



Choline and betaine intake among brazilian picky-eater children: an observational cross-sectional study

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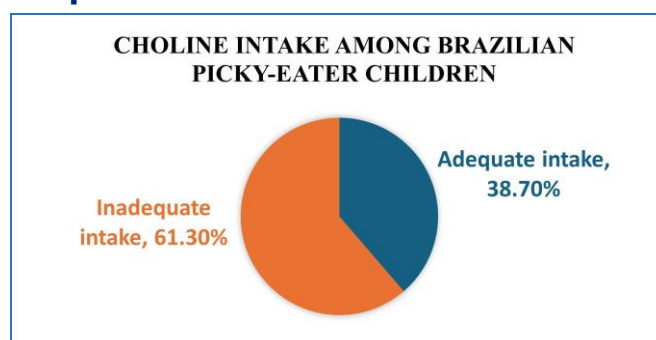
Abstract

Introduction: Choline is a phospholipid component, considered by the Institute of Medicine (IOM), since 1998, as an indispensable nutrient for human beings. After ingestion, free choline is absorbed by the intestinal epithelium by carrier-mediated transport and accumulates in all tissues. In children, low choline levels are related to impairments in synaptic transmission, synaptic plasticity and learning processes, damage to the neuronal membrane, communication and visual-motor deficits and lower academic performance. **Objective:** To evaluate choline and betaine intake in a sample of Brazilian picky eaters aged between 2 and 5 years. **Methods:** This an observational cross-sectional study included 62 children classified as picky eaters, assessed during their first visit to a pediatric clinic in Ribeirão Preto, Brazil. Dietary intake was evaluated using a 24-hour dietary recall. Choline and betaine intakes were analyzed using nutrition analysis software, supplemented with data from the USDA food composition database. Choline intake adequacy was determined based on the Dietary Reference Intakes. **Results:** Median choline intake was 177.2 mg/day (IQR: 116.7–261.2), while betaine intake reached a median of 18.5 mg/day (IQR: 10.9–36.1). Choline intake was below the Adequate Intake (AI) in 61.3% (n=38) of the participants. No dietary reference values are established for betaine intake. Anthropometric z-scores indicated a sample with preserved nutritional

status. **Conclusion:** Brazilian picky eater children have reduced choline intake and this fact can lead to the consequences that have been observed by the deficiency of this nutrient, especially negative repercussions for neurodevelopm.

Keywords: Choline. Choline Deficiency. Betaine. Food Fussiness. Picky-eater. Neurodevelopmental Disorders. Preschool Children.

Graphical Abstract



Source: Own authorship.

Introduction

Choline is a phospholipid component, considered by the Institute of Medicine (IOM), since 1998, as an indispensable nutrient for human beings [1]. Despite being synthesized in small quantities by the liver, this biosynthesis is not enough to meet the needs of most individuals and it is recommended to ingest daily food

sources of choline, such as eggs, livers, milk, meat, cauliflower and peanuts, or betaine, a bioactive compound derived from choline responsible for some of its activities, found in wheat and spinach [1-3]. After ingestion, free choline is absorbed by the intestinal epithelium by carrier-mediated transport and accumulates in all tissues, especially in the liver, kidney, mammary gland, placenta, and brain [1].

The IOM, through the Dietary Reference Intakes (DRI), defines the daily recommended choline intake value by age group (Adequate Intake – AI), as well as the Tolerable Upper Intake Level (UL), as indicated in Table 1 [4]. However, it is estimated that about 50% of the population has genetic polymorphisms that result in increased methyl requirements, for which folate and choline are the main dietary sources [5].

For these individuals, the daily intake recommendation established by the DRIs would be insufficient. Wallace et al. highlight the importance of replacing the AI values with Estimated Average Requirement (EAR) and Recommended Daily Allowance (RDA) values, that would be closer to the population's real choline requirement [6].

Table 1. Recommended daily intake of choline in childhood.

| Age | Gender | UL (mg) | AI (mg) |
|----------------|--------|---------|---------|
| 0 to 6 months | M/F | - | 125 |
| 7 to 12 months | M/F | - | 150 |
| 1 to 3 years | M/F | 1.000 | 200 |
| 4 to 8 years | M/F | 1.000 | 250 |
| 9 to 13 years | M | 2.000 | 375 |
| 9 to 13 years | F | 2.000 | 375 |
| 14 to 18 years | M | 3.000 | 550 |
| 14 to 18 years | F | 3.000 | 400 |

Source: Institute of Medicine [7].

Among its main functions, the donation of methyl groups for the synthesis of Sadenosylmethionine, constitution of the neurotransmitter acetylcholine, constitution of phosphatidylcholine and sphingomyelin (phospholipids predominant in cell membranes) and performance in lipid transport and metabolism stand out. Indirectly, choline also acts on homocysteine methylation, renal cells for adaptation to osmotic stress, and as a precursor to platelet activating factor [1,2]. More specifically, early in life, the development of the central nervous system and the closure of the neural tube are directly related to the supply of choline, via the

placenta, and later breast milk [3]. In turn, the availability of choline for the fetus and infant is dependent on the maternal intake of this nutrient [3].

Choline deficiency in humans is associated with kidney and pancreatic dysfunctions, development of atherosclerosis and nonalcoholic liver disease, and impairments in memory, cognitive function, and growth [1,5]. In children, low choline levels are related to impairments in synaptic transmission, synaptic plasticity and learning processes, damage to the neuronal membrane, communication and visual-motor deficits and lower academic performance [8,9].

Studies conducted in Europe, the United States, and Canada have observed that most populations did not meet the recommended daily intake of choline [3,6,10-13]. According to the NHANES (National Health and Nutrition Examination Survey) study, carried out in the United States, it concluded that children of both sexes in a situation of food insecurity are more likely to not reach the recommended daily intake of choline. The same study points out that, in adolescents, less than 5% of the evaluated population of adolescents ingested amounts of choline higher than the AI [10].

In Brazil, according to data from ELANS (Estudio Latinoamericano de Nutrición y Salud), 83.5% of women between 15 and 49 years of age have deficient choline consumption [14]. Hamlin et al., when evaluating 288 children with Autism Spectrum Disorder, between 1 and 11 years old, noted that more than 69% had choline intake below the AI for their age [15]. Mayneris-Perxachs et al. [16], in a study based on urinary choline metabolites, observed that Brazilian children between 6 and 24 months with a weight-for-age ratio below the z-score -2 had lower concentrations of these metabolites.

Feeding difficulties are characterized by reduced acceptance of food, either temporarily or persisting into adulthood, and may include types such as neophobia, food selectivity, food phobia, or low appetite [17,18]. In general, they have an early manifestation, between 2 and 5 years of age, influenced by the experiences acquired during the food introduction phase [19]. It is estimated that, worldwide, the prevalence of feeding difficulties in children ranges from 8% to 50% [20]. In Brazil, studies in different geographic areas indicate prevalences between 34 and 44% [21-24].

Depending on the intensity of the rejection of food, the child may present growth and development disorders and nutritional deficiencies, as well as emotional harm and impacts on the family's well-

being. In these children, inadequate intake of vitamins E, D, and C, folate, iron, calcium, and zinc, and protein are often observed [18,25]. In addition, the most rejected food groups, in most cases, are fruits and vegetables [19,26].

This study aimed to evaluate choline and betaine intake in a sample of Brazilian picky eaters aged between 2 and 5 years.

Methods

Study design

This is an observational cross-sectional study that followed the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) rules. Available at: <https://www.strobe-statement.org/checklists/>. Accessed on: 08/21/2025. This study used extended baseline data from a randomized, controlled, single-blind clinical trial [18] conducted between December 2019 and August 2022 at a private pediatric clinic in Ribeirão Preto, São Paulo, Brazil.

Ethical Approval

The study was approved by the Research Ethics Committee of the Federal University of São Carlos (UFSCar), under approval number 3.510.241, and was registered in the Brazilian Clinical Trials Registry (ReBEC) under the Universal Trial Number (UTN: U1111-1223-7015) and registration number RBR-6pxpvx. Written informed consent was obtained from all participants' parents or legal guardians prior to enrollment.

Eligibility criteria

Medical doctors and nutritionists practicing in Ribeirão Preto were invited to refer children whose families reported feeding difficulties. All children referred to the clinic during the study period were screened according to eligibility criteria, comprising a convenience sample. Inclusion criteria were age between 24 and 60 months and being a picky eater [27]. A total of 67 children were referred, of whom 64 met the inclusion criteria. Two children were excluded due to the following exclusion criteria: cow's milk protein allergy, lactose intolerance, inability to feed orally, neoplasms, renal or hepatic failure, ongoing treatment for heart disease, genetic syndromes, anorexia nervosa, autism spectrum disorder, attention deficit hyperactivity disorder (ADHD), chronic diarrhea, inflammatory bowel diseases, or growth and developmental delay associated with chronic conditions. The final sample consisted of 62 children. The participant selection flowchart is presented in Figure 1.

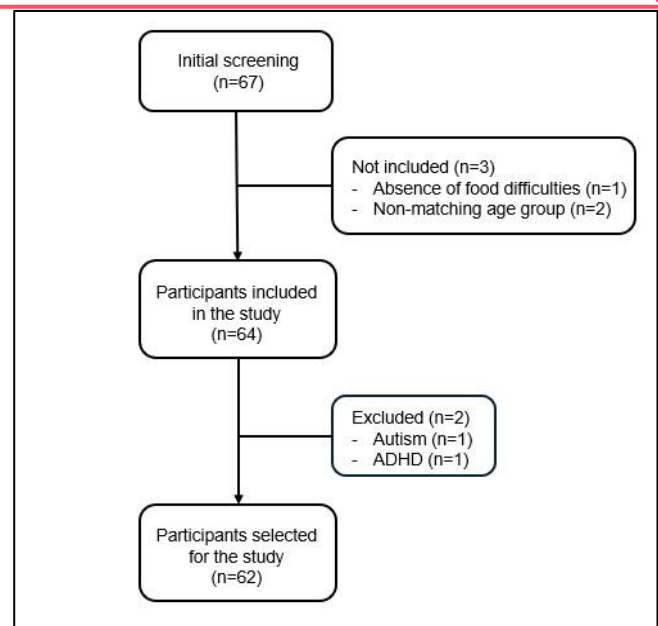


Figure 1. Participant selection flowchart. Source: Own authorship.

Anthropometric assessment

Body weight was measured using a digital electronic scale (Welmy®, Santa Bárbara d'Oeste, Brazil), with participants wearing only undergarments. Height was measured using a wall-mounted stadiometer (Seca®), with the child standing barefoot, upright, and with the back of the head touching the wall. Measurements followed a standardized protocol [28]. BMI was calculated and z-scores for weight, height, and BMI were derived according to WHO standards. Given the rapid physical growth typical of pediatric populations, the WHO recommends the use of z-scores for all anthropometric assessments in children [28].

Dietary intake assessment

Dietary intake was assessed using a 24-hour dietary recall (24HR) administered following the multiple-pass method, which consists of three steps [29]. Adequate intake (AI), as defined by the Dietary Reference Intakes (DRIs), was used to assess the adequacy of choline intake [7]. Betaine intake adequacy could not be determined, as there are currently no established dietary recommendations for this compound. Dietary data were double-checked before being entered into Nutrilife® software (Nutrilife Nutrition Software, Maringá, Brazil), which was used to analyze nutrient intake. The choline (mg) and betaine (mg) contents of foods were obtained from the United States Department of Agriculture (USDA) database and manually entered into the software [30].

Statistical analysis

Descriptive analyses were performed for anthropometric and dietary intake variables. Qualitative

variables were presented as absolute frequency (%). Quantitative variables were described as medians and interquartile ranges (non-normally distributed data). The normality of data was assessed using the Kolmogorov-Smirnov test. All statistical analyses were conducted using IBM SPSS Statistics software, version 22.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 62 children participated in the study, of whom 59.7% (n=37) were male. The median age was 3 years. Median values, interquartile ranges, and minimum– maximum values of anthropometric indicators are presented in Table 2.

Table 2. Anthropometric data of study participants (n=62).

| | Median (Q1 – Q3) | Minimum – Maximum |
|--------------------------|----------------------|-------------------|
| Weight (kg) | 15.5 (13.5 – 17.6) | 9.5 – 31.1 |
| Height (cm) | 100.0 (94.0 – 105.2) | 76.0 – 118.0 |
| BMI (kg/m ²) | 15.8 (14.8 – 17.0) | 12.9 – 23.3 |
| Weight-for-age z-score | 0.09 (-0.7 – 0.8) | -2.6 – 3.8 |
| Height-for-age z-score | -0.3 (-0.7 – 0.5) | -3.7 – 1.7 |
| BMI-for-age z-score | 0.3 (-0.4 – 1.24) | -1.9 – 4.7 |

Source: Own authorship.

The median daily intake of choline and betaine was 177.2 mg and 18.5 mg, respectively (Table 3). Based on the AI values established by the DRIs (Table 1), it was found that 61.3% (n=38) of participants had inadequate choline intake.

Table 3. Daily intake of choline and betaine among study participants (n=62).

| | Median (Q1 – Q3) | Minimum – Maximum |
|------------------|-----------------------|-------------------|
| Choline (mg/day) | 177.2 (116.7 – 261.2) | 3.5 – 697.5 |
| Betaine (mg/day) | 18.5 (10.9 – 36.1) | 0.14 – 132.8 |

Source: Own authorship.

Discussion

Eating difficulties are extremely frequent complaints in the offices of pediatricians and nutritionists. International data suggest prevalences that can reach 50% [20] and, in Brazil, it is believed that the numbers are similar [21-24]. Nogueira-de-Almeida et al. [19] showed, in a 2022 article, that in a set of 1,000 mothers interviewed throughout Brazil, 62% of them reported the presence of feeding

difficulties when their children were between 1 and 4 years old. The repercussions of this situation can include problems in various biopsychosocial spheres in addition to numerous nutritional deficiencies [18,25].

Nogueira-de-Almeida et al. [18] in a study published in 2023 found high prevalences of inadequate intake of several nutrients in a group of 35 picky eaters aged between 2 and 5 years: iron (27.8%), calcium (38.9%), zinc (38.9%), magnesium (27.8%), vitamin A (44.4%), vitamin D (83.3%), vitamin C (22.2%), vitamin B12 (11.1%) and folate (77.8%). Other researchers have also identified several nutritional deficiencies in picky eaters [31], however, to date, we have not found publications that evaluated choline intake in this group. Wertz et al. published a study in 2014 in which they evaluated children with fetal alcohol spectrum disorder (in this group, 31.6% were picky eaters) and found that more than half of the children had choline intake below 80% of the recommendations [32].

No reference values are described for betaine. According to a document from the EFSA, for adults, the mean choline intake estimate from the background diet ranges between 269 and 468 mg/day [33]. Assuming that all dietary choline is ultimately oxidised to betaine, the mean exposure to betaine would range between 302 and 526 mg/day by considering the molecular weight of betaine and choline [33]. Using the same understanding as the EFSA, the average of betaine converted from choline in the children of the present study would be 198 mg/day. Direct consumption of betaine was 18.5 mg/day. The sum of these two ways to obtain betaine leads to a total of 216.5 mg/day. Although the EFSA data refer to adults, the intake observed in the present study is possibly lower than desired. Betaine acts as a donor of methyl groups in several metabolic pathways and deficiencies can lead to elevated homocysteine levels in the blood, increasing the risks of cardiovascular and neurological diseases [34].

The main food sources of choline are eggs, meats, liver, milk, cauliflower and spinach. The low consumption of several of these foods is common among picky eaters [35]. Therefore, insufficient choline consumption would indeed be expected in this group. In fact, the data from the present study showed that 61.3% of the children evaluated did not meet the recommendation and the average consumption (177.2 mg/day) was below the AI reference values (200 mg/day between 2 and 3 years and 250 mg/day between 4 and 5 years).

Although nutritional care is relevant throughout the life cycle, in the first 2,200 days the child needs differentiated attention, since the effects of omissions

or care in this age group can have lifelong impacts [36]. As far as choline is concerned, it is able to help with neurodevelopment and the attainment of cognitive abilities [37]. Wiederman et al. [38] evaluated dietary choline intake and status in healthy 1- and 2-year-old children and demonstrated that most children did not achieve AI and that higher plasma concentrations of betaine (choline metabolite) were associated with better visual-motor development at 2 years of age. Low choline levels in children are related to cognitive impairment, due to impairment of synaptic transmission, damage to the neuronal membrane and synaptic plasticity, problems in learning and memory processes, communication deficits, and lower academic and visuomotor performance [9,38-40]. Nilsson et al. showed that plasma choline concentration was significantly and positively associated with academic performance, regardless of confounding factors evaluated [9].

Other aspects relevant to pediatric health are also related to choline. Regarding growth, Semba et al. [41] showed, in a study published in 2016, that low linear growth in young children in Malaysia was associated with low serum choline. In preterm infants, Bernhard et al. showed that choline deficiency can contribute to impaired growth of lean body mass and lung and neurocognitive developments, even with sufficient macronutrient supply and adequate weight gain [42].

In Brazil, urinary choline metabolites were measured among 326 children aged 6 to 24 months with weight-for-age (W/A) z-scores lower than -2 or greater than -1. Children with W/A less than -2 had lower concentrations of urinary choline metabolites, signifying changes in choline metabolism among underweight children [16]. Innis & Hasman, in a 2006 study, warn that choline depletion may contribute to clinical complications found in cystic fibrosis [43]. In 2011, another study by Innis' group showed that, in these children, choline depletion is associated with a reduction in peripheral leukocyte acetylcholine [44]. Children with Autistic Spectrum Disorders (ASD) generally have insufficient choline intake, which may contribute to some metabolic abnormalities observed in this condition [15].

Gabis et al. [45] showed that the combination treatment of donepezil hydrochloride with choline supplement demonstrated a sustainable effect on receptive language skills in children with ASD for 6 months after treatment, with a more significant effect in those under 10 years of age. Among children aged 2 to 5 years with fetal alcohol syndrome, Wozniak et al showed that choline supplementation led to greater nonverbal intelligence, greater visual-spatial ability,

greater working memory capacity, better verbal memory, and fewer behavioral symptoms of attention deficit hyperactivity disorder than the placebo group [46,47]. In 2025, this same group confirmed these findings, focusing on memory-related outcomes [48].

Another study focused on the effect of choline supplementation on school-aged children with ADHD. Thirty-six children between the ages of 4 and 14 years received either a placebo or a phosphatidylserine supplement 200 mg/d for two months. Their ADHD symptoms based on DSM IV, auditory short-term memory, working memory, and mental performance related to visual stimuli were assessed. Children who received the choline supplement showed significant improvements in ADHD symptoms and auditory short-term memory. The supplement was well tolerated and resulted in zero adverse effects [49]. Among children with NASH, Zoher et al found that choline associated with docosahexaenoic acid (DHA) may improve steatosis and reduce AST and glucose concentrations [50].

Limitations

- 1) The definition of Picky-eater diagnosis does not have a widely accepted international standard, and the criteria used were necessarily chosen by the authors.
- 2) The analyses related to choline and betaine were based on a dietary survey, and the results are subject to the limitations of this methodology.
- 3) Reference tables for dietary surveys often do not include the choline and betaine levels of some foods, and manual input of these levels was necessary for some foods.

Conclusion

In conclusion, Brazilian picky-eater children have reduced choline intake, and this fact can lead to the consequences that have been observed by the deficiency of this nutrient, especially negative repercussions for neurodevelopment.

CRedit

Author contributions: **Conceptualization-** Carlos Alberto Nogueira-de-Almeida, Maria Eduarda Nogueira-de-Almeida, Fábio da Veiga Ued; **Data curation-** Carlos Alberto Nogueira-de-Almeida, Maria Eduarda Nogueira-de-Almeida, Fábio da Veiga Ued; **Formal Analysis-** Carlos Alberto Nogueira-de-Almeida; **Investigation-** Carlos Alberto Nogueira-de-Almeida, Maria Eduarda Nogueira-de-Almeida, Fábio da Veiga Ued; **Methodology-** Carlos Alberto Nogueira-de-Almeida, Maria Eduarda Nogueira-de-Almeida; **Project administration-** Carlos Alberto Nogueira-de-Almeida;

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Writing - original draft- Carlos Alberto Nogueira-de-Almeida, Maria Eduarda Nogueira-de-Almeida, Fábio da Veiga Ued; **Writing-review & editing-** Carlos Alberto Nogueira-de-Almeida, Maria Eduarda Nogueira-de-Almeida, Fábio da Veiga Ued.

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Not applicable.

Ethical Approval

The study was approved by the Research Ethics Committee of the Federal University of São Carlos (UFSCar), under approval number 3.510.241, and was registered in the Brazilian Clinical Trials Registry (ReBEC) under the Universal Trial Number (UTN: U1111-1223-7015) and registration number RBR-6pxpvx. Written informed consent was obtained from all participants' parents or legal guardians prior to enrollment.

Informed Consent

It was applicable.

Funding

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Data Sharing Statement

No additional data are available.

Conflict of Interest

The authors declare no conflict of interest.

Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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