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Research Article

Nutritional and Metabolic Parameters of Children and Adolescents with Phenylketonuria

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Abstract

Objective: To evaluate the anthropometric and biochemical characteristics of children and adolescents with phenylketonuria.

Methods: Retrospective study with anthropometric and biochemical data collection from patients with phenylketonuria in the age group 2-19.9 years. Nutritional status was classified according to the World Health Organization. Biochemical tests were compared to current recommendations.

Results: A total of 84 patients (71.8%) were eligible, with a median age of 10.7 years (2.4-19.9 years). There was predominance of eutrophy (n = 58, 69%) with presence of overweight and obesity in 24 (28.5%) patients. The biochemical tests revealed hyperphosphatemia in 46 (55%), hypertriglyceridemia in 27 (50%), vitamin B12 elevated in 34 (41.2%), selenium deficiency in 10 (13.7%), insufficient zinc in 7 (8.9%), low globulin in 21 (26.9%), low HDL in 35 (59.3%) and elevated phenylalanine level in 28 (34.5%) patients in the sample. Overweight and obesity were correlated with low HDL (p= 0.04) and lowest adequate frequency of LDL (p = 0.09). Higher phosphorus values were associated with lower body weight (r = -0.72) and age (r = -0.75), as well as vitamin B12 in the same parameters (r= -0.67 and r= -0, 68). A positive correlation of phenylalanine with body weight and age (r = 0.62 and r = 0.66) was observed.

Conclusion: Most patients presented eutrophy according to anthropometric parameters and appropriate biochemical tests, except HDL, and moderate metabolic control of the disease. However, attention should be paid to the presence of overweight and need for biochemical monitoring of triglycerides, selenium, zinc, HDL, and phenylalanine.

ABBREVIATIONS

PKU: Phenylketonuria; Phe: phenylalanine; FEPE: Ecumenical Foundation for the Protection of the Exceptional; W/A: weight-for-age; H/A: height-for-age; W/H: weight-for-height; BMI/A: body mass index by age; WHO: World Health Organization; LDL: low density lipoproteins; HDL: high density lipoproteins; BMI: body mass index; HGM-CoA: 3-hydroxy-3-methylglutaryl coenzyme A.

INTRODUCTION

Phenylketonuria (PKU) is a hereditary disease caused by a deficiency in the activity of the hepatic enzyme L-phenylalanine-4-hydroxylase, involved in the metabolism of phenylalanine (Phe) [1]. This is the most prevalent disorder among inborn errors of amino acid metabolism [2]. The prevalence of PKU varies according to region, with 1 in 10,000 births in the United States, 1 in 15,839 births in Brazil, 1 in 20,000 births in Europe [3,4].

The absence of Phe metabolism results in high levels of this amino acid in the bloodstream, compromising brain development in childhood and brain functions at any stage of life [5]. The diagnosis of this disease when performed at neonatal screening and accompanied by immediate onset of a diet excluding foods containing Phe - such as meats, fish, eggs, legumes, milk and dairy products, among others, and supplemented with micronutrients and Phe-free amino acids, allows cognitive development close to normal [6-8]. However, as a result of dietary restriction of protein, these patients generally consume a diet rich in simple carbohydrates and lipids, which may increase the risk of developing overweight and obesity [9].

Another relevant aspect is an increased susceptibility to micronutrient deficiencies due to the intense restriction of Phe

source foods such as proteins, of less than 10 g/day [10,11]. The practice of adding vitamin, mineral and trace element supplements in Phe-free formulas has been the treatment of this disease over the past 20 years, with the Phe-free formulas being the main source of the micronutrients for the majority of patients. However, micronutrient sources are chemically derived, which impacts their bioavailability [11].

Some studies have found deficiencies of pre-albumin, selenium, vitamin D, iron, copper and zinc in this population [1,11-13]. In contrast, folic acid levels were found to be increased in part of this population [1,11].

These changes may be caused by the composition of the free-Phe food formulas provided free of charge by governments as well as the fact that foods with low amounts of Phe that are nutrient rich are difficult to access and costly [14]. Moreover, foods poor in Phe may become monotonous, which may aggravate nutritional deficiencies [14]. Faced with this scenario and considering the lack of information on the anthropometric and biochemical profile of children and adolescents with PKU in the State of Paraná, this present study may help in the evolution of nutritional treatment, quality of life and improvement of nutritional programs for this population. The objective of this study was to evaluate the anthropometric and biochemical characteristics of children and adolescents with PKU residing in the State of Paraná.

MATERIALS AND METHODS

This is a cross-sectional study with retrospective data collection on anthropometric and biochemical parameters of children and adolescents with PKU attended at the Ecumenical Foundation for the Protection of the Exceptional (FEPE) in Curitiba (PR, Brazil).

The Reference Service in Neonatal Screening in Parana, accredited by the Ministry of Health, is the FEPE. This institution specializes in preventive health, specialized care and free social assistance for pregnant women and patients with multiple genetic deficiencies, such as cystic fibrosis, congenital hypothyroidism, congenital adrenal hyperplasia, hemoglobinopathies and PKU [15].

The Reference Neonatal Screening outpatient clinic specializing in FEPE PKU presents, on average, six new cases of PKU per year, with 30 weekly consultations and 117 patients between 2 and 19 years of age. The study sample was obtained from the population with PKU attended in this outpatient clinic and who met the inclusion and exclusion criteria.

Patients were invited to participate in the study that included the following inclusion criteria: presenting a PKU diagnosis, being in clinical follow-up for at least one year, aged between 2 and 20 years, of both sexes. Written informed consent was given for all subjects by one caregiver with parental responsibility and written assent was obtained from the subjects if appropriate for their age (7-18 years) and level of understanding. This work was approved by the Ethics Committee on Research in Human Beings of the Sector of Health Sciences of the Federal University of Paraná under nº 2.294.271 and was carried out in accordance with the Declaration of Helsinki.

Patients who did not have data on anthropometric weight and height assessment or did not perform biochemical exams in the last two years were excluded.

For the anthropometric evaluation, data were collected on sex, weight and height at the time of the last consultation performed in the prior two years. The data obtained were evaluated by means of the weight-for-age (W/A), height-for-age (H/A), weight-for-height (W/H) and body mass index by age (BMI/A) indexes for children aged 2 to 19.9 years; H/A, BMI/A, H/A for children aged 5 to 9.9 years, BMI/A, H/A for children and adolescents aged 10 to 19.9 years. The results were classified according to categories established by the World Health Organization (WHO) [16].

Serum calcium, total cholesterol and fractions, triglycerides, ferritin, phosphorus, total proteins and fractions, selenium, vitamin B12, 25-OH-vitamin D and zinc collected in the last 24 months of these patients were examined. The values found were compared with the current literature, according to the age group [17-20].

The Phe values were defined by the mean of three consecutive previous measurements performed close to the date of the biochemical tests collected for the study. The results were compared with the recommendation of the Ministry of Health (0 to 12 years - to maintain between 2 and 6 mg/dL levels, over 12 years - to maintain levels between 2 and 10 mg/dL) [4].

Statistical analysis was performed considering the significance level of 5% and Student's t-tests, Mann-Whitney test, Fisher's exact test and Pearson's chi-square test were applied. Pearson's correlation coefficient was calculated to estimate association between biochemical exams, body weight and age (Statistica v. 10.0 - Statsoft®).

RESULTS

Among the 117 children and adolescents with PKU treated in FEPE, 84 (71.8%) patients participated in the study. Exclusions were due to the lack of serum tests in the last two years. Among the patients included, 46 (54.8%) were female and 38 (45.2%) were male, with a median age of 10.7 years (2.4-19.9 years).

In the evaluation of the BMI/A and W/H indices, a statistically significant difference was observed between the female and male sexes ($p = 0.02$ and $p = 0.04$, respectively). In females, there was a higher frequency of eutrophy in the BMI/A index ($p = 0.02$) and a higher risk of overweight in the W/H index ($p = 0.04$). On the other hand, males showed a higher frequency of thinness and marked thinness in relation to females, according to the BMI/A index. The H/A index showed low/very low height for age in 11.9% ($n = 11$) of the study population and was similar between groups ($p > 0.05$). The W/A index showed a predominance ($n = 35$, 87.5%) of adequate weight for age with no difference between genders ($p > 0.05$) and very low weight/low weight for age in 4 (24.9%) of the male patients (Table 1).

There was a significant difference between the male and female participants in exams for vitamin D ($p = 0.01$), total cholesterol ($p = 0.01$) and LDL ($p = 0.04$). Ferritin values were higher in males, with a borderline significance level ($p = 0.08$) (Table 2).

When comparing the results of the biochemical tests according to the reference values, low High Density Lipoproteins (HDL) was observed in 59.3% (n = 50) of the cases, and insufficient globulin values in 26.9% (n = 22). Deficiencies of calcium, selenium, vitamin B12, vitamin D, zinc and albumin were observed less frequently. Values higher than the reference values most frequently observed included phosphorus (55%, n = 46), hypertriglyceridemia in 50% (n = 27), vitamin B12 (41.2%, n = 34) and Phe (34.5%, n = 28). It was observed that 6% (n = 5) used zinc supplementation, 7.1% (n = 6) calcium, 13% (n = 11) vitamin D, of iron, 3.5% (n = 3) of vitamin B12 and 10.7% (n = 9) of selenium. There was no difference, however, between genders (p> 0.05) (Figure 1).

High Density Lipoproteins was found in adequate levels in only 16.7% (n = 3) of overweight / obese patients according to the BMI/A index in relation to eutrophic (42.5%, n = 17) (p = 0.04), and there was a lower frequency of adequate LDL (p = 0.09) in this population. In addition, there was no association between anthropometric indices and biochemical tests (Table 3).

A strong negative correlation was observed between the values of phosphorus and vitamin B12 with body weight and age; that is, higher values of phosphorus associated with lower weight (r = -0.72) and age (r = -0.75), and moderate negative correlation of vitamin B12 (r = -0.67 and r = -0.68). In relation to Phe, a moderate positive correlation was observed between body weight and age (r = 0.62 and r = 0.66). There was no association between phenylalanine levels and other biochemical tests (data not shown).

DISCUSSION

The present study demonstrated that the nutritional status of the majority of the children and adolescents with PKU treated at the FEPE clinic in Paraná was adequate. There was a relevant frequency of overweight and obesity, mainly in the female sex, as well as the relation between overweight and obesity with inadequacy of HDL and LDL, and higher levels of phosphorus and vitamin B12 in the younger population with lower weight.

Supporting the results of the present study, a study by Mazzola et al., [14], with children with Brazilian PKU after five years (n = 27) showed that in 74.0% of the sample the patients were eutrophic according to BMI and 22% were overweight or obese. A study carried out in Spain showed that 56.4% of the patients were considered to be eutrophic according to the BMI/age index, 4.4% presented thinness and 39.1% were overweight or obese [1], values higher than those found in the present study.

Burrage et al. [9], found eutrophy values for most of their patients and also found a higher frequency of overweight in women according to BMI. Despite the above, our results from the W/H index should be viewed with caution, since this evaluation included only 5 girls and 7 boys. There are studies that point out that there is no significant difference between patients with PKU and control group and in both sexes, regarding the preponderance of overweight and obesity [14,21]. Regarding the W/A index, there was no difference between the sexes in this study.

Similar to the results of this study, the Cardiovascular Risk Study in Adolescents (ERICA) analyzed Brazilian adolescents with no PKU between 12 and 17 years of age and found the overweight sample to be 25%, according to the BMI/A index [22]. In addition, in a national study of Family Budgets (*Pesquisa de Orçamentos Familiares* - POF), found the prevalence of overweight ranged from 22 to 27% in the Southern region of Brazil, in adolescents aged 10 to 19 years without PKU [23]. These studies suggest that the percentage of overweight in the population with PKU evaluated in the Southern region is similar to that of the healthy population analyzed in recent studies.

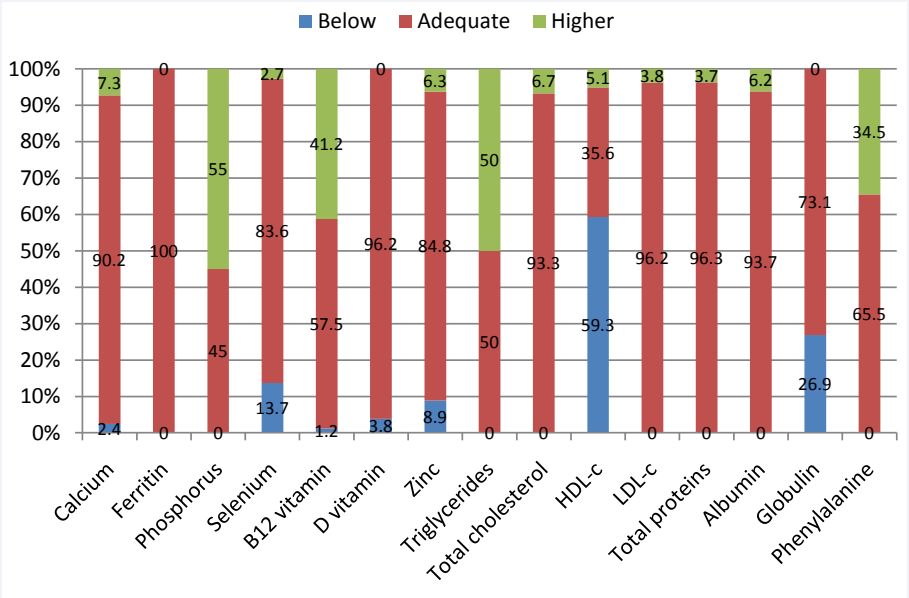

Figure 1 Adequacy of biochemical tests according to reference values of children and adolescents between 2.4 and 19.9 years old with phenylketonuria - State of Paraná, Brazil.
Note: Pearson's Chi-square test and Fisher's exact test: p> 0.05.

Table 1: Anthropometric indices of children and adolescents between 2.4 and 19.9 years with phenylketonuria - State of Paraná, Brazil, 2019.

Anthropometric indices	Total sample (n = 84)	Women (n = 46)	Male (n = 38)	p
Body mass index/age (F = 46; M = 38)				
Accentuated thinness	1 (1.2%)	0 (0.0%)	1 (2.6%)	0.023[1]
Thinness	1 (1.2%)	0 (0.0%)	1 (2.6%)	
Eutrophy	58 (69.0%)	30 (65.2%)	28 (73.7%)	
Overweight	18 (21.4%)	12 (26.1%)	6 (15.8%)	
Obesity	6 (7.1%)	4 (8.7%)	2 (5.3%)	
Height/age (F = 46; M = 38)				
Low	8 (9.5%)	6 (13.0%)	2 (5.3%)	1.00[1]
Very low	2 (2.4%)	0 (0.0%)	2 (5.3%)	
Adequate	74 (88.1%)	40 (87.0%)	34 (89.4%)	
Weight/Height (F = 5; M = 7)				
Eutrophy	9	2	7	0.04[2]
Overweight	3	3	0	
Weight/age (F = 24; M = 16)				
Very low weight for age	1 (2.5%)	0 (0.0%)	1 (6.2%)	0.13[1]
Low weight for age	3 (7.5%)	0 (0.0%)	3 (18.7%)	
Appropriate weight for age	35 (87.5%)	23 (95.8%)	12 (75.0%)	
Hight /weight for age	1 (2.5%)	1 (4.2%)	0 (0.0%)	

NOTE: [1]Chi-square test; [2]Fisher exact test. Eutrophy and overweight in the index Height/age index: values only in absolute frequency (n < 10). F = female M = male.

Table 2: Biochemical examinations of children and adolescents aged between 2.4 and 19.9 years with phenylketonuria - State of Paraná, Brazil.

Biochemical examination	Women (n = 46)	Male (n = 38)	p
Calcium (mg/dL) (F = 46; M = 36)	9.9 ± 0.6	9.8 ± 0.6	0.94[1]
Ferritin (ng/ml) (F = 45; M = 37)	41.2 (15.5 – 134.9)	56.7 (18.9 – 157.3)	0.08[2]
Phosphorus (mg/dL) (F = 42; M = 38)	4.7 ± 0.7	4.6 ± 0.8	0.63[1]
Selenium (mg/L) (F = 40; M = 33)	82.0 (3.1 – 147.0)	77.0 (7.2 – 160.0)	0.25[2]
B12 vitamin (pg/ml) (F = 44; M = 36)	858.0 (179.0 – 1909.0)	688.0 (216.0 – 2000)	0.56[2]
D vitamin (ng/ml) (F = 44; M = 36)	31.9 (17.2 – 83.0)	38.9 (18.8 – 70.0)	0.01[2]
Zinc (ug/dL) (F = 44; M = 35)	92.0 (0.9 – 130.8)	90.5 (0.8 – 155.1)	0.67[2]
Total cholesterol (mg/dL) (F = 36; M = 24)	138.7 ± 27.1	120.8 ± 28.3	0.01[1]
HDL (mg/dL) (F = 36; M = 23)	45.6 ± 11.2	43.5 ± 9.9	0.46[1]
LDL (mg/dL) (F = 33; M = 20)	73.0 (31.8 – 191.2)	53.0 (33.0 – 103.0)	0.04[2]
Triglycerides (mg/dl) (F = 33; M = 21)	84 (33 - 186)	84 (23 – 275)	0.74[2]
Total proteins (g/dL) (F = 45; M = 36)	7.1 ± 0.4	7.0 ± 0.6	0.20[1]
Albumin (g/dL) (F = 44; M = 36)	4.5 ± 0.3	4.5 ± 0.3	0.77[1]
Globulin (g/dL) (F = 43; M = 36)	2.6 ± 0.4	2.5 ± 0.5	0.25[1]
Phenylalanine (mg/dL) (F = 46; M = 36)	6.2 (1.1 – 17.5)	6.7 (1.6 – 16.3)	0.45[2]

NOTE : [1]T Student Test [2]Mann Whitney Test ; F = female ; M = male ; HDL: High Density Lipoproteins; LDL: Low Density Lipoproteins.

The high prevalence of overweight and obesity indicate the need for implementation of strategies such as increased physical activity practice and as well as nutritional guidance for healthy food selection [9].

Another important point is adherence to the metabolic formula, which can have an unpleasant and monotonous taste and, therefore, seem disagreeable [7]. Food restrictions can result in consumption of foods containing sugars, are free of Phe, but which may favor weight gain in this population [9].

In addition, maintenance of rigid diet is associated with abnormal eating behaviors that may promote obesity in older children as they gain autonomy for their food intake choices [9]. In addition, adherence to strict diet may place a social burden on patients, and may lead them to refrain from practicing sports and other physical activities [24].

As for growth, a Spanish study followed the growth rate from 6 months to 18 years in 279 patients with PKU and reported impairment in children and adolescents over the years [24]. On the other hand, another study with children and adolescents with PKU in São Paulo found only a 5% prevalence of short stature for

age, a percentage that was slightly lower than that found in our study [25]. According to the POF, the prevalence of short stature in children without PKU, from 2 to 9 years old was approximately 6.4% and therefore, a lower percentage than the one found here [23].

Regarding the biochemical tests, the majority of patients studied had adequate serum levels of proteins, vitamins and minerals; but the values of HDL and globulin were low (Figure 1). Other deficiencies found less frequently were calcium, selenium, vitamin B12 and vitamin D, with no significant difference between the sexes (p> 0.05). A study conducted in Turkey indicated that vitamin D deficiency was present in 53.6% of PKU patients and 47.2% of control subjects [26]. Lower values were found by Crujeiras et al. [1], with 14% of patients with vitamin D insufficiency. However, Macdonald et al. [27], found that vitamin D levels were higher in phenylketonuric individuals with good adherence to diet compared to patients who did not. This result may be associated with an adequate intake of a food formula supplemented with vitamin D [27]. Different brands have different levels of vitamin D in their composition, so it is necessary to correlate the food consumption of this population with serum levels.

The trace element selenium was insufficient in a small part of the study population. Crujeiras et al. [1], observed 25% of selenium insufficiency in the phenylketonuric population examined, an excessively larger value than that found in the present study. Another study in children aged 1 to 4 years showed that selenium concentrations decreased with increasing age, as opposed to Phe, which tended s to increase [10]. Additionally, in Minas Gerais, a study compared food intake of patients with PKU of 4 to 10 years with the Dietary Reference Intake and concluded that selenium supplementation in these patients is essential due to the direct relationship of the dosage of glutathione peroxidase with selenium levels and for its correlation with oxidative stress, since supplementation of selenium controls biochemical parameters linked to the oxidative condition [28]. Insufficient serum levels of selenium in patients with PKU can be justified by decreased tubular reabsorption, increased urine excretion, redistribution of mineral metabolic reservoirs and rupture in intestinal absorption [5,11].

Zinc insufficiency was found in a small part of the sample studied. Studies have found 71% of plasma zinc levels below the reference value, even with adequate dietary intake. This effect may be associated with the fact that zinc, as a supplement in the metabolic formula, has its bioavailability decreased compared to zinc available in products of animal origin [11]. In addition, interaction with other available ions in the metabolic formula, such as calcium, may interfere with absorption of the mineral. As with selenium, zinc in individuals with PKU may have decreased tubular reabsorption, increased urine excretion, redistribution of mineral metabolic reservoirs, and rupture of intestinal absorption [5,11]. Other authors have demonstrated, however, that the metabolic formula is sufficient to achieve adequate levels of zinc [26]. Because of these differences, individual case assessment becomes necessary.

Mineral calcium was found to be insufficient in a small part of the study sample, which indicates that the majority of patients with PKU had adequate serum levels of this mineral. Several authors have reported that in order to obtain the expected bone development in each stage of life, individuals with PKU depend on the supplementation of this mineral, since many factors can compromise intake and absorption and negatively interfere with bone mass; these include elevated levels of Phe, restricted dietary intake of these patients and the presence of antinutritional

Table 3: Frequency of appropriate biochemical exams according to nutritional status by BMI/age of children and adolescents between 2.4 and 19.9 years with phenylketonuria - State of Paraná, Brazil.

Biochemical examination	Eutrophic (n = 58)	Overweight/Obesity (n = 24)	p
Calcium (n = 80)	53 (92.9%)	20 (87.0%)	0.19[1]
Ferritin (n = 82)	56 (100.0%)	24 (100.0%)	1.00[2]
Phosphorus (n = 78)	28 (50.9%)	8 (34.8%)	0.22[2]
Selenium (n = 71)	43 (86.0%)	16 (76.2%)	0.22[1]
B12 vitamin (n = 78)	33 (60.0%)	12 (52.2%)	0.27[1]
D vitamin (n = 76)	51 (96.2%)	22 (95.6%)	1.00[2]
Zinc (n = 77)	46 (85.2%)	19 (82.6%)	0.22[1]
Cholesterol (n = 59)	39 (95.1%)	16 (88.9%)	0.57[2]
HDL (n = 58)	17 (42.5%)	3 (16.7%)	0.04[1]
LDL (n = 52)	36 (100.0%)	14 (87.5%)	0.09[2]
Triglycerides (n = 54)	18 (47,4%)	8 (53,3%)	0,93[2]
Total proteins (n = 79)	54 (96.4%)	22 (95.6%)	1.00[2]
Albumin (n = 78)	51 (92.7%)	22 (95.6%)	1.00[2]
Globulin (n = 76)	39 (70.9%)	17 (80.9%)	0.56[2]
Phenilalanine (n = 82)	39 (67.2%)	16 (66.7%)	1.00[2]

Note: [1]Pearson´s chi-square test; [2]Fisher exact test. HDL: High Density Lipoproteins; LDL: Low Density Lipoproteins.

factors which interfere in the bioavailability of this mineral. Other factors include hereditary intrinsic factors such as race, sex and hormone levels and extrinsic factors such as nutritional status, mechanical strength, eating habits, presence of chronic diseases, use of medications, decreased tubular reabsorption, increased urinary excretion, redistribution of metabolic reservoirs minerals and rupture in intestinal absorption [5,11]. It is noteworthy that cases of osteopenia, osteoporosis and fractures in the phenylketonuric population are increasingly evident and increasing, which reinforces the importance of sufficient supply of this micronutrient [25].

Vitamin B12 was also found to be insufficient in the smallest portion of the sample. There is evidence that adults with PKU are at risk of vitamin B12 deficiency [29]. On the other hand, studies have shown that patients with PKU may have higher vitamin B12 levels relative to the PKU population and state that metabolic formulas are sufficient to reach desired values of this vitamin [26].

Similar to the present study, 93% of the serum ferritin samples were within the reference value in a study by Evans et al. [11], and the incidence of iron deficiency was not higher in PKU patients when compared to the control group. Despite the high iron intake, both dietary and supplementary, the study found no correlation between the nature of food consumed and results [11].

It should be noted that serum levels of calcium, selenium, vitamin B12 and zinc were found to be high in part of the sample. This may be associated with the food formula and/or the specific supplementation with these nutrients, since patients were monitored periodically, as part of a service protocol that prescribed supplementation when necessary.

The high phosphorus value in the study sample may be due to the Phe-free food formula prescribed for this population, thus corroborating the adequacy of the total protein and albumin tests evaluated. In addition, the highest phosphorus level was found in younger children with lower age and lower body weight, a result that is the opposite of that found by other authors [30]. Arslan and Kose found that 38.8% of PKU patients had pre-albumin values above the reference range while the frequency was 22.1% in the control group [26]. The opposite was demonstrated in other studies where 34.6% of patients were deficient in this marker [1,6]. Pre-albumin is a more sensitive predictor of plasma protein status than albumin and total protein [26]. The globulins are closely related to chronic inflammation and can play important roles in tumor occurrence and progression [31]. However, Chen et al. [32], report that low serum globulin level is related to favorable survival outcomes in cancer patients. Our search did not find studies on globulin levels in phenylketonurics. Dietary intake should be studied to elucidate questions regarding the protein status of individuals.

Our work also registered a small portion of the sample with high levels of total LDL cholesterol, while low HDL was found in the majority of the studied population. Other studies found that total cholesterol and LDL were lower in PKU children who were on dietary intake than the control group. HDL did not show any difference in their levels in both groups [33], Lipid metabolism is impaired in PKU, and patients presented altered serum lipoprotein values, including total cholesterol, HDL, LDL, and apolipoproteins AI, AII and B low, explained by the compromise of the cholesterol synthesis caused by the decreased expression of the enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HGM-CoA) reductase, responsible for controlling the rate of cholsterogenesis [33,34]. This information may explain the results found in our study, where overweight and obese children and adolescents had low HDL and lower LDL frequency. High total cholesterol and elevated LDL are important risk factors for cardiovascular diseases, the leading cause of death in the world and therefore must be monitored and controlled [35].

The presence of hypertriglyceridemia found in the population of our study corroborates the results described by other authors [21,34,36]. This situation may be due to different realities of patterns of physical activity and food consumption among different countries. It also suggests an indicator of overweight and metabolic syndrome in this population [9,21,34].

Also, in our stu`dy, a significant portion of the sample registered elevated Phe levels. Similar results were found previously with a 44% inadequacy of Phe levels in a study conducted with children and adolescents with PKU in São Paulo [25]. Rigorous dietary control was able to maintain 100% Phe concentrations within the reference values [4,7]. The amount of Phe consumed should be sufficient for protein synthesis and growth, but its tolerance is influenced individually by factors such as growth, protein catabolism, hydroxylation rate, amino acid dosage without Phe, biopterin treatment, blood concentration of Phe and pregnancy [27]. In addition, serum Phe is also influenced by eating habits and life in each country, thus requiring multidisciplinary life-long follow-up [12].

The adequacy of the serum exams and the growth curves found are justified by the monitoring and efficient treatment undergone. Although the present study presents the anthropometric and biochemical profile of children and adolescents with PKU in the state of Paraná, this is presented as a limitation to the study, in the absence of a dietary analysis of the patients.

CONCLUSION

The nutritional profile of children and adolescents with PKU in Paraná was characterized by individuals who are mostly eutrophic, with adequate height for age in both sexes and adequate weight for age. Additionally, there was an important frequency of overweight and obesity. Hypertriglyceridemia and inadequate metabolic control of the disease were observed in part of the sample, while a small portion showed deficiency of selenium, zinc, HDL, reinforcing the need for adequate consumption of recommended foods, food formulae, nutritional supplementation as well as the practice of physical exercises. Further studies on the bioavailability and absorption of macro and micronutrients in Phe-free formulas and in the supplementation used by these patients are needed.

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