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Original Research Article

Association between dietary Folate intake and Obesity in Children and Adolescent

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Conflict of interest: Nil

Abstract:

Objectives: The present study was to evaluate the association between dietary folate intake, vitamin B12 and obesity in children and adolescent at tertiary care centre, Bihar, India.

Methods: We were performed anthropometric measurements, including waist circumference (WC), height, and weight. BMI was computed. General obesity was defined using sex- and age specific BMI cutoffs for children's BMI, and abdominal obesity was characterized using the criterion of WHtR ≥ 0.5. Serum folate and vitamin B12 concentrations were determined using an automatic electrochemical luminescence analyzer. Participants' dietary intake was evaluated using a semi-quantitative food frequency questionnaire (FFQ).

Results: A total of 456 children and adolescents with a median age of 10.88 years were enrolled. Among them 57.73% were boys and 46.27% were girls. The majority of the participants were lived in urban area (84%) and 16% lived in rural areas. 60.96% participants were in age group of 6-11 years and 39.04% participants were in age group of 12-17 years. General obesity was seen in 52(11.40%) participants. And abdominal obesity as observed in 56(12.28%) participants. Participants with high concentrations of both folate and vitamin B12 (the highest quartile for each vitamin) had lower odds of general ($P < 0.0001$) and abdominal obesity ($P < 0.0001$) compared with those with moderate levels of both vitamins.

Conclusions: Serum vitamin B12 are inversely associated with obesity in children and adolescent. High level of serum folate and vitamin B12 are associated with low risk of obesity. Low level of serum B12 may be the risk of general and abdominal obesity in children and adolescent population.

Keywords: Serum folate, Serum Vitamin B12, General obesity, Abdominal obesity.

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Introduction

Overweight is rising among children, increasing the risk of metabolic syndrome, type 2 diabetes, and obesity in adulthood [1, 2]. For adequate prevention, it is important to identify factors that influence the development of overweight in early life. One of the mechanisms that might be involved in the early development of overweight is DNA methylation. DNA methylation is a mechanism in which gene expression is altered in response to environmental influences, such as nutrition and physical activity [3].

Obesity among children and adolescents has become a global public health crisis [4]. The global prevalence of obesity among children and adolescents, aged 5–19 years, has risen dramatically from 0.7% to 5.6% in girls and 0.9% to 7.8% in boys between 1975 and 2016[5]. Obesity is related to a complex range of factors, of which micronutrient status may be an etiological cause and effect [6,7].

Folate and vitamin B12 are vital water-soluble vitamins directly involved in one-carbon metabolism, encompassing processes such as DNA methylation, redox defense, protein and nucleic acid biosynthesis, and other metabolic pathways [8,9]. Deficiency in these vitamins can disrupt one-carbon metabolism, resulting in increased reactive oxidant production and insulin resistance, as well as inhibition of protein synthesis and promotion of lipogenesis [10-11]. Moreover, folate is associated with leptin secretion, gut microbiota composition, and epigenetic gene modifications related to fat and energy metabolism [11,12]. Vitamin B12 plays a significant role in glucose, amino acid, and lipid metabolism through the tricarboxylic acid cycle [9]. A study involving pregnant and postnatal rats revealed that dietary restriction of folate and vitamin B12 results in increased visceral and total body fat, respectively, and altered lipid metabolism in the offsprings [13]. These findings suggest that

inadequate folate or vitamin B12 status could be a potential risk factor for obesity. Objective of the present study was to evaluate the association between dietary folate intake and obesity in children and adolescence at tertiary care centre, Bihar, India.

Material & Methods

The present study was conducted in the Department of Pediatrics, Jan Nayak Karpoori Thakur Medical College and Hospital, Madhepura, Bihar, India during a period from January 2024 to June 2024.

A total of 456 school-aged children and adolescents with age <6 to >18 years were surveyed.

We were excluded the participants with implausible energy intake (falling below the 1st percentile or above the 99th percentile for energy intake) [14]. Parents or guardians of participants, aged 6–11 years, provided written informed consent for them to participate. Participants, aged 12–17 years, along with their legal guardians, provided written informed consent for participation.

Anthropometric Measurements: We were performed anthropometric measurements, including waist circumference (WC), height, and weight, from all the participants before breakfast, who were wearing light clothes and no shoes.

Body weight was measured using calibrated electronic digital scales with a 0.01 kg resolution, while height was measured using height measuring bars with a 0.01 cm resolution.

BMI was computed as weight (kg)/height (m2).

WC was measured using a non-elastic tape in a horizontal plane halfway between the lowest rib edge and iliac crest. The waist-to-height ratio (WHtR) was determined by dividing the WC (cm) by height (cm). General obesity was defined using sex- and age specific BMI cutoffs for children's BMI, and abdominal obesity was characterized using the Indian criterion of WHtR ≥ 0.5.

Serum Folate and Vitamin B12 Concentrations: Venous blood samples were obtained from all participants after an overnight fast between 8:00 and 10:00 am. After a 30-minute standing period, serum was collected after centrifuging the blood at 3,000 rpm and 4 °C for 15 minutes. The samples were the cooled at 4 °C and transported to the laboratory for analysis on the same day. Serum folate and vitamin B12 concentrations were determined using an automatic electrochemical luminescence analyzer. The coefficient of variation for the analytical techniques was 4.27% and 6.89% for serum folate and 2.49% and 3.17% for vitamin B12.

Assessment of Covariates: The socio-demographic indicators comprised age, sex, region (rural and urban areas). Lifestyle variables included total energy intake, multivitamin or B-vitamin supplement use, physical activity, passive smoking, and alcohol consumption.

Participants' dietary intake was evaluated using a semi-quantitative food frequency questionnaire (FFQ) that had been verified for validity and reliability before the survey [15]. Parents or guardians answered food consumption questionnaires for children < 12 years of age; children and adolescents aged 12–17 years answered questions with assistance from their caregivers. The FFQ consists of 57 food and beverage items consumed by children and adolescents. Daily energy intake of each participant was determined [16]. Multivitamin or B-vitamin supplement use by participants was dichotomized into "used" and "not used" in the month prior to the survey. Physical activity levels were assessed using total moderate-to-vigorous intensity physical activity (MVPA) time, encompassing housework, school and outside physical activity, and active commute time, including walking or biking. Passive smoking status was defined based on exposure to tobacco products and was classified into the following groups: daily, not daily, and never. Alcohol consumption status was categorized as never, former (30 days ago), or current drinker (within the past 30 days). Serum high-sensitive C-reactive protein (hs-CRP) and creatinine concentrations were determined using an automatic modular analyzer. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration formula from the serum creatinine values [17].

Results

A total of 456 children and adolescents with a median age of 10.88 years were enrolled in our study. Among them 57.73% were boys and 46.27% were girls. The majority of the participants were lived in urban area (84%) and 16% lived in rural areas. 60.96% participants were in age group of 6-11 years and 39.04% participants were in age group of 12-17 years. General obesity was seen in 52(11.40%) participants. And abdominal obesity as observed in 56(12.28%) participants.

Table 1: Demographic characteristics of population

Variables	Total population (N=456)	General obesity (N0) (404)88.56%	General obesity (Yes) (52) 11.40%
Gender			
Male	245 (53.73%)	215(87.75%)	30(12.24%)
Female	211(46.27%) 1	189(89.57%)	22 (10.43%)
Age group (years)			
6–11	278(60.96%)	242(87.05%)	36(12.94%)
12–17	178 (39.04%)	162(91.01%)	16(8.99%)
Region			
Urban	383(84%)	337(87.99%)	46(12.01%)
Rural	73(16%)	65(89.04%)	8(10.96%)
Passive smoking			
Never	302(66.23%)	268(88.74%)	34(11.26%)
Not daily	142(31.14%)	128(90.14%)	14(9.86%)
Every day	12(2.63%)	8(66.67%)	4(33.33%)
Alcohol consumption			
Never	385(84.43%)	354(91.95%)	31(8.05%)
Former	54(11.84%)	38(70.37%)	16(29.63%)
Current	17(3.73%)	12(70.59%)	5(29.41%)

Median serum folate and vitamin B12 concentrations were 6.98ng/mL and 552.2 pg/mL respectively. We compared to those with obesity were more likely to be boys, younger, urban residents, passive smokers, and exhibited higher hs-CRP and eGFR levels but lower vitamin B12 concentrations.

Serum vitamin B12 concentrations were inversely associated with BMI. The inverse associations of serum vitamin B12 with BMI and WC were almost roughly linear across the distribution of vitamin B12 values.

Serum vitamin B12 concentrations and serum folate were observed to be positively associated with WC. Serum vitamin B12 levels were inversely associated with general obesity and abdominal obesity after adjusting for all potential confounding factors.

We were evaluated the potential interaction between serum concentrations of folate and vitamin B12 using logistic regression analysis. Participants with high concentrations of both folate and vitamin B12 (the highest quartile for each vitamin) had lower odds of general ($P < 0.0001$) and abdominal obesity ($P < 0.0001$) compared with those with moderate levels of both vitamins. Conversely, low serum vitamin B12 concentrations in combination with high serum folate concentrations were positively associated with higher odds of abdominal obesity ($P = 0.016$). Higher odds of general obesity were observed only for low serum vitamin B12 concentrations in combination with moderate serum folate concentrations ($P = 0.022$).

Table 2: Life style and investigative variables of population.

Variables	Total population (N=456)	General obesity (N0) (404)88.56	General obesity (Yes) (52) 11.40%
Total energy intake (kcal/day)	442(96.93%)	214(48.42%	228(51.58%)
Multivitamin or B-vitamin supplements	8(1.75%)	7(87.50%)	1(12.5%)
MVPA (minutes/day)	6(1.32%)	6(100%)	0
BMI (kg/m2)	18.5±2.14	17.3±2.24	26.12±1.64
WC (cm)	62.5±4.67	61.6±3.86	78.6±3.88
WHtR	0.32±0.13	0.32±0.12	0.45±0.13
Abdominal obesity	456	400	56(12.28%)
Biochemistry			
Serum folate (ng/mL)	6.8	6.8	6.8
Serum vitamin B12 (pg/mL)	552.2	557	523.4
hs-CRP (mg/L)	0.2	0.2	0.8
eGFR (mL/min per 1.73 m2)	147.8	147.8	151.5

Discussions

Obesity during childhood and adolescence not only disturbs growth, endocrine balance and psychosocial development during puberty [18], but also exerts long-term health effects in adulthood, amplifying susceptibility to cardiovascular pathology,

metabolic disorders and several cancers [19]. Even more alarming, obesity in these early life stages is associated with an increased risk of premature death in adulthood [20]. Timely and effective interventions on child and adolescent obesity are therefore of critical public-health importance [20].

In the present study, we found that high concentrations of vitamin B12, but not folate, were independently associated with a reduced likelihood of both general and abdominal obesity. Participants with high serum folate and vitamin B12 levels exhibited lower odds of general and abdominal obesity than those of participants with moderate concentrations of these vitamins. Our findings provide new insights into the relationship of serum folate and vitamin B12 with childhood obesity.

Several studies from the United Kingdom and India have observed that decreased vitamin B12 concentrations during pregnancy are associated with increased BMI and general obesity risk among pregnant women [21, 22]. Identical outcomes have been reported in children and adolescents. The risk of low vitamin B12 status is more than 4-fold higher among children and adolescents with obesity than among normal-weight individuals [23].

Our study represents the first reporting of such inverse associations of serum vitamin B12 levels with anthropometric indices and the odds of obesity among children and adolescents. Several mechanisms may explain these results. First, low serum vitamin B12 levels may interfere with one-carbon metabolism, preventing the generation of methionine from homocysteine, thereby reducing protein synthesis and lean tissue deposition [24]. Second, as a critical cofactor for methylmalonyl-coa mutase in the tricarboxylic acid cycle, low vitamin B12 levels may affect caloric expenditure control and energy availability [25]. Conversely, obesity could also decrease the serum vitamin B12 levels through reduced dietary intake or absorption, increased catabolism and sequestration in the adipose tissue [24], or through changes in gut microbiota composition or function that could affect the biosynthesis and metabolism of vitamin B12 [26, 27].

Our results suggested that the association between serum folate levels and WC could be confounded by serum vitamin B12 levels, which may partly explain the discrepancies between our findings and those of other studies. We observed that participants with high serum levels of both folate and vitamin B12 had low odds of developing general and abdominal obesity. However, an increase in serum folate levels in participants with low levels of vitamin B12 increased their probability of experiencing abdominal obesity. Abdominal obesity is strongly associated with insulin resistance. High folate levels may mask and exacerbate the effects of vitamin B12 deficiency, which in turn impairs DNA synthesis, especially of mitochondrial DNA, leading to the development of insulin resistance [21, 28]. A study conducted in India reported that newborns of mothers with high folate and low vitamin B12 concentrations exhibited elevated insulin resistant and greater susceptibility to visceral obesity [29]. Another study from France also revealed that consecutive patients with obesity in the highest tertile of red blood cell folate levels and the lowest tertile of plasma B12 levels exhibited high levels of insulin resistance [30]. Therefore, we speculated that insulin resistance might mediate the association between the high folate and low vitamin B12 levels and abdominal obesity.

In the current study, we also found that participants in the upper B12 quartile exhibited decreased odds of developing general and abdominal obesity as serum folate levels increased. Folate levels in the body may affect the circulating levels of active vitamin B12 and are related to its availability in the body tissues [31].

We found the direct association between folate and obesity is weak and that obesity may be primarily modified by altering the active level and availability of vitamin B12. The mechanism underlying the interaction of folate and vitamin B12 levels with obesity is not yet fully understood and requires further investigation.

This study had several limitations. First, owing to the cross-sectional nature of the study, we could not confirm a causal relationship among serum folate and vitamin B12 levels, anthropometric indices, and obesity. And second sample size was small.

Dietary and nutritional strategies are central to the prevention of obesity in children and adolescents [32]. Folate, a water-soluble B-vitamin that cannot be endogenously synthesized, is essential for key metabolic processes [33]. From a physiological functional perspective, folate plays a crucial role in one carbon unit metabolism and is an essential cofactor for DNA synthesis and repair, as well as epigenetic regulation, such as DNA methylation [34]. These basic physiological processes are involved in regulating gene expression related to energy metabolism, fat production, and appetite regulation [35].

Conclusions

The present study concluded that the serum vitamin B12 are inversely associated with obesity in children and adolescent. High level of serum folate and vitamin B12 are associated with low risk of obesity. Low level of serum B12 may be the risk of general and abdominal obesity in children and adolescent population.

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