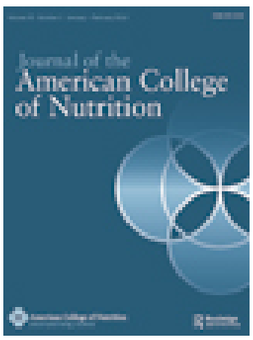

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Usefulness of the StrongKids Screening Tool in Detecting Anemia and Inflammation in Hospitalized Pediatric Patients

Carolina Araújo dos Santos[a], Carla de Oliveira Barbosa Rosa[a], Sylvia do Carmo Castro Franceschini[a], Heloísa Helena Firmino[b] and Andréia Queiroz Ribeiro[a]

[a]Department of Nutrition and Health, Federal University of Viçosa, Minas Gerais, Brazil; [b]Nutrition Support Team, Department of Dietetics, São Sebastião Hospital, Viçosa, Minas Gerais, Brazil

ABSTRACT

Objective: To assess whether the nutritional risk classified by StrongKids is associated with anemia and inflammation (total leukocytes and C-reactive protein (CRP)), as well as to compare the ability of StrongKids with anthropometry in identifying these changes in hospitalized pediatric patients.

Methods: Cross-sectional study with patients admitted to the pediatric ward of a public hospital in Brazil, from 2014 to 2018. The experimental protocol included: nutritional risk screening by StrongKids; weight and height measurements; and biochemical tests (complete blood count and C-reactive protein – CRP). Sensitivity, specificity, positive predictive value and negative predictive value were calculated to assess the ability of StrongKids and anthropometry to identify patients with the biochemical changes.

Results: The study included 482 patients (54.2% male), with a median age of 2.7 years. The frequency of nutritional risk (medium or high) was 85.9% and the prevalence of malnutrition (acute and/or chronic) was 20.2%. Overall, of the patients evaluated, 40.2% had anemia, 28.2% leukocytosis, and 78.0% high CRP. Children and adolescents classified as at nutritional risk (moderate/high) had lower levels of hemoglobin and higher levels of CRP and total leukocytes, as well as a higher frequency of leukocytosis, high CRP and the three alterations combined when compared with individuals at low risk. No association was found between anthropometric variables and biochemical alterations. The sensitivity of nutritional screening was high to detect all biochemical alterations and was superior to the anthropometric assessment.

Conclusion: StrongKids was associated with alterations in biochemical parameters with a better performance than anthropometry.

Abbreviations: BMI: Body Mass Index; BMI/A: Body Mass Index-for-age; CRP: C-reactive protein; Hb: hemoglobin; HFA: height-for-age; HR: high risk; IQR: interquartile range; LR: low risk; MR: moderate risk; NPV: negative predictive value; OR: odds ratio; PPV: positive predictive value; SENS: sensitivity; SPEC: specificity; StrongKids: Screening Tool for Risk on Nutritional Status and Growth; WFA: weight-for-age; WFH: weight-for-height; WHO: World Health Organization

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Malnutrition; pediatrics; nutritional screening; anemia; inflammation

Introduction

Hospital malnutrition in children and adolescents is still a frequent and underdiagnosed condition (1). Despite advances in health care, its occurrence has not reduced in the last 20 years (2). The consequences are severe and include a higher incidence of complications, longer hospitalization, increased hospital costs, and higher mortality (3–5). In Brazil, there are no national epidemiological data on the prevalence of hospital malnutrition in children and adolescents, but it is believed that the rates may be higher than 50% (6). Initiatives have been encouraged to improve this scenario, with emphasis on actions for screening, diagnosis, management and treatment (7).

Nutritional screening allows the identification of individuals who are malnourished or at nutritional risk and determines whether a detailed nutritional assessment is necessary (8,9). In adults and elderly, this practice is well established, with validated and internationally recommended methods for different clinical contexts (10–12). However, there is still no consensus on nutritional risk screening for pediatric patients, and the available tools are scarce and little used (13). In practice, the nutritional approach to hospitalized children is not standardized and is mainly based on the anthropometric measurements, which detect alterations already installed (14).

In this context, Hulst et al. (15) proposed the Screening Tool for Risk on Nutritional Status and Growth (StrongKids), which is considered the best method for pediatric nutritional risk screening in comparative studies among other tools (14, 16). It is the only method that has been translated and cross-culturally adapted to Portuguese (17), but little is known about how it interrelates with objective

CONTACT Carolina Araújo dos Santos carolaraujors@hotmail.com Ed Centro de Ciências Biológicas II, Campus Universitário, s/n°, Universidade Federal de Viçosa, CEP 36570.900, Viçosa, Minas Gerais, Brazil.

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indicators commonly used in pediatric nutritional assessment in Brazil (18).

Biochemical assessment is an important part of a complete nutritional assessment (19) and is useful for the diagnosis of deficiencies, detection of metabolic alterations, and identification of changes related to the underlying disease with nutritional impact (19,20). A systematic review of the scientific evidence related to the performance of StrongKids (18) showed that few studies have evaluated the association of this method with biochemical parameters and, to the best of our knowledge, no research has been carried out in Brazil for this purpose.

From the foregoing, the aim of this study was to verify if the StrongKids is associated with biochemical variables of nutritional interest, such as hemoglobin (Hb), total leukocytes, and C-reactive protein (CRP), as well as to compare the ability of both StrongKids and anthropometry in identifying alterations in these parameters.

Materials and methods

A cross-sectional study was conducted with children and adolescents admitted to the pediatric ward of a public hospital in Viçosa (Brazil), from August 2014 to June 2018. The inclusion criteria were: children from 1 month to 18 incomplete years old; hospital length of stay at least 24 hours (15); and biochemical tests (complete blood count and/or CRP) within one week of nutritional screening.

Sociodemographic data were gathered through a questionnaire applied to parents/caregivers before the nutritional screening. Information on the length of hospital stay, diagnosis at admission and biochemical data were obtained from medical records.

The Portuguese version of StrongKids (17) was applied to inpatients within 48 hours after hospital admission. According to the final score, the patients were classified as low risk (LR) = 0 point, moderate risk (MR) = 1–3 points, or high risk (HR) = 4–5 points.

The weight and height were measured and the following anthropometric indexes were established: weight-for-age (WFA), weight-for-height (WFH), height-for-age (HFA), and Body Mass Index (BMI)-for-age (BMI/A). According to World Health Organization (WHO) growth charts (21,22), the z-scores of the indices were calculated using WHO Anthro and WHO AnthroPlus softwares.

Standard deviation z-scores < -2 for WFH ($<$ 5 years old) or for BMI/A ($\geq$ 5 years old) were considered to indicate acute malnutrition. For chronic malnutrition, the criterion was HFA < -2 z-score (23). Overall malnutrition was defined as the presence of chronic and/or acute malnutrition (15, 24). Preterm infants (gestational age <37 completed weeks) had their age corrected up to 24 months (25) and patients with cerebral palsy or Down syndrome were excluded from the anthropometric analysis since the growth curves used do not apply to this group.

The diagnosis and classification of anemia (mild, moderate or severe) was based on WHO recommendations (26) (Supplementary material, Table 1). Identification of leukocytosis used the cuttof proposed by Bahia, Froede and Delgado (2013) (Supplementary material, Table 2) (27). Levels of C-reactive protein (CRP) higher than 5 mg/dL were considered elevated (28).

The distribution of the numerical data was verified by graphical analysis, asymmetry and kurtosis coefficients, and by the Shapiro-Wilk test. Comparison of biochemical parameters according to the categories of nutritional risk was performed by the Kruskal-Wallis test and complemented by the Dunn's multiple comparison test. The comparison according to the presence (MR or HR) or absence (LR) of risk was performed by the Mann-Whitney test. The association between the frequency of nutritional risk and biochemical alterations was assessed by Pearson's chi-square test or Fisher's exact test (LR *vs.* MR/HR) and by the chi-square test for trend (LR *vs.* MR *vs.* HR). Sensitivity (SENS), specificity (SPEC), positive predictive value (PPV), and negative predictive value (NPV) were also calculated to compare the ability of StrongKids and anthropometry to identify patients with biochemical alterations. The estimation of the odds ratio (OR) and its respective 95% confidence interval (95% CI) was used to verify the association between longer hospital stay and the presence of nutritional risk, malnutrition and biochemical alterations.

This study was approved by the Human Research Ethics Committee of the Federal University of Viçosa (n. 841.492/2014; CAAE: 20488013.9.0000.5153). All the parents or caregivers of the participated children signed the Informed Consent Form. The statistical analyses were performed using STATA for Windows (version 13.0), with a significance level of 5%.

Results

In the period when the data was gathered, 763 children were admitted to the pediatric ward. Of these, 641 (84.0%) were assessed by nutritionist and met the inclusion criteria for StrongKids utilization. In all of the screened patients, the complete application of the tool was possible. No parent/caregiver refused to participate in the study and in all patients StrongKids was fully applied. Of the total number of children who had nutritional screening, 482 (75.2%) met the inclusion criteria of this study (i.e. StrongKids and biochemical data) and were included in the final sample. Anthropometric assessment was possible in a sub-sample, since the growth curves did not apply to certain conditions, such as cerebral palsy or Down Syndrome, and in some cases was not possible to measure weight and height (Figure 1).

The median age was 2.7 years (IQR: 0.9–6.4 years). More than half of the children were male (54.2%) and most of them were under 5 years of age (69.5%) and resided in the urban area (74.3%). The median length of hospital stay was 5 days (IQR: 4–7), ranging from 1 to 48 days. The main diagnoses at hospital admission were respiratory diseases (32%), infectious and parasitic diseases (10.8%), digestive diseases (5.6%), genitourinary diseases (5.6%), and poisoning, injuries or other external causes (4.7%).

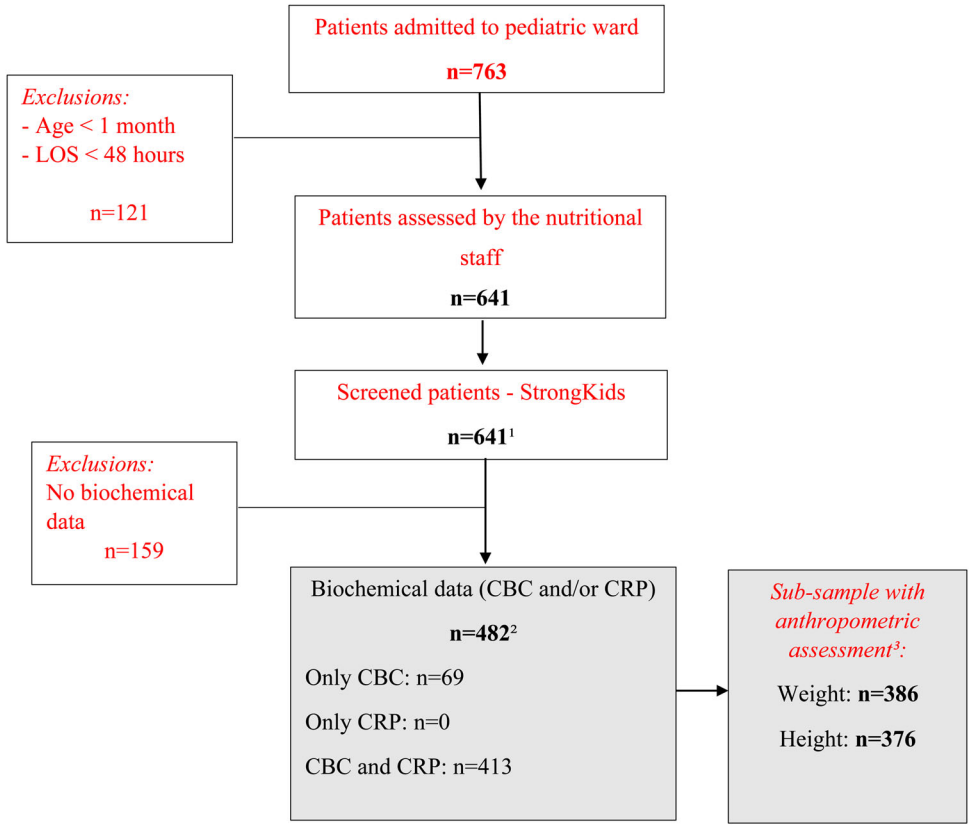

Figure 1. Study sample. [1]All patients assessed by the nutritional staff were screened by StrongKids. No data loss related to refusal to participate or incomplete data. [2]No significant differences in age, sex, StrongKids score, StrongKids nutritional risk category, or anthropometric indices compared with the patients with no biochemical tests ($p > 0.05$ for the *Mann-Whitney* Test or *Pearson's* Chi-square). [3]Exclusions: cerebral palsy or Down Syndrome ($n = 36$), impossibility of measuring weight ($n = 60$) and height ($n = 70$) for reasons such as inability to stand due to pain, fracture or risk of falling, need for absolute rest or use of continuous monitoring system. LOS: length of hospital stay; CBC: complete blood count; CRP: C-reactive protein.

StrongKids screening showed 85.9% of nutritional risk (moderate or high) and the prevalence of malnutrition (acute and/or chronic) according anthropometry was 20.2%. The most frequent biochemical alteration was elevated CRP (78.0%) (Table 1).

The biochemical parameters had significant differences according to the nutritional risk classification in all comparisons. Hemoglobin levels were higher in the non-risk group (LR), while total leukocytes and CRP were higher in at-risk patients (MR or HR). The comparison among the three risk categories (LR, MR and HR assessed separately) showed significant difference only for CRP, which was lower in the LR category than in the MR category (Figure 2).

A significant association was found between nutritional risk (LR *vs.* MR/HR) and the presence of leukocytosis, elevated CRP and these three combined alterations (Figure 3A). When assessing the three risk categories separately (LR *vs.* MR *vs.* HR), we identified an increasing linear trend in the frequency of anemia and the three combined alterations as nutritional risk increased (Figure 3B).

There was no association between malnutrition (acute, chronic, or general) and the biochemical alterations investigated ($p > 0.05$ in Pearson's chi-square test for all comparisons). The comparison between patients with and without anthropometry also showed no significant differences in the parameters of interest ($p > 0.05$ in Mann-Whitney test).

The sensitivity of StrongKids in detecting anemia, leukocytosis, and elevated CRP was high (88.7%, 91.2%, and 89.1%, respectively). StrongKids classified as at nutritional risk 98.1% of the individuals with the three combined alterations. The sensitivity of anthropometry was lower for all alterations (isolated or combined), although the specificities were higher than StrongKids screening (Table 2). In addition, the ability of StrongKids to identify patients with anemia increased as this condition was more severe: mild anemia (sensivity 82.2%), moderate anemia (sensivity 93.8%), severe anemia (sensivity 100%) (data not shown).

The association with a longer hospital stay (according to the sample median) was found for malnutrition (OR: 1.71; CI95%: 1.02–2.88), nutritional risk (OR: 2.031; CI95%: 1.21–3.41), anemia (OR: 1.68; CI95%: 1.15–2.45), and elevated CRP (OR: 1.84; CI95%: 1.15–2.93).

Discussion

This study identified the association between nutritional risk and lower Hb, higher inflammation markers, as well as higher frequency of leukocytosis, elevated CRP, and the three combined alterations. In addition, StrongKids showed much higher sensitivity than anthropometry in identifying

Table 1. Nutritional screening, nutritional assessment and biochemical data of the hospitalized pediatric patients.

	n	%
Nutritional Screening – StrongKids (n = 482)		
Items		
Presence of underlying illness with a risk of malnutrition or expected major surgery	226	46.9
Poor nutritional status judged by subjective clinical assessment	152	31.5
Excessive diarrhea (≥ 5 per day) and/or vomiting (>3 times/day) in the last few days	94	19.5
Reduced food intake during the last few days before admission	281	58.3
Pre-existing dietetically advised nutritional intervention	85	17.6
Inability to consume adequate intake because of pain	24	5.0
Weight loss or poor weight gain	122	25.3
Classification		
Low risk (0 points)	68	14.1
Medium risk (1–3 points)	308	63.9
High risk (4–5 points)	106	22.0
Nutritional assessment – Anthropometry		
Acute malnutrition[a] (n = 379)	33	8.7
Chronic malnutrition[b] (n = 376)	51	13.6
Overall malnutrition[c] (n = 386)	78	20.2
Biochemical data (n = 482)		
Anemia	194	40.2
Mild	90	18.7
Moderate	97	20.1
Severe	7	1.4
Leukocytosis (n = 482)	136	28.2
Elevated CRP (n = 413)	322	78.0

CRP: C-reactive protein.
[a]Weight-for-height < −2 standard deviation (< 5 years) or Body Mass Index-for-age < −2 standard deviation (≥ 5 years).
[b]Height-for-age < −2 standard deviation (all ages).
[c]Acute and/or chronic malnutrition.

biochemical alterations, which is a desirable feature for screening tools (29).

The frequency of nutritional risk (MR/HR) was high (85.9%), pointing to a worrying scenario, which is also shown by other studies in the country. In Brasilia, a study with 271 hospitalized children detected risk prevalence of 78.6% (30), similar to the frequency detected by studies in Porto Alegre, which ranged from 72.2% (31) to 75.4% (32). Lower but still worrying prevalence was found in Pelotas (71.3%) (33), Goiás (69%) (34), and Recife (58.3%) (35). These results draw attention to the magnitude of nutritional risk in pediatrics and confirm the need for systematic nutrition screening routines for this group.

The anthropometric assessment showed that about 1/5 of the participants had overall malnutrition (chronic and/or acute). Despite differences in sample size and diagnostic criteria, anthropometric deficits are common in hospitalized pediatric patients, with prevalence ranging from 19 to 58% in studies conducted in Brazil (36) and from 6.1% to 45.6% in Europe and the United States (13, 37,38).

We found that 40.2% of the children and adolescents admitted to the hospital had anemia, which is defined as a condition that results from a deficiency of one or more essential nutrients, regardless of the cause of such deficiency (26). Symptoms of decreased Hb content and the consequent impairment of oxygen transport to tissues include fatigue, poor appetite, generalized tiredness, reduced physical capacity, mental confusion, shortness of breath, and apathy (39). In addition to the consequences in childhood related to impaired cognitive and motor growth and development (40), anemia directly affects the immune response (41–43). It has also been associated with longer hospital stays, susceptibility to infections, greater mortality in hospitalized patients, and up to 50% increase in care costs (44–46). In our study, the median Hb was significantly higher in the LR group than in the MR/HR group (12.0 g/dl *vs.* 11.5 g/dl). A meta-analysis that involved more than 12,000 children (9 of the 10 selected studies were conducted in hospitals) showed that for each 1 g/dL increase in Hb, the risk of death is reduced by 24%. The authors suggest that approximately 1.8 million deaths in children aged 28 days to 5 years could be prevented each year by increasing 1 g/dL in Hb (47).

Studies evaluating the frequency of anemia in hospitalized children identified prevalence ranging from 54.8% (48) to 70.7% (49). In Brazil, most studies are regional and/or with convenience samples (50). The largest nationwide study ever conducted, which evaluated anemia in 3,499 community children under 5 years of age, identified a prevalence of 20.9% (51). There are no such national data for the Brazilian hospital environment.

It is of note that studies conducted in hospitals generally present higher frequencies of anemia than those carried out in the community, such as day care centers (10.2%–10.9%) (52,53), schools (13.4%–39.3%) (54,55), outpatient clinics (9.5%–36.7%) (56–58), and home visits (26%) (59). This difference can be explained by the impact of the underlying disease or occurrences during hospitalization. Infectious diseases, for example, can cause anemia through multiple mechanisms, including poor nutrient absorption and metabolism, ineffective erythropoiesis, and increased nutrient losses (39). The occurrence of blood loss, use of medication, and reduced food intake (approximately 60% of parents/caregivers reported this reduction), also contribute to a higher frequency of anemia in hospitalized children.

Total leukocyte count and elevated CRP were use as inflammation markers (60,61), although CRP shows better performance for this purpose (62,63). CRP is an acute phase protein synthesized in the liver in response to inflammation,

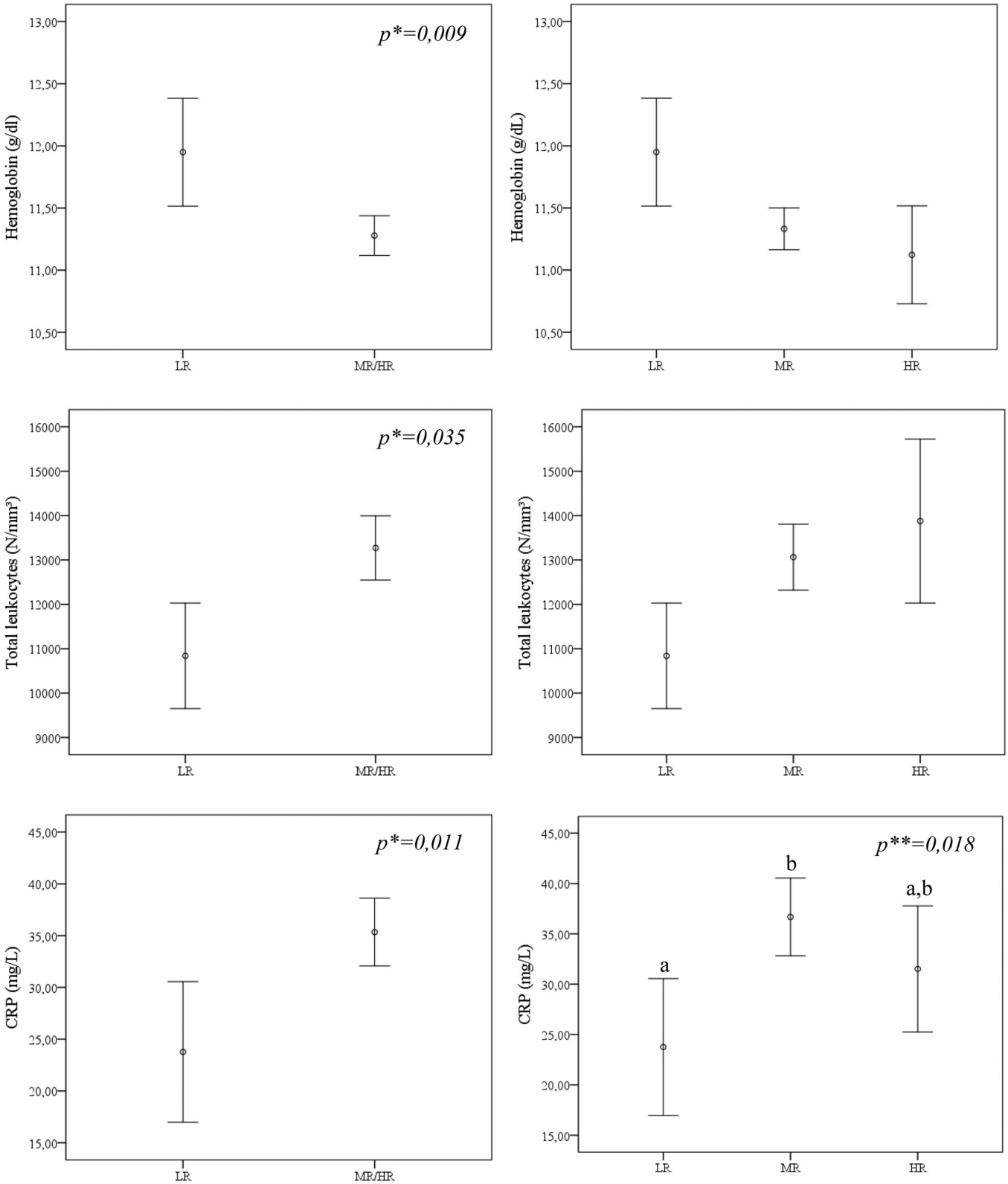

Figure 2. Biochemical parameters (means and 95% confidence intervals) according to nutritional risk categories. LR: low risk; MR: moderate risk; HR: high risk; CRP: C-reactive protein. *Mann-Whitney Test. ***Kruskal-Wallis, Dunn's* post hoc. Different letters indicate significant differences between groups.

infection, and tissue damage (64). Its greatest utility is in the assessment of inflammatory conditions, without, however, accurately identifying the etiology (65). CRP levels increase 4 to 6 hours after the inflammatory trigger (infectious or not), double every 8 hours, and peak after 36–48 hours. Levels will remain high as long as the inflammatory process is active and will rapidly decrease as inflammation decreases due to the short plasma half-life of about 4–7 hours. Since CRP plasma half-life is constant, the only determinant of its levels is the synthesis rate, which reflects the intensity of the inflammatory process (66,67).

The CRP concentration is not affected by anemia, protein levels, age or sex of the patient, nor is it altered in situations of immunosuppression, renal dysfunction, and corticosteroid use (67). Delgado et al. (2008) (68) found that hospitalized children and adolescents keep CRP synthesis preserved even with malnutrition. The authors note that although this process favors infection control, it can also have a significant impact on nutritional status during hospitalization.

Systemic inflammatory response causes metabolic dysregulation, which is characterized by muscular proteolysis (hypercatabolism), negative nitrogen balance that is proportional to lesion intensity (68), reduced protein synthesis (69), and increased resting energy expenditure (63). Behavioral changes that frequently accompany inflammation such as anorexia, drowsiness, and lethargy aggravate this problem (70). Inflammation is recognized as an important cause of malnutrition (71), and its presence is already incorporated in the guidelines for the diagnosis of malnutrition (61, 72).

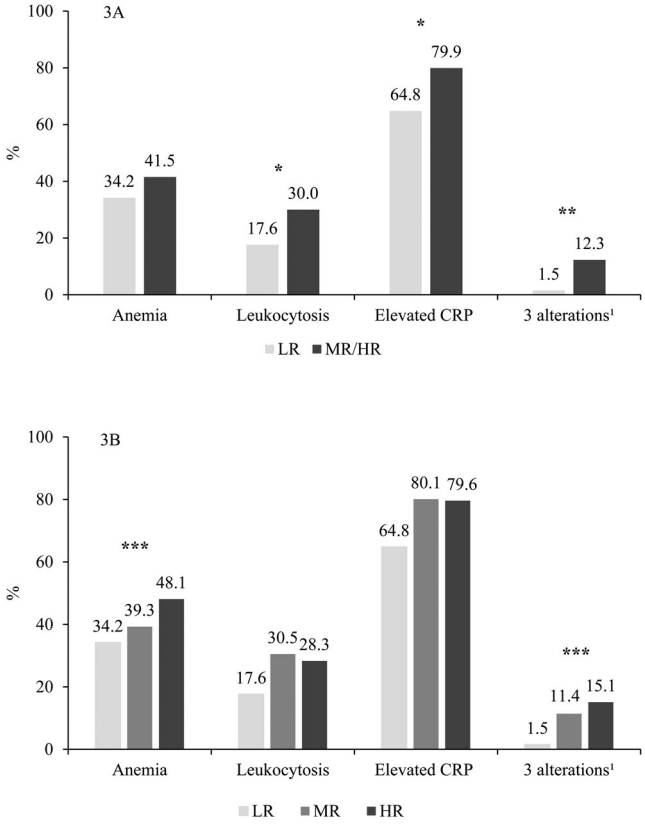

Figure 3. Frequency of biochemical alterations according to StrongKids classification into two (3A) and three categories (3B). *$p<0.05$ in Pearson's chi-square test; **$p < 0.05$ in Fisher exact test; ***$p < 0.05$ in Chi-square test for trend.

Our study identified 28.2% of the patients with leukocytosis. It is a condition of multiple etiologies (73) and, although the increase in total leukocytes occurs in pregnancy, intense physical exercise, stress, obesity, smoking, and other conditions, is a suggestive sign of infection, especially in pediatrics (74,75). The condition has been associated with higher mortality in hospitalized malnourished children (76) and higher risk of pneumonia (77). Leukocyte evaluation is also reported for the determination of etiological causes of malnutrition, as well as CRP (61).

A previous literature systematic review (18) has shown that few studies have been conducted to evaluate the relationship between StrongKids and biochemical parameters, all in China. Li et al. (2017) (78) evaluated 106 children with biliary atresia and found lower Hb contents in the HR group (10.6 g/dl) than in the MR group (11.6 g/dl). Lower albumin levels were also observed in the HR group, but without differences in the contents of bilirubin, creatinine, and blood urea nitrogen. In addition, children classified in the HR group had a higher risk of the inflammatory complication cholangitis. Song et. al (2017) (79) studied 2874 hospitalized children and adolescents with liver disease and identified lower levels of serum albumin and prealbumin in the MR group compared with HR). In this study, however, no difference in Hb was found (MR: 11.3 g/dl; HR: 11.2 g/dl). Cao et al. (2014) (2), in a study with 1325 patients from a pediatric hospital, found a higher frequency of infectious complications in the HR group, but without differences in the contents of Hb, CRP, albumin, and globulin. The authors point out that although these biochemical markers are important indicators of nutritional status, their levels may vary depending on the underlying disease. In our study, even with this possible influence, StrongKids was sensitive to detect the alterations investigated, especially when they were combined.

What our results point out is that even patients at risk (who may not be malnourished) also already have alterations in biochemical profile, and that the screening, in this sense, is even more sensible to identify patients with abnormalities that increase the probability of malnutrition. The results corroborate the StrongKids' value in this way, since it was able to be associated with variables of nutritional

Table 2. Predictive ability of StrongKids and anthropometry to identify biochemical alterations in hospitalized pediatric patients.

	Anemia				Leukocytosis				Elevated CRP				3 alterations[d]			
	SENS	SPEC	PPV	NPV	SENS	SPEC	PPV	NPV	SENS	SPEC	PPV	NPV	SENS	SPEC	PPV	NPV
StrongKids																
Nutritional risk (n = 414/482)	88.7	16.0	41.5	67.6	91.2	16.2	30.0	82.4	89.1	20.9	79.9	35.2	98.1	15.6	12.3	98.5
Anthropometry																
Acute malnutrition[a] (n = 33/379)	10.1	92.2	45.4	61.3	11.6	92.5	39.4	71.4	9.8	93.2	83.3	23.1	15.0	92.0	18.2	90.2
Chronic malnutrition[b] (n = 51/376)	14.2	86.8	39.2	62.8	11.9	85.8	25.5	70.5	12.8	82.9	71.1	22.4	7.9	85.8	5.9	89.2
Overall malnutrition[c] (n = 78/386)	21.3	80.5	41.0	61.7	22.1	80.6	32.1	71.4	20.6	79.2	76.8	23.0	22.5	80.1	11.5	89.9

SENS: sensitivity; SPEC: specificity; PPV: positive predictive value; NPV: negative predictive value; CRP: C-reactive protein.
[a]Weight-for-height < -2 standard deviation (< 5 years) or Body Mass Index-for-age < -2 standard deviation (≥ 5 years).
[b]Height-for-age < -2 standard deviation (all ages).
[c]Acute and/or chronic malnutrition.
[d]Anemia, leukocytosis and elevated CRP.

interest (biochemical data) that are not directly measured by the tool. The relationship between malnutrition and inflammation has already been demonstrated in the literature (although no significant association with anthropometry was found in this study), but evidence related to a screening method for nutritional risk (which precedes malnutrition) is highly relevant—especially in children.

Our study has several limitations. Firstly, this is a single-centre experience and may not be representative of the whole Brazilian pediatric population. Secondly, it was not possible obtain biochemical and anthropometric data to all the eligible patients for nutritional screening, which reflects a reality in clinical practice. However, the comparison between the groups with and without these data showed that they are comparable, not differing in relevant characteristics. Thirdly, the cause of anemia (malnutrition, inflammation, blood loss or some diseases) cannot be determined, since data on ferritin levels and components of the complete blood count were not available. Lastly, since it is a cross-sectional study, no causality could be inferred from nutritional risk, biochemical abnormalities and malnutrition.

The main strength of this study is that it provides new information on the relationship between a pediatric screening tool and relevant biochemical abnormalities. To the best of our knowledge, this is the first study to demonstrate these aspects in a Brazilian population, corroborating the tool's usefulness in this county. As study strengths, we also highlight the large number of participants and the representativeness of the sample (75.2% of the patients eligible for nutritional screening were included). We also highlight that in 100% of the patients screened by StrongKids it was possible to fully apply the tool. There was no difficulty in understanding the questions or unanswered items by the parents/caregivers. This indicates the applicability and feasibility of the StrongKids in clinical practice.

Conclusion

The nutritional risk assessed by StrongKids was related to biochemical alterations (inflammation and anemia), with higher sensitivity to identify abnormalities compared to anthropometry. CRP was the most frequently alteration related to changes in risk category. These results contribute to the tool's usefulness and corroborate its relationship with variables of nutritional relevance. In addition, the high prevalence of nutritional risk identified alerts of the importance of including nutrition screening in pediatric hospital care.

Disclosure statement

No potential conflict of interest.

ORCID

Carolina Araújo dos Santos http://orcid.org/0000-0001-5947-8744
Carla de Oliveira Barbosa Rosa http://orcid.org/0000-0003-1463-3055
Sylvia do Carmo Castro Franceschini http://orcid.org/0000-0001-7934-4858
Heloísa Helena Firmino http://orcid.org/0000-0001-7165-275X
Andréia Queiroz Ribeiro http://orcid.org/0000-0001-6546-1252

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