

Daily branch chained amino acid intakes and the risk of obesity among women with prior gestational diabetes mellitus

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Research

Keywords: oral branched chain amino acids, gestational diabetes mellitus, obesity risk, postpartum

Posted Date: February 18th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-202675/v1>

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Abstract

Background

Some studies have found that branched amino acid (BCAA) is associated with the risk of obesity among general population, however, not all the results were consistent. The present study aimed to investigate the association of daily BCAA intakes with the risk of postpartum overweight and abdominal obesity among women with prior gestational diabetes mellitus (GDM).

Methods

We performed a cross-sectional study of 1263 women with prior GDM at 1–5 years post-delivery. Logistic regression models were used to estimate the association of daily dietary intakes of BCAAs with the risk of overweight and abdominal obesity.

Results

The multivariable-adjusted odds ratio (OR) across quartiles of daily BCAA intakes were 1.42 (95% confidence interval [CI] 1.02–1.97), 1.00 (reference), 1.21 (95% CI 0.88–1.68), and 1.31 (95% CI 0.95–1.81) for general overweight, and 1.38 (95% CI 0.99–1.90), 1.00, 1.19 (95% CI 0.86–1.64), and 1.43 (95% CI 1.04–1.98) for abdominal obesity, respectively. Only women with the lowest quartile of daily BCAA intakes significantly increased the risks of general overweight (OR 1.49; 95 %CI 1.06–2.09) and abdominal obesity (OR 1.50; 95 %CI 1.08–2.11) compared with women at quartile 2 of daily BCAA intakes after further adjustment of daily energy intake.

Conclusions

The present study indicated U-shaped associations between daily BCAA intakes and the risk of general overweight and abdominal obesity among women with prior GDM.

Introduction

Gestational diabetes mellitus (GDM) is one of the most common complications during pregnancy (1), and has clinical impacts on maternal and fetal health during the perinatal and postpartum period (2) (3). The estimated global prevalence of GDM is 12.8% according to the 9th edition of International Diabetes Federation atlas (4). A recent meta-analysis has shown that the prevalence of GDM in mainland China is 14.8% (5). Women with GDM have a 7.43-fold higher risk of postpartum diabetes than women with normal blood glucose during pregnancy (6). Postpartum obesity is one of most important risk factors for postpartum diabetes among women with GDM (7). Our recent study indicated that the 1-year early

postpartum lifestyle intervention led to significant weight loss in women with prior GDM, the effect of which was more pronounced in women who were overweight at baseline (8).

Over the past decades, more researchers have assessed the association of daily branch chain amino acid (BCAA) intakes with the risks of obesity and related metabolic disorders, however, the results were inconsistent. BCAAs include a group of essential amino acids, such as leucine, isoleucine and valine. These three BCAAs account for one third of the dietary essential amino acids and make up for 20% of the total protein content (9). Several studies demonstrated that high BCAA levels were associated with increased risks of obesity, insulin resistance and type 2 diabetes in adults and children (10) (11) (12) (13). Nevertheless, data from the “INTERMAP STUDY” showed that higher BCAA intake had a lower prevalence of overweight and obesity in middle aged East Asian and Western adults (14). Although women with prior GDM have high prevalence of postpartum overweight and obesity (15), no studies have assessed whether the postpartum daily BCAA intakes would influence the risks of general overweight and abdominal obesity among women with prior GDM. In the present study, we examined associations between daily dietary intakes of BCAAs and the risks of postpartum general overweight and abdominal obesity among women with a history of GDM.

Methods

Study population

Tianjin GDM Prevention Program is an early postpartum lifestyle-intervention trial in Tianjin, China (16). The detailed study design and methods were previously described (8, 16). The inclusion criteria were: (1) women diagnosed with GDM from 2005 to 2009; and (2) the baseline age of 20–49 years old. All pregnancies at 26–30 gestational weeks were enrolled in a one-hour oral glucose tolerance test (OGTT) with 50-g glucose load (16). Women with a glucose reading ≥ 7.8 mmol/L were invited to the Tianjin Women’s and Children’s Health Center to undergo a two-hour OGTT with 75-g glucose load. According to the 1999 World Health Organization (WHO)’s criteria, either diabetes (fasting glucose ≥ 7.0 mmol/L or 2-hour glucose ≥ 11.1 mmol/L) or impaired glucose tolerance (IGT) (2-hour glucose ≥ 7.8 mmol/L and < 11.1 mmol/L) would be diagnosed as GDM (17). The exclusion criteria were: (1) age < 20 or ≥ 50 years old; (2) presence of any chronic diseases that could seriously reduce life expectancy or the ability to participate in the study; and (3) unwilling to give informed consent or communicate with study staff, losing contact during the screening visit. Finally, a total of 1 263 GDM women finished the baseline survey during August 2009 to July 2011 and were included in the present study (16). We collected written informed consents from all participants. This study was approved by the Human Subjects Committee of the Tianjin Women’s and Children’s Health Center.

Questionnaires and measurements

At the baseline survey, all participants completed a self-administered questionnaire and underwent a physical examination. They also completed the 3-day 24-hour food records taught by a dietician. The self-administered questionnaire included socio-demographics (age, marital status, education, income,

and occupation), family history of diabetes, pregnancy outcomes (pre-pregnancy weight, weight gain in pregnancy and number of children), postpartum weight, smoking habits (non-smoking, former smoking, current smoking), passive smoking status, alcohol intake, leisure time physical activity (0 minute/day, < 30 minutes/day, and ≥ 30 minutes/day). Dietary assessments were obtained from the 3-day 24-h food records, which were carried out on three continuous days (two weekdays and one weekend day). The food was weighed separately with a scale before being cooked or the portion sizes were estimated. After completion, the records were reviewed and coded by a dietitian. Food was divided into 18 groups and averages of the 3-day food energy and nutrient intakes including BCAAs (including leucine, isoleucine, and valine) were calculated according to the Chinese food ingredient list published in 2002 (18) via a dietary analyzing software developed by the China CDC. The performance of 3-day 24-h food records was validated in the China National Nutrition Survey in 2002 (19).

Physical examinations included body weight (wearing light clothes), height (without shoes), and waist circumference measurements by specially trained doctors using standardized protocols. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm. Waist circumference was measured midway between the lowest rib and the iliac crest with a flexible anthropometric tape on the horizontal plane with the participant in standing position. Waist circumference was measured to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing their weight in kilograms by the square of height in meters. The BMI cut-points in the Chinese population were $24 \leq \text{BMI} < 28 \text{ kg/m}^2$ for overweight and $\text{BMI} \geq 28 \text{ kg/m}^2$ for obesity (20); abdominal obesity was defined as waist circumference ≥ 80 cm for women (21).

Statistical analysis

Demographic and lifestyle data were revealed according to the quartiles of daily BCAA intakes. One-way ANOVA and chi-square tests were used to assess the differences in continuous and categorical variables according to the quartiles of daily intakes of BCAAs. Logistic regression was used to estimate the odds ratio (OR) and 95% confidence interval (CI) of general overweight and abdominal obesity by quartiles of daily BCAA intakes. The analyses were first adjusted for age (Model 1); then for education, family income, family history of diabetes, current smoking, passive smoking, current alcohol drinking, leisure time physical activities, and sitting time (Model 2); and further for daily energy intake (Model 3). We used the restricted cubic spline nested in logistic regression to test whether there was a dose-response or nonlinear association of daily BCAA intake as a continuous variable with the risk of obesity. All the statistical analyses were performed with SPSS statistics V.25.0 for Windows software package (IBM) and SAS for Windows version 9.3 (SAS Institute Inc., Cary, NC, USA). Two-sided $P < 0.05$ was considered statistically significant.

Results

General characteristics of the study population according to quartiles of daily BCAA intakes are presented in Table 1. Current alcohol drinking, daily energy intake, energy intake from fat, energy intake from protein, and energy intake from carbohydrate were positively associated daily BCAA intakes.

Table 1
Baseline characteristics by different levels of daily branched-chain amino acid intake

	Quartiles of branched-chain amino acids				P value
	1	2	3	4	
No. of participants	315	317	315	316	
Age, years	32.0 ± 3.36	32.4 ± 3.70	32.5 ± 3.44	32.6 ± 3.55	0.18
Body mass index, kg/m ²	24.6 ± 4.24	23.7 ± 3.65	23.9 ± 3.75	24.4 ± 4.00	0.01
Body mass index categories, %					0.13
<24 kg/m ²	50.5	59.0	54.9	51.6	
≥24 kg/m ²	49.5	41.0	45.1	48.4	
Education, %					0.20
<13 years	27.6	22.1	21.3	19	
≥13 to < 16 years	66.7	69.7	71.4	72.5	
≥16 years	5.7	8.2	7.3	8.5	
Family income, %					0.79
<5000 yuan/month	27.6	30.0	24.8	27.5	
5000 ~ 7999 yuan/month	38.7	35.6	37.8	35.4	
≥8000 yuan/month	33.7	34.4	37.5	37.0	
Current smokers, %	3.2	0.9	2.2	1.6	0.22
Passive smokers, %	52.4	52.7	54.3	56.0	0.79
Current alcohol drinkers, %	20.0	25.5	22.5	32.0	0.01
Leisure time physical activity, %					0.62
0 min/day	50	52.4	55.3	48.3	
1 ~ 29 min/day	48.7	44.9	42.4	49.2	
≥ 30 min/day	1.3	2.8	2.3	2.5	
Sitting time at home, h/day	3.21 ± 2.01	3.30 ± 2.33	3.03 ± 1.87	3.35 ± 2.16	0.02
Dietary intakes					

Values are means ± SDs, or %.

	Quartiles of branched-chain amino acids				P value
	1	2	3	4	
Energy consumption, kcal/day	1325 ± 320	1587 ± 329	1779 ± 306	2078 ± 422	< 0.001
Energy intake from protein, %	15.1 ± 2.57	15.8 ± 2.19	16.6 ± 2.29	18.0 ± 2.77	< 0.001
Energy intake from fat, %	31.6 ± 6.60	33.2 ± 6.55	33.7 ± 5.56	35.3 ± 6.17	< 0.001
Energy intake from saturated fat, %	7.36 ± 2.18	7.94 ± 2.09	7.97 ± 1.76	8.66 ± 2.06	< 0.001
Energy intake from monounsaturated fat, %	13.2 ± 2.97	13.6 ± 2.96	13.5 ± 2.48	14.0 ± 2.55	0.004
Energy intake from polyunsaturated fat, %	11.1 ± 2.73	11.7 ± 2.95	12.3 ± 2.69	12.7 ± 3.30	< 0.001
Energy intake from carbohydrate, %	53.3 ± 7.63	50.9 ± 6.85	49.7 ± 6.04	46.7 ± 6.65	< 0.001
Branched chain amino acids, mg/day	3627 ± 913	5592 ± 422	7251 ± 495	10491 ± 2225	< 0.001
Isoleucine, mg/day	931 ± 236	1421 ± 120	1841 ± 143	2671 ± 569	< 0.001
Leucine, mg/day	1674 ± 429	2581 ± 203	3337 ± 247	4817 ± 1015	< 0.001
Valine, mg/day	1022 ± 270	1590 ± 151	2073 ± 159	3003 ± 659	< 0.001
Values are means ± SDs, or %.					

There were U-shaped associations of daily dietary intakes of BCAAs, isoleucine, leucine, and valine with the risk of general overweight (Table 2 and Fig. 1) among women with prior GDM. The multivariable-adjusted (age, education, family income, family history of diabetes, current smoking, current alcohol drinking, leisure time physical activities, and sitting time – model 2) odds ratios (ORs) for general overweight across quartiles of daily BCAA intakes were 1.42 (95% confidence interval [CI] 1.02–1.97), 1.00 (reference), 1.21 (95% CI 0.88–1.68), and 1.31 (95% CI 0.95–1.81), respectively. Women with the lowest or highest quartile of daily intakes of isoleucine and leucine had a significantly increased risk of general overweight compared with women at quartile 2 of daily isoleucine and leucine intakes (reference group) in the multivariable-adjusted analyses (Model 2). After further adjustment of daily energy intake, an increased risk of general overweight was only found among women with the lowest quartile of daily intakes of BCAAs (OR 1.49; 95 %CI 1.06–2.09), isoleucine (OR 1.48; 95 %CI 1.06–2.07), leucine (OR 1.51;

95 %CI 1.08–2.11), and valine (OR 1.44; 95 %CI 1.03–2.02) compared with women at quartile 2 of daily intakes of BCAAs, isoleucine, leucine, and valine (reference group), respectively.

Table 2
Odds ratios of overweight by different dietary intake levels of branched chain amino acids

	No. of participants	No. of cases	Odds ratio (95% confidence intervals)		
			Model 1	Model 2	Model 3
Branched chain amino acids					
Quartile 1	315	156	1.41 (1.03, 1.93)	1.42 (1.02, 1.97)	1.49 (1.06, 2.09)
Quartile 2	317	130	1	1	1
Quartile 3	315	142	1.18 (0.86, 1.62)	1.21 (0.88, 1.68)	1.17 (0.84, 1.63)
Quartile 4	316	153	1.35 (0.98, 1.84)	1.31 (0.95, 1.81)	1.20 (0.83, 1.72)
Isoleucine					
Quartile 1	315	155	1.37 (1.00, 1.87)	1.43 (1.03, 1.98)	1.48 (1.06, 2.07)
Quartile 2	316	131	1	1	1
Quartile 3	316	138	1.10 (0.80, 1.50)	1.15 (0.83, 1.59)	1.12 (0.80, 1.56)
Quartile 4	316	157	1.40 (1.02, 1.91)	1.40 (1.01, 1.93)	1.31 (0.91, 1.87)
Leucine					
Quartile 1	315	158	1.44 (1.05, 1.97)	1.45 (1.05, 2.01)	1.51 (1.08, 2.11)
Quartile 2	316	130	1	1	1
Quartile 3	316	134	1.06 (0.77, 1.45)	1.04 (0.75, 1.44)	1.01 (0.73, 1.41)
Quartile 4	316	159	1.45 (1.06, 1.99)	1.42 (1.03, 1.97)	1.32 (0.92, 1.90)
Valine					
Quartile 1	315	158	1.42 (1.04, 1.94)	1.38 (0.99, 1.91)	1.44 (1.03, 2.02)
Quartile 2	316	131	1	1	1

Model 1 adjusted for age; Model 2 adjusted for age, education, family history of diabetes, family income, current smoking, passive smoking, current alcohol drinking, leisure time physical activities, and sitting time; Model 3 adjusted for variables in Model 2 plus daily energy intake.

	No. of participants	No. of cases	Odds ratio (95% confidence intervals)		
			Model 1	Model 2	Model 3
Quartile 3	316	138	1.10 (0.80, 1.51)	1.07 (0.77, 1.48)	1.03 (0.74, 1.43)
Quartile 4	316	154	1.35 (0.98, 1.84)	1.28 (0.93, 1.77)	1.17 (0.81, 1.68)
Model 1 adjusted for age; Model 2 adjusted for age, education, family history of diabetes, family income, current smoking, passive smoking, current alcohol drinking, leisure time physical activities, and sitting time; Model 3 adjusted for variables in Model 2 plus daily energy intake.					

After adjustment for age, education, family income, family history of diabetes, current smoking, current alcohol drinking, leisure time physical activities, and sitting time, U-shaped associations of daily intakes of BCAAs, isoleucine, leucine, and valine, with the risk of abdominal obesity (Table 3 and Fig. 1) were still observed among women with prior GDM. After further adjustment of daily energy intake, an increased risk of abdominal obesity was only found among women with the lowest quartile of daily intakes of BCAAs (OR 1.50; 95 %CI 1.08–2.11), isoleucine (OR 1.42; 95 %CI 1.02–1.99), leucine (OR 1.48; 95 %CI 1.06–2.07), and valine (OR 1.60; 95 %CI 1.15–2.24) compared with women at quartile 2 of daily intakes of BCAAs, isoleucine, leucine, and valine (reference groups), respectively.

Table 3
Odds ratios of central obesity by different dietary intake levels of branched chain amino acids

	No. of participants	No. of cases	Odds ratio (95% confidence intervals)		
			Model 1	Model 2	Model 3
Branched chain amino acids					
Quartile 1	315	166	1.38 (1.01, 1.88)	1.38 (0.99, 1.90)	1.50 (1.08, 2.11)
Quartile 2	317	142	1	1	1
Quartile 3	315	152	1.15 (0.84, 1.57)	1.19 (0.86, 1.64)	1.11 (0.80, 1.54)
Quartile 4	316	170	1.43 (1.05, 1.96)	1.43 (1.04, 1.98)	1.21 (0.84, 1.74)
Isoleucine					
Quartile 1	315	164	1.28 (0.94, 1.76)	1.32 (0.95, 1.82)	1.42 (1.02, 1.99)
Quartile 2	316	145	1	1	1
Quartile 3	316	149	1.05 (0.77, 1.44)	1.12 (0.81, 1.54)	1.05 (0.76, 1.46)
Quartile 4	316	172	1.41 (1.03, 1.92)	1.44 (1.04, 1.99)	1.24 (0.86, 1.78)
Leucine					
Quartile 1	315	168	1.37 (1.00, 1.87)	1.36 (0.99, 1.88)	1.48 (1.06, 2.07)
Quartile 2	316	144	1	1	1
Quartile 3	316	143	0.98 (0.72, 1.35)	0.98 (0.71, 1.35)	0.92 (0.66, 1.28)
Quartile 4	316	175	1.48 (1.08, 2.03)	1.49 (1.08, 2.05)	1.26 (0.87, 1.80)
Valine					
Quartile 1	315	172	1.53 (1.12, 2.10)	1.46 (1.06, 2.02)	1.60 (1.15, 2.24)
Quartile 2	316	146	1	1	1

Model 1 adjusted for age; Model 2 adjusted for age, education, family history of diabetes, family income, current smoking, passive smoking, current alcohol drinking, leisure time physical activities, and sitting time; Model 3 adjusted for variables in Model 2 plus daily energy intake.

	No. of participants	No. of cases	Odds ratio (95% confidence intervals)		
			Model 1	Model 2	Model 3
Quartile 3	316	142	1.19 (0.87, 1.63)	1.17 (0.85, 1.61)	1.08 (0.78, 1.50)
Quartile 4	316	170	1.48 (1.08, 2.02)	1.44 (1.04, 1.99)	1.19 (0.83, 1.71)
Model 1 adjusted for age; Model 2 adjusted for age, education, family history of diabetes, family income, current smoking, passive smoking, current alcohol drinking, leisure time physical activities, and sitting time; Model 3 adjusted for variables in Model 2 plus daily energy intake.					

Discussion

The present study found U-shaped associations of daily intakes of BCAAs, isoleucine, leucine, and valine with the risks of general overweight and abdominal obesity among women with a history of GDM. A significantly increased risk of obesity was observed among women with the lowest quartiles of daily BCAA intakes compared with women at quartile 2 of BCAA intakes.

The prevalence of obesity has increased rapidly in China (22). Many factors account for the rapid increase in obesity, including more sedentary behavior and a high energy/high fat diet (22). The present study indicated that daily lower and higher intakes of BCAAs were associated with higher risks of general overweight and abdominal obesity among women with prior GDM. BCAAs are a group of essential amino acids, which are not produced in body but can only be obtained from the diet (23). Several studies have assessed the association between daily consumptions of BCAAs and the risk of obesity, and results were full of controversy. The “INTERMAP STUDY” and one study in northern China supported the inverse association between daily BCAA intake and the risks of general overweight/obesity and abdominal obesity (14) (24). However, another Chinese study indicated positive associations of daily BCAA intake with mean values of BMI and waist circumference, as well as the risks of metabolic syndrome and cardiovascular disease (25). Several clinical trials have also evaluated the association between daily BCAA levels and the risk of obesity. A protein-restricted diet could help improve metabolic indexes, including obesity and insulin resistance (26). Another animal study pointed out that the restriction of dietary BCAAs significantly decreased body weight and adiposity, and increased energy expenditure (27). However, very few studies have assessed the effects of dietary BCAA restriction on metabolism in humans (28). Two trials have found that weight loss induced by either gastric bypass surgery or sleeve gastrectomy among severely obese patients causes the same decline in circulating BCAAs (29, 30).

GDM is a serious pregnancy complication worldwide (31). Women with a history of GDM have a marked increase in type 2 diabetes risk later in life (32). It has been found that women exposed to GDM generally have a higher BMI after delivery, (15) and postpartum obesity is one of most important risk factors of postpartum diabetes (33). However, very few studies have assessed how BCAA intakes influence the risks of overweight and central obesity among women with a history of GDM. The present study found that

daily higher and lower intakes of BCAAs, isoleucine, leucine, and valine assessed by a 3-day 24-hour food record were associated with increased risks of general overweight and abdominal obesity among women with prior GDM.

The mechanisms of BCAAs and metabolic disorders are complicated. Studies in human and rodent adipose tissues have demonstrated a reduced expression and activity of mitochondrial branched-chain aminotransferase (BCATm) and branched-chain keto acid dehydrogenase (BCKDH) in an obese condition (34) (35). Another study has suggested that impaired adipokine signaling (leptin versus adiponectin) is a key element in the obesity-driven changes in circulating BCAA levels (36). Moreover, elevated BCAA levels are highly effective activators of the mTOR signaling pathway and persistent activation of mTORC1 promotes insulin resistance through serine phosphorylation of IRS-1 and IRS-2 (37) (38). Thus, the increased circulating BCAAs might have a connection with obesity. Although diet is the only source of BCAAs and 80% of the dietary BCAAs reach blood circulation (39), the relationship between BCAA intakes and obesity risk was not coincident with the BCAA concentrations. As many investigations indicated that BCAA supplementation had an inverse association with weight, the potential mechanisms were postulated as follows: first, leucine directly into brain could activate the hypothalamic mTOR signaling and decrease food intake and body weight (40) (41). Second, leucine supplementation stimulated the increase of leptin, which can suppress dietary appetite and food intake resulting in decreasing body weight (42) (43). Third, the hydrolysis of dietary protein releases leucine in the gastrointestinal tract, which can stimulate the production of cholecystokinin and glucagon-like peptide 1 (anorexigenic hormones) and thus inhibit the production of ghrelin (orexigenic hormones) by activating the mammalian target of rapamycin (44). On the contrary, some other researchers insisted that restriction of BCAA intakes was a approach for weight loss through stimulating the induction of FGF-21 expression, which has shown the effect on weight loss (45).

There were some strengths in the present study. First, this is a large epidemiological study of GDM and this study enrolled a large amount of women with a history of GDM in Tianjin, China. Second, the quantity of BCAA intakes was measured by a 3-day 24-hour food record that is different from previous studies and more practical for adjustment of the daily diet structure. Third, as far as we know, many investigations focused on the association of dietary BCAA intakes with the risk of obesity in the general population. This is the first study aiming at women with prior GDM in a short postpartum period. There were also some limitations in the present study. First, this study had a cross-sectional design that limited the reference as the causal association between daily BCAA intakes and the risk of obesity. Second, the present study only aimed at women with GDM in China. It could not represent the general population. Therefore, future studies are needed to verify the situation in larger regions worldwide. Third, the measurement of BCAA intakes in our study was only in a short term, which may be less representative of individuals' long term dietary patterns.

Conclusion

The present study indicated that the daily lowest quartile of BCAA intakes was significantly associated with great risks of general overweight and abdominal obesity among women with a history of GDM after a short time of delivery. Only moderate BCAA intakes were beneficial for weight control and avoiding abdominal obesity. In the future, more clinical trials are needed to verify this issue.

Abbreviations

BCAA
Branched chain amino acids
GDM
Gestational diabetes mellitus
OR
Odds ratio
CI
Confidence interval
OGTT
Oral glucose tolerance test

Declarations

Ethics approval and consent to participant: the present study was approved by the Biomedical Ethics Board of Tianjin Women's and Children's Health Center. The ethics approval number was 2013-03-01

Consent for publication: not applicable

Availability of data and materials: the datasets generated and analysed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Competing interests: the authors declared that they had no competing interests.

Funding: This study is supported by the grant from European Foundation for the Study of Diabetes (EFSD)/Chinese Diabetes Society (CDS)/Lilly programme for Collaborative Research between China and Europe. Dr. Hu was partly supported by the grant from the National Institute of Diabetes and Digestive and Kidney Diseases (R01DK100790) and the National Institute of General Medical Sciences (U54GM104940) of the National Institutes of Health.

Authors' contributions: Y.S., and G.H. designed the study, acquired data, performed statistical analyses, and drafted the manuscript. J.L., W.L., S.Z., H.L., P.S., P.W., L.W., H.T. and J.T. designed the study and critically revised the manuscript for important intellectual content. C.Z., X.Y., Z.Y. and L.H. critically revised the manuscript for important intellectual content.

Acknowledgements: We would like to appreciate all families for participating in the Tianjin Gestational Diabetes Mellitus Prevention Program. G.H. is the guarantor of this work and, as such, has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Individual participant data will not be available to share.

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Figures

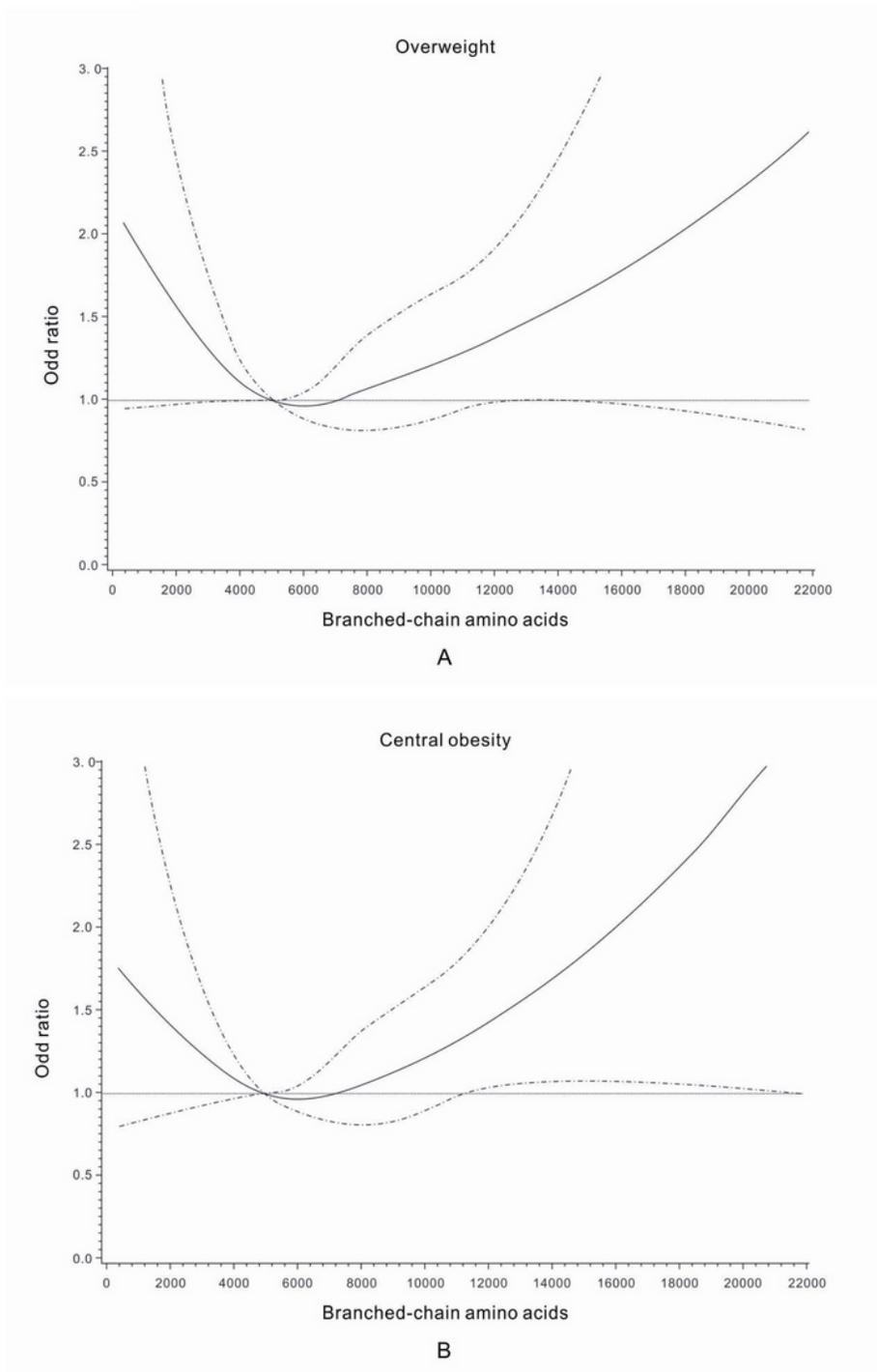


Figure 1

Odds ratios for general overweight (A) and central obesity (B) by different dietary intake levels of branched-chain amino acids (mg/day). Adjusted for age, education, family history of diabetes, family income, current smoking, passive smoking, current alcohol drinking, leisure time physical activities, and sitting time.