietary recalls and compared with the Chinese Dietary Reference Intakes (DRIs) 2013. The potential socio-demographic and behavioral factors were analyzed using multivariate logistic model to identify strong influential factors. Results: We found that mean daily energy intake was 1655.0 kcal (SD: 619.3 kcal) and 1360.3 kcal (SD: 552.1 kcal) for male and female patients, respectively. The mean daily energy intake was significantly lower than that has been recommended by DRI (i.e., 2250 and 1800 kcal for males and females, respectively), with 87.4% of the male patients and 59.9% of female patients failed to consume adequate energy. The protein intakes were 44.6 g (SD: 18.2 g) and 35.9 g (SD: 12.3 g) for male and female patients, respectively, which were lower than the recommended values by DRI (i.e., 65 and 55 g for males and females, respectively). Most male (90.8%) and female (58.4%) TB patients had insufficient daily protein intake. Further analyses suggested that mean daily intakes of many micronutrients, were insufficient, while for most of patients, intakes of vitamin E and sodium were sufficient. We identified that unemployment was a risk factor for low energy intake ($p<0.05$) and out-home-eating was a protective factor for low protein intake ($p<0.01$). Conclusions: In impoverished areas in China, intakes of macronutrients and most micronutrients in TB patients were inadequate compared with DRIs, especially for unemployed patients and patients eating at home. These findings suggested that public health actions are needed to promote education on TB patients about significance of nutritional support, and, further interventions in TB patients' nutritional intakes are also required.
Keywords: Tuberculosis patients; Nutrient intakes; Socio-demographic factors; Behavioral factors

Background

Tuberculosis (TB) is an airborne disease caused by *Mycobacterium tuberculosis* and is the first leading cause of death from single infectious agents. According to World Health Organization (WHO), there were estimated 10.0 million people developed TB disease and 1.6 million people died from TB in 2017. China is in 2nd place among 30 TB high burden countries, with a reported incidence of 63 per 100,000 persons per year in 2017[1].

The interactions between tuberculosis and malnutrition are well appreciated. TB will result in malnutrition and malnutrition can predispose to TB. TB increases the basal metabolic rate (BMR)[2], thus requiring more energy to maintain body function, leading to weight loss. However, due to reduction in appetite and gastrointestinal disorder[3], food intake will decrease in TB patients, resulting in undernutrition. Malnutrition will in turn lead to impaired immune function[4, 5], as nutritional deficiency alters the interaction between macrophages and T-lymphocytes[6], thus increasing the risk of getting infected firstly. Moreover, although most people who get infected will not manifest symptoms as their immune system manages to control the bacteria, malnourished person are more likely to develop active TB because the infection is no longer constrained by their immune systems[7].

Three studies in China[8-10] reported previously that protein and caloric intakes in TB patients were inadequate as well as some micronutrients. Insufficient protein and caloric intakes will hinder the functions of some generalized host defense mechanisms that are essential for combating TB[11]. Besides, both vitamins and minerals play important roles in immunity[12], deficiency of one or more of these nutrients will impair person's resistance to any infection[13].

Assessment of nutrient intakes is critical in nutritional management of patients with TB. Until now, only one research group conducted studies on nutrient intakes in TB patients in China, however, they did not examine associated factors about nutrient intakes. Moreover, to our knowledge, until now there are no studies conducted to evaluate the nutritional status of TB patients with reference to the latest Chinese Dietary Reference Intakes (DRIs) 2013[14]. We carried out this community-based study to evaluate nutrient intake levels of TB patients by comparing them with both current dietary recommendations in China and local general population, and to examine associated factors of nutrient intakes among TB patients.

Methods

Study Context

This cross-sectional study was undertaken as part of the project "Investigation of nutrition and diet of patients with pulmonary tuberculosis in poor areas in China" supported by the WHO Regional Office in the Western Pacific. It was conducted from November 2015 to April 2017 in two counties, that is, Lingyun county located in Guangxi province and Lin county located in Shanxi Province. These two counties were national impoverished counties and behaved well in their routine work. TB case notification rates in 2016 were 63.16 per 100,000 in Lin county and 106.97 per 100,000 in Lingyun county, respectively.

Participants

Adult patients (age≥18 years) with active TB registered in *Tuberculosis management information system* from Nov 1st, 2015 through May11th, 2017 and signed consent form were recruited. Patients with extrapulmonary tuberculosis, and those aged 18 years and below or with severe complications were not eligible for the study. Pregnant or breast-feeding women, and those who refused to sign the consent form were also excluded.

Sample Size

As BMI is commonly used in nutrition assessment, we applied the prevalence of BMI<18.5 which is also defined as malnutrition[15]],[in the calculation of sample size. We assumed that the prevalence of malnutrition in the general population in poor areas and TB patients would be 6.7% [16]and 25.0%[2], respectively, and the required sample size was calculated to detect difference in the two proportions. The probability of a type I error was set at 0.05, the power of the study was estimated at 90% and the design effect was set at 1, determining a sample size of TB patients was 77 per study site. Considering

participants' refusal, we expanded the sample size to 150 per study site, and the final sample size of TB patients was 300 totally.

Socio-demographic and behavioral factors

Data for associated factors were taken from a questionnaire on personal information, including socio-demographic data (age, gender, education level, marital status, occupation and household income level) and behavioral data (alcohol consumption, smoking status and eating out-of-home). Age was categorized into 3 groups, 18-49 years, 50-64 years, 65 years and above, based on Chinese Dietary Reference Intakes (DRIs) 2013[14]. Education level was categorized into 2 groups[17], that is, primary school and below, junior middle school and above. Household income level was evaluated by annual household income and was categorized into 3 groups, <20,000 yuan, 20,000-40,000 yuan, and ≥40,000 yuan[17]. Alcohol consumption was defined as drinking wine, beer and Chinese spirit now or ever. A smoker was defined as smoking now or smoking previously but have stopped smoking in the evaluation period. Eating out-of-home was defined as eating at least one meal away from one's own home or their residents' home during the survey[18]. Severity of TB was grouped into two categories based on the result of chest x-ray. If the lesion is confined to two lung fields then it is defined as mild. If the lesion covers more than two lung fields or there're cavities, it is defined as severe[19].

Assessment of Nutrient intake

Trained staff performed face-to-face interviews on each participant to obtain dietary intake data through a 2-day 24-hour dietary recall (24hdr) questionnaire, which was adapted from the method of 3-day 24hdr[20]. Participants were instructed to record all food intake at home and away from home in the previous 2 days (one weekday and one weekend day). Consumptions of condiments were also recorded through a questionnaire. All investigations were completed after the patient registering in *Tuberculosis management information system* and before anti-tuberculosis treatment. Data for dietary intake of general population was obtained from a 3-day 24hdr questionnaire (two weekdays and one weekend day).

Total energy, four kinds of macronutrients and sixteen kinds of micronutrients were evaluated. Nutrient intakes of each patient were calculated based on Chinese Food Composition Tables (CFCT) 2004[21].

We also evaluated TB patients' nutritional intake by applying Chinese dietary reference intakes (DRIs) 2013, with mean daily nutrient intakes compared with Recommended Nutrient Intakes (RNIs) and Adequate Intakes (AIs). Recommended Nutrient Intakes is an estimate of the amount of a nutrient that meets the requirements of most people (97%-98%) within a specific physiological group (sex, age, body size, physical activity, type of diet). Adequate Intakes means a recommended intake value based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of healthy people[14].

Statistical analysis

Data of daily nutrient intakes were presented as means ± standard deviation (SD). As dietary recommendations are different for men and women, we compared TB patients' daily nutrient intakes with DRIs by gender. Since protein-calorie malnutrition (PCM) is the most common form of undernutrition in TB patients[11], we only examine factors related to insufficient energy and protein intakes. Univariate logistic regression analysis was used to identify potential risk factors associated with inadequate energy and protein intakes in 300 TB patients. Age, gender, county and severity of TB were considered to be possible confounders in the multiple logistic regression model with stepwise selection. Patients were classified into two groups: below RNI/AI and above RNI/AI. A P-value of less than 0.05 was considered statistically significant. All analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC, USA).

Quality Control

The study was carried out on the basis of CHNS 2015, from which the investigating method and tool were used in our study. All on-site investigations were carried out by the county-level CDC and interviewers were trained with a standard protocol. Data was checked for completeness and accuracy on the day of investigation and sampled by provincial CDC for verification later. All data was double-entered into a database specially designed for this project.

Results

Characteristics of the subjects

Almost all notified TB patients registered from Nov 1st, 2015 to May 11th, 2017 in Lin county were included in our study, while TB patients enrolled in our study accounted for less than 40% of all notified TB patients in Lingyun county during that period.

The majority (53.7%) of TB patients aged between 18 and 49, with the mean age being 45.5 years old (SD±18.7). More than half (68.7%) of them were males. Most TB patients were married, employed and didn't attend junior middle school, with annual household income less than 20, 000 RMB yuan. Only 39.7% of them tended to have alcohol consumption and 46.7% of them were smokers.

Daily energy and nutrient intake

Recommendations for daily energy intake was 2250 kcal in males and 1800 kcal in females, and for daily protein intake was 65 g in males and 55 g in females. Thus, the average daily energy (1655.0 kcal in males, 1360.3 kcal in females) and protein (44.6 g in males and 35.9 g in females) intakes of TB patients were inadequate in both genders (Table 2). 87.4% male patients' and 59.9% female patients' daily energy intakes were below RNI/AI, as well as 90.8% male patients' and 58.4% female patients' daily protein intakes. As for micronutrients, in male TB patients, the mean daily intake of retinol, niacin, vitamin E, sodium, iron, Manganese, copper and Phosphorus were all higher than RNI/AI, while calcium (216.3 mg) intake was severely less than RNI/AI (800 mg). In female TB patients, the intakes of vitamin E, copper and

sodium were higher than RNI/AI. However, the intakes of riboflavin, potassium and calcium were severely inadequate.

Factors associated with low energy and low protein intakes in 300 TB patients

As shown in table 4, univariate analysis suggested that being unemployed was associated with inadequate energy intake and annual household income with 40,000 RMB yuan and above was a protective factor. In multivariate analysis (see Table 5), after adjusting for other factors, unemployed participants were more likely to have low energy intake (OR: 3.542; 95%CI:1.471, 8.530)(p<0.01). Meanwhile, lower protein intake was associated with eating at home. The possibility of low protein intake for people eating out-of-home was much lower than those eating at home (OR: 0.328; 95CI%:0.133, 0.809)(p<0.05).

Discussion

Our study demonstrated that intakes of both macronutrients and selected micronutrients were inadequate in most TB patients. Protein-calorie malnutrition (PCM), characterized by inadequate intakes of both protein and total calories[11], was common in TB patients, with both the male and female TB patients taking energy and protein below RNI/AI. This finding was consistent with some published studies[8-10] in China. PCM will reduce the effectiveness of some components that play important roles in cell-mediated immunity[11]. Also, mean daily intakes of many micronutrients were below RNI/AI, especially calcium, in our study, the mean daily intake of which was much lower than RNI/AI in all the women and 99.5% of men. A survey conducted in China revealed that TB patients did not take enough fish, shrimp and dairy products[22], which are all calcium-rich food. This may explain the insufficient intake of calcium. Calcium participates in many physiological activities in the body such as affecting endocrinologic consequences and regulating activities of enzymes and its deficiency will cause low immunity in TB patients[9]. Our study also showed that over 95% TB patients didn't have adequate intakes of riboflavin, zinc and selenium. Riboflavin is associated with the metabolisms of iron and niacin and its deficiency will compromise oxidant defense mechanisms[23]. Zinc has an essential role in vitamin A metabolism and supplementation of zinc will increase immune function in TB patients[24]. Selenium is reported to have an important function in maintaining the immune process and is beneficial for the clearance of mycobacteria[25]. However, sodium consumption was higher than RNI/AI in TB patients. Researches conducted in other populations[26-28] in China also showed that high sodium consumption remained a public health problem. Nevertheless, the quality of diet seemed to improve in some ways, as the mean daily intake of vitamin E was much higher than RNI/AI in both genders compared with previous studies[8-10]].[9].[.

Furthermore, we discerned that eating out-of-home was related to higher intake of protein. Relevant studies conducted among other populations in China[29-31] also demonstrated that there was an increase in protein intake while eating out-of-home. The reason for this phenomenon may be that people tend to choose food with better tastes and higher nutritional values when they eat away from home[30].

According to some surveys, eating out more frequently was associated with higher socio-economic status (measured by higher education level and household income)[29, 32, 33]. This may because people with higher socio-economic status are more likely to afford frequent away-from-home food consumption. We also discovered that the inadequate energy intake was significantly higher among unemployed TB patients, being consistent with studies[34, 35]][conducted in other countries. This is most likely because that persons with low socio-demographic status will not be able to afford nutritious food.

Malnutrition will also have an impact on the treatment of TB. Malnutrition will reduce the level of protein in the patient's body, and thus delayed the recovery of lesions. This is probably because sufficient protein, on the one hand, helps the recovery of lesions during the treatment. On the other hand, increases the number of drug carriers in the treatment, therefore, concentration of anti-tuberculosis drugs in the blood will rise, promoting sputum conversion[36]. A study in China showed that 56% of patients' sputum culture were negative after 20 days of treatment in the nutritional support group, which was significantly higher than 28% in the general treatment group[37].

Limitations and Strengths

There are some limitations in our study. On the one hand, we used the 24hdr method to evaluate the nutrient intakes, and this method has its own shortcomings. Reliance on the memory of participants and recall bias could result in an underestimation of nutrient intakes[38]. Additionally, considering that more times we interviewed, less cooperate would TB patients be as they were worried about being discriminated against, we took the 2-day 24hdrs method instead of the commonly used 3-day 24hdrs, thus the reliability may decrease. A study conducted among African American youth showed that reliability estimates for 3-day 24hdrs ranged from 27%-62%, but for 2-day 24hdrs, ranged from 19%-52% [39]. And, when measuring the consumption of condiments, we didn't take the household weighing method commonly used in nutrition survey. On the other hand, we hope to enroll all eligible TB patients in these two counties notified from Nov 1st, 2015 to May 11th, 2017. However, almost all notified TB patients in Lin county were included in our study, while TB patients enrolled in our study accounted for less than 40% of all notified TB patients in Lingyun county during that period. Moreover, we measured social-economic status of TB patients only by annual household income and this was not enough to capture the economic disparities. All of these may result in that our findings could not be generalized to all the local people.

Although limitations existed, our study has outstanding strengths. Firstly, different from previous hospital-based studies, our study is a community-based study initiated in comparing TB patients' nutrient intakes with the latest DRIs and examining the associated factors in TB patients' nutrient intake. Moreover, we collected the same information for local general population and make comparisons between these two groups, avoiding the influence of different dietary patterns in various areas.

Conclusions

Our study showed that in poor areas in China, the intakes of macronutrients and most micronutrients in TB patients were lower than DRIs, especially for those unemployed and eating at home. These findings suggested that the public health actions are needed to promote education on TB patients about significance of nutritional support, and, further interventions in TB patients' nutritional intakes are also required.

Abbreviations

TB: tuberculosis; DRIs: Dietary Recommended Intakes; RNI: Recommend Nutrient Intake; AI: Adequate Intake; WHO: World Health Organization; BMR: basal metabolic rate; CHNS: China Health and Nutrition Survey; 24hdr: 24-hour dietary recall; CFCT: Chinese Food Composition Tables; SD: standard deviation; PCM: protein-calorie malnutrition; CDC: center for disease control and prevention.

Declarations

Ethics approval and consent to participate

The present study protocol was approved by the China CDC Institutional Ethics Review Board (NO. 201532) and The Ethic Review Committee of the WHO Regional Office in the Western Pacific (2015.22.CHN.3.STB). All those agreed to participate in the survey had to provide informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Zhewen Ren: analyzed the data, completed statistical analysis and wrote the initial draft of the manuscript. Fei Zhao: conceived the research idea, conducted the data collection. Hui Chen and Dongmei Hu: made contributions to data analysis. Wentao Yu and Xiaoli Xu: supervises the data collection and analysis. Dingwen Lin, Fuyi Luo, Yueling Fan and Haijun Wang: participated in the implementation of the

study. Jun Chen and Liyun Zhao: designed the study and contributed to the protocol conception. All authors' read and approved the final manuscript.

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Tables

Table 1 Socio-demographic and behavioral characteristics for 300 TB patients

Characteristics		N	N%
Socio-demographic factors			
Age group	18-49	161	53.7
	50-64	86	28.7
	≥65	53	17.7
	Mean (±SD)	45.5 (±18.7)	
Gender	Male	206	68.7
	Female	94	31.3
Education	Primary school and below	161	53.7
	Junior middle school and above	139	46.3
Marital status	Married	209	69.7
	Other marital status	91	30.3
Occupation	Employed	178	59.3
	Unemployed	122	40.7
	<20,000	136	45.3
	20,000-40,000	79	26.3
Annual household income[a]	≥40,000	20	6.7
	Refusal or unknown	65	9.7
	Mean (±SD)	18203.1 (±17622.2)	
Behavioral factors			
Alcohol consumption	Yes	119	39.7
	No	181	60.3
Smoking status	Smoker	140	46.7
	Non-smoker	160	53.3
Eating out-of-home	Yes	58	19.3
	No	242	80.7

[a] 65 patients who refused or with missing data were excluded from this analysis

Table 2 Daily energy and macronutrient intakes of TB patients compared with DRIs

Energy and macronutrient intakes	Males (n=206)			Females (n=94)		
	RNI/AI	Mean (SD)	Below RNI/AI(%)	RNI/AI	Mean (SD)	Below RNI/AI(%)
Calories (Kcal)	2250	1655.0 (619.3)	180(87.4)	1800	1360.3 (552.1)	78(83.0)
Total Protein (g)	65	44.6 (18.2)	187(90.8)	55	35.9 (12.3)	86(91.5)
Total Fat (g)	-	73.0 (50.5)	-	-	68.9 (48.3)	-
Total Carbohydrates (g)	-	212.1 (117.2)	-	-	154.8 (58.0)	-
Total fiber (g)	-	7.6 (4.3)	-	-	5.7(2.6)	-

Table 3 Daily micronutrient intakes of TB patients compared with DRIs

Micronutrient intakes	Males (n=206)			Females (n=94)		
	RNI/AI	Mean (SD)	Below RNI/AI(%)	RNI/AI	Mean (SD)	Below RNI/AI(%)
Retinol (µg)	800	807.5 (994.0)	135(65.5)	700	603.9 (626.7)	68(72.3)
Thiamin (mg)	1.4	0.9(0.5)	180(87.4)	1.2	0.7(0.3)	88(93.6)
Riboflavin (mg)	1.4	0.6(0.3)	203(98.5)	1.2	0.5(0.2)	94(100)
Niacin (mg)	12	12.6(5.3)	94(45.6)	15	10.3(4.7)	78(83.0)
Vitamin E (mg)	14	53.6 (39.6)	13(6.3)	14	57.1(40.0)	4(4.3)
Vitamin C (mg)	100	96.6 (75.3)	130(63.1)	100	70.2(55.8)	74(78.7)
Potassium (mg)	2000	1309.2 (636.7)	180(87.4)	2000	1011.7 (351.0)	94(100)
Sodium (mg)	1500	2204.4 (1204.8)	67(35.5)	1500	2054.5 (1123.4)	28(29.8)
Calcium (mg)	800	216.3 (126.2)	205(99.5)	800	176.9 (86.5)	94(100)
Magnesium (mg)	330	221.0 (112.0)	174(84.5)	330	166.0 (56.6)	92(97.9)
Iron (mg)	12	14.2(6.8)	86(41.8)	20	10.8(3.7)	92(97.9)
Manganese (mg)	4.5	4.7(2.3)	126(61.2)	4.5	3.5(1.3)	83(88.3)
Zinc (mg)	12.5	5.5(2.9)	196(95.2)	7.5	4.1(1.5)	90(95.7)
Copper (mg)	0.8	1.2(1.2)	72(35.0)	0.8	0.9(0.3)	53(56.4)
Phosphorus (mg)	720	745.7 (382.1)	116(56.3)	720	571.8 (173.0)	74(78.7)
Selenium (µg)	60	26.3 (15.3)	200(97.1)	60	20.2(10.2)	93(98.9)

Table 4 Factors associated with low energy and low protein intakes using univariate regression analysis in 300 TB patients

Associated factors		Energy OR(95%CI)	P	Protein OR(95%CI)	P
Socio-demographic factors					
Age	18-49	1.0		1.0	
	50-64	1.032(0.498, 2.138)	0.9319	2.039(0.730, 5.698)	0.1741
	≥65	2.252(0.746, 6.797)	0.1499	1.542(0.498, 4.778)	0.4530
Area	Lin county	1.0		1.0	
	Linyun county	0.639(0.329, 1.240)	0.1856	1.509(0.676, 3.369)	0.3158
Gender	male	1.0		1.0	
	female	0.704(0.358, 1.386)	0.3098	1.092(0.460, 2.593)	0.8415
Severity	mild	1.0		1.0	
	severe	0.851(0.425, 1.704)	0.6486	0.859(0.370, 1.911)	0.7224
Education	Primary school and below	1.0		1.0	
	Junior middle school and above	1.503(0.547, 2.207)	0.8780	0.923(0.418, 2.037)	0.8429
Marriage	Married	1.0		1.0	
	unmarried	1.708(0.781, 3.735)	0.1797	0.859(0.370, 1.991)	0.7224
Occupation	Employed	1.0		1.0	
	Unemployed	3.364(1.499, 7.550)	0.0033	1.412(0.612, 3.257)	0.4181
Annual household income	<20,000	1.0		1.0	
	20,000-40,000	0.766(0.333, 1.762)	0.5311	0.905(0.336, 2.438)	0.8437
	≥40,000	0.289(0.097, 0.866)	0.0266	0.499(0.126, 1.969)	0.3207
Behaviroral factors					
Alcohol consumption	No	1.0		1.0	
	Yes	1.372(0.690, 2.731)	0.3670	1.350(0.585, 3.113)	0.4821
Smoking status	Non-smoker	1.0		1.0	
	Smoker	0.766(0.399, 1.472)	0.4243	0.482(0.213, 1.092)	0.0802
Eating out-of-home	No	1.0		1.0	

			OR(95%CI)	P	OR(95%CI)	P
		Yes	0.628(0.294, 1.228)	0.2280	0.302(0.132, 0.693)	0.0047

Note: Intake above RNI/AI was assigned as 0, intake below RNI/AI was assigned as 1. The sample size of analysis of annual household income was 235

Table 5 Factors associated with low energy and low protein intakes using multivariate regression analysis in 300 TB patients

Associated factors			OR(95%CI)	P
Energy	Age	18-49	1.0	
		50-64	1.010(0.452, 2.260)	0.9800
		≥65	1.916(0.560, 6.555)	0.3002
	Gender	Male	1.0	
		female	0.512(0.246, 1.067)	0.0741
	Area	Lin county	1.0	
		Linyun county	0.631(0.286, 1.394)	0.2550
	Severity	mild	1.0	
		severe	1.192(0.546, 2.605)	0.6595
	Occupation	Employed	1.0	
		Unemployed	3.542(1.471, 8.530)	0.0048
	Annual household income	<20,000	1.0	
		20,000-40,000	1.242(0.536, 2.877)	0.6132
		≥40,000	0.366(0.115, 1.163)	0.0885
Protein	Age	18-49	1.0	
		50-64	1.460(0.490, 4.353)	0.4927
		≥65	0.985(0.285, 3.401)	0.9813
	Gender	Male	1.0	
		female	1.133(0.468, 2.741)	0.7817
	Area	Lin county	1.0	
		Linyun county	1.284(0.489, 3.370)	0.6122
	Severity	mild	1.0	
		severe	0.690(0.266, 1.792)	0.4461
	Eating out-of-home	No	1.0	
		Yes	0.328(0.133, 0.809)	0.0155

Note: Intake above RNI/AI was assigned as 0, intake below RNI/AI was assigned as 1. The sample size of analysis of annual household income was 235