Original Article

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Evaluation of Eating Behaviors in Breath-holding Spells in Pediatrics: A Case-control Study

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Abstract

Aim: Breath-holding spells (BHS) are associated with various etiologies, including potential behavioral disorders. While factors like iron deficiency have been studied, the role of other micronutrients and specific eating behaviors remains under-investigated. Therefore, this study aimed to investigate vitamin deficiencies (folate and B12) and evaluate the eating behaviors of children with BHS.

Methods: This prospective, single-center, case-control study was conducted between June and September 2024. The study included 35 patients with BHS and 35 age- and sex-matched healthy controls. Blood and vitamin levels were compared, and the Children's Eating Behaviour Questionnaire (CEBQ) was administered to assess and compare eating patterns between the groups.

Results: Logistic regression analysis was performed to identify significant predictors for being in the patient group. Each unit increase in folate was associated with a 33% reduction in odds ratio (OR=0.67, p<0.001), and each unit increase in hemoglobin was associated with a 69% reduction in OR (OR=0.31, p=0.007). Regarding eating behaviors, only the "slow eating" subscale was a significant predictor; each point increase on this scale decreased the odds of being a patient by 13% (OR=0.87, p=0.025), indicating that faster eating is a risk factor. Ferritin, vitamin B12, and other CEBQ subscales, including "emotional overeating" and "enjoyment of food", were not significant predictors in the final model.

Conclusion: This study identifies folate deficiency and anemia as significant risk factors for BHS. This study is the first to report that children with BHS exhibit specific eating behaviors, such as rapid eating. These findings suggest that the clinical management of children with BHS should include screening for folate deficiency and providing guidance on observed eating behaviors.

Keywords: Breath-holding spells, feeding behavior, anemia, folic acid deficiency, infant

Introduction

Breath-holding spells (BHS) are common, generally benign paroxysmal events in early childhood that are often distressing to caregivers. The onset usually happens before the child is 18 months old, and up to 33% of cases have a family history of the condition (1). The pathophysiology is primarily linked to a dysregulation of the autonomic nervous system, with cyanotic spells precipitated by emotional triggers and pallid spells caused by vagally mediated cardiac inhibition (1-3). Supporting this neurophysiological basis, one study found significantly prolonged interpeak latencies in brainstem auditory evoked potentials among children with BHS, suggesting that delayed myelination of the brainstem may be a contributing factor (4,5).

Beyond autonomic dysfunction, both nutritional and psychosocial factors have been implicated in BHS. The link between iron deficiency and increased irritability is well-

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established, and specific temperamental traits like low frustration tolerance have also been identified in these children (6,7). However, the roles of other micronutrients and specific eating behaviors, which could be linked to both temperament and nutritional status, remain under-investigated. We hypothesized that children with BHS would exhibit distinct eating behaviors (such as emotional or rapid eating) and have lower levels of specific micronutrients, particularly folate, compared to healthy controls.

While the roles of iron deficiency and temperament have been explored, the potential contribution of other micronutrient deficiencies and specific eating behaviors to BHS remains under-investigated. We hypothesized that children with BHS would exhibit distinct eating behaviors and have lower levels of key hematological parameters, particularly folate, compared to healthy controls. Therefore, the aim of this study was to test this hypothesis by evaluating eating behaviors and investigating the association between BHS and serum levels of folic acid and other hematological parameters. By identifying these nutritional and behavioral patterns, this study could contribute to a more comprehensive clinical assessment and provide a basis for targeted therapeutic approaches.

Materials and Methods

Compliance with Ethical Standards

This study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Gaziosmanpasa Training and Research Hospital (approval no.: 20, date: 05.06.2024). Written informed consent was obtained from the parents or legal guardians of all participating children prior to their inclusion in the study.

Study Design and Participants

This prospective, single-center, case-control study was conducted at the Gaziosmanpasa Training and Research Hospital in Istanbul, Türkiye, between June 2024 and September 2024. The study included a patient group and a control group, with participants aged between 2 and 6 years.

The patient group consisted of 35 children with a diagnosis of BHS, recruited from the pediatric neurology outpatient clinic. Inclusion criteria were an established diagnosis of BHS confirmed by clinical evaluation and review of family-recorded videos. Exclusion criteria included the presence of epilepsy, cardiac rhythm disorders, or other chronic neuropsychiatric conditions (e.g., autism spectrum disorder), as well as regular medication use. All patients had normal cranial magnetic resonance imaging, sleep electroencephalogram (EEG), and electrocardiogram (ECG) findings. The Denver Developmental Screening Test was administered to all participants to ensure age-appropriate development.

The control group consisted of 35 healthy children matched for age, sex, and socio-economic status, recruited from the general pediatrics clinic. These children had no known acute or chronic diseases and were not on regular medication. For the control group, blood test results were obtained from the hospital's information system for age- and sex-matched healthy children who underwent routine blood tests during the same study period. The participant selection process is summarized in a flow diagram (Figure 1).

Procedures and Data Collection

For all participants, data on age, gender, height, weight, breastfeeding history, and number of siblings were collected. Body mass index (BMI) was calculated, and all participants were confirmed to be within the 5^{th} and 95^{th} percentiles for their age.

Eating behaviors were assessed using the Turkish validated version of the Children's Eating Behaviour Questionnaire (CEBQ), a 35-item parent-report tool that scores eight subscales of eating behavior (8,9).

Step 1. Total Number of Patients Screened: Potentially eligible patients followed in the Pediatric Neurology Clinic (n=42)
Step 2: Exclusion: Excluded Patients (n=7) **Refused to participate in the study (n=5)** **Incomplete test results (n=2) (EEG, MRI, ECG, Blood Results)**
Step 3: Case Group - Number of Patients with Breath-Holding Seizures Included in the Analysis as the Final Case Group (n=35)
Step 4: Control Group **Number of Healthy Children Matched by Age, Gender, and Socioeconomic Status Who Met the Inclusion Criteria and Included in the Analysis as the Control Group (n=35)**

Figure 1. Study flow diagram

The questionnaire is used in various patient groups and healthy populations and is an internationally validated tool (10-12).

For the patient group, blood samples were collected to measure serum levels of ferritin, vitamin B12, folate, and hemoglobin (Hb).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0. Descriptive statistics were presented as mean ± standard deviation for normally distributed variables and frequency (percentage) for categorical variables. Group comparisons were conducted using the independent samples t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Categorical variables were compared using the chi-squared test. Correlations were assessed using Pearson or Spearman's rho tests where appropriate. A p-value of <0.05 was considered statistically significant.

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0. The normality of the distribution for continuous variables was assessed using the Kolmogorov-Smirnov test. Descriptive statistics were presented as mean ± standard deviation for normally distributed variables and as median (interquartile range) for non-normally distributed variables, while categorical variables were presented as frequency (percentage). For group comparisons, the independent samples t-test was used for normally distributed data, and the Mann-Whitney U test was used for non-normally distributed data. Categorical variables were compared using the chi-squared test. Correlations were assessed using Pearson or Spearman's rho tests where appropriate. A p-value of <0.05 was considered statistically significant.

Post-hoc power analysis was performed using the G*Power 3.1.9.7 program for an achievable sample size. In the post-hoc power analysis, the effect size was associated with power $(1-\beta)=0.895$ and power $(1-\beta)=0.882$ for the independent sample t-test when the significance criterion was $d=0.7$ and $\alpha=0.05$, with the number of samples for the first group being 35, and the number of samples for the second group being 35. The statistical power $(1-\beta)$ was found to be 0.917 for the chi-squared test, with an effect size of $d=0.4$, a significance level of $\alpha=0.05$, and a total sample number of 70. For the correlation analysis, the effect size was calculated as power $(1-\beta)=0.967$, when the significance criterion was $\alpha=0.05$ and the number of samples was 70.

Results

Sample Characteristics

The study included a total of 70 children, comprising 35 patients with BHS and 35 healthy controls. The two groups were well-matched, showing no statistically significant differences in gender, age, BMI, number of siblings, or history of breastfeeding (Tables 1, 2).

Comparison of Blood Parameters

The comparison of blood parameters revealed key differences between the groups (Table 3). Folate and Hb values were significantly lower in the patient group (p<0.001 for both). No significant differences were found for ferritin, vitamin B12, or other hematological parameters.

Although the mean folate level in the patient group was statistically lower, the rate of clinical folate deficiency (defined as a serum level <5.3 ng/mL) was found in 22.8% of patients (n=35) compared to 11.42% of controls (n=35).

Comparison of Eating Behaviors (CEBQ)

While the total CEBQ score did not differ between the groups, analysis of the subscales revealed significant behavioral differences (Table 4). The patient group scored

Table 1. Demographic findings

Total number (n, %)	**70 (100%)**
Female	40 (57.1%)
Male	30 (42.9%)
Groups (n, %)	**70 (100%)**
Patient	35 (50%)
Control	35 (50%)
Patient group (n, %)	**35 (100%)**
Female	20 (57.1%)
Male	15 (42.9%)
Control group (n, %)	**35 (100%)**
Female	20 (57.1%)
Male	15 (42.9%)
Age (year) (mean ± SD)	**3.31±1.22**
Patient	3.1±1.42
Control	3.52±0.95
Body mass index (kg/m²) (mean ± SD)	**19.51±4.15**
Patient	18.83±4.22
Control	20.2±4.02
Number of siblings (mean ± SD)	**1.47±1.2**
Patient	1.57±1.38
Control	1.37±1
History of breastfeeding (month) (mean ± SD)	**15.84±9.75**
Patient	13.9±9.29
Control	17.77±9.95
Type of breath-holding spells for the patient group (n, %)	**35 (100%)**
Cyanotic	16 (%45.7)
Pallid	19 (%54.3)

SD: Standard deviation

significantly higher on "emotional overeating" ($p=0.021$) and "enjoyment of food" ($p=0.002$). Conversely, the patient group scored significantly lower on the "slow eating" subscale ($p=0.03$), indicating a tendency to eat faster.

Predictors of Breath-Holding Spells: A Logistic Regression Analysis

In order to predict whether individuals were in the patient or control group, binary logistic regression analysis was performed using six different blood values (ferritin, B12, folic acid, Hb, white blood cells, and platelets). The logistic regression model was found to be statistically significant, χ^2 (6, n=70, n=42.24, $p<0.001$). The model explained 60% of the variance in health status (Nagelkerke R2) and correctly classified 77.1% of the cases. As a result of the analysis, the coefficients of folic acid and Hb levels were significant ($p<0.05$). When other variables were held constant, it was found that each unit increase in folic acid levels (e.g., 1 ng/mL) reduced the odds of being in the disease group by 33% [(OR=0.67, 95% confidence interval (CI): (0.54, 0.84), $p<0.001$)]. In other words, individuals with low folic acid levels were more likely to be ill. Similarly, each unit increase in Hb levels (e.g., 1 g/dL) reduced the odds of being in the disease group by 69% [OR=0.31, 95% CI: (0.14, 0.73), $p=0.007$]. The coefficients for other blood values (ferritin, B12, white blood cells, and platelets) were not statistically significant.

In the binary logistic regression analysis applied to predict whether individuals were in the control or patient group according to the scores obtained from the nutrition questionnaire, only the coefficient of the "slow eating" subscale was found to be significant; $p<0.05$. Each unit (e.g., 1 point) increase recorded in the "slow eating" score decreased the probability of being in the patient group by 13% [OR=0.87, 95% CI: (0.77, 0.98), $p<0.025$]. This result revealed that individuals who tend to eat faster were more likely to be part of the patient group. The coefficients of the total score obtained from the nutrition questionnaire and the other seven subscales (food craving, emotional overeating, food aversion, drinking craving, satiety craving, emotional undereating, and food pickiness) were not significant in the binary logistic regression model; $p>0.05$.

Discussion

In this study, we tested the hypothesis that children with BHS would exhibit distinct hematological and behavioral profiles compared to healthy controls. Our findings provide significant support for this hypothesis on two main fronts. First, supporting the hematological component, we found that children with BHS had significantly lower levels of Hb and folate. Second, supporting the behavioral component, we identified for the first time that children with BHS display specific eating patterns, namely a tendency for higher emotional overeating, greater enjoyment of food,

Table 2. Comparison of the patient group and the control group in terms of BMI, age, number of siblings and history of breastfeeding

	Patient group	Control group	
	[mean ± SD (median)]	**[mean ± SD (median)]**	**p**
Age	3.10±1.42 (2.87)	3.52±0.95 (3.79)	[a]p=0.156
Body mass index (kg/m2)	18.83±4.22 (18.12)	20.20±4.02 (19.83)	[a]p=0.169
Number of siblings	1.57±1.38 (1)	1.37±1 (1)	[b]p=0.774
Type of breath-holding spells for the patient group (month)	13.9±9.29 (17)	17.77±9.95 (24)	[b]p=0.075

Data are presented as mean ± standard deviation (median). Group comparisons were performed using the [a]Independent Samples t-test or the [b]Mann-Whitney U test SD: Standard deviation

Table 3. Comparison of blood values between the patient group and the control group

	Patient group	Control group	
	[mean ± SD (median)]	**[mean ± SD (median)]**	**p**
Ferritin (ng/ml)	53.25±142.7 (23.6)	30.55±29.72 (20.3)	[a]p=0.953
Vitamin B12 (pg/mL)	473.51±317.21 (398)	418.91±121.09 (388)	[a]p=0.972
Folic acid (ng/mL)	10.11±5.71 (8)	16.1±2.64 (15.6)	[a]p=0.000
Hemoglobin (g/dL)	11.39±1.32 (11.5)	12.32±0.7 (12.3)	[a]p=0.000
White blood cell count (/µL)	9968.29±2390.97 (10000)	8965.43±2622.35 (8780)	[b]p=0.099
Platelet count (/µL)	340942.86±105688.76 (357000)	316542.86±86290.67 (315000)	[a]p=0.106

Data are presented as mean ± standard deviation (median). Group comparisons were performed using the [a]Mann-Whitney U test or the [b]Independent samples t-test SD: Standard deviation and faster eating. These parallel findings suggest a more complex interplay between nutritional status and behavior in the etiology of BHS.

This study should be considered a preliminary investigation into the complex relationship between BHS and hematological status. While the literature has predominantly focused on iron deficiency as a trigger for BHS, our results suggest that anemia itself, potentially influenced by the observed low folate levels, rather than iron store depletion (as indicated by normal ferritin levels), may be a key factor (13-15). This aligns with recent research demonstrating a relationship between folate/B12 deficiencies and spells and suggests that the clinical approach to anemic children with BHS should include a comprehensive assessment of all vitamins implicated in hematopoiesis, not just iron (16).

The most novel contribution of our study is the identification of specific eating behaviors in children with BHS. While initial group comparisons showed that children with BHS had higher scores for "emotional overeating" and "enjoyment of food", our logistic regression model identified that only the "slow eating" subscale was a significant independent predictor of group membership (OR=0.87, p=0.025). The odds ratio of less than one indicates that lower scores on this scale—reflecting a tendency for faster eating—were significantly associated with being in the patient group. This suggests that while emotional and hedonic aspects of eating may differ between the groups, the most robust and defining behavioral characteristic of children with BHS in our study is a tendency to eat more quickly. This finding of faster eating may be consistent with the known temperamental traits of children with BHS, such as higher impulsivity or lower frustration tolerance (7).

Table 4. Comparison of nutrition questionnaire scores between the patient group and the control group

	Patient group	Control group	
	[mean ± SD (median)]	**[mean ± SD (median)]**	**p**
Total score	92.34±16.72 (94)	86.63±11.33;(86)	[a]p=0.099
Subscale scores			
Food enthusiast	11±5.88 (9)	8.14±3.58 (7)	[b]p=0.078
Emotional overeating	6.69±2.19 (6)	5.69±2.29 (5)	[b]p=0.021
Enjoyment of food	16.69±5.73 (16)	12.57±4.6 (11)	[b]p=0.002
Drink enthusiast	8.29±3.49 (8)	7.37±2.4 (7)	[b]p=0.428
Satiety enthusiast	20.43±5.76 (19)	22.09±5.89 (22)	[a]p=0.238
Slow eating	10.06±3.66 (10)	12.46±4.72 (12)	[b]p=0.03
Emotional undereating	11.2±3.63 (11)	11.4±3.34 (11)	[b]p=0.559
Food selectivity	8±3.4 (8)	6.91±2.54 (7)	[a]p=0.134

Data are presented as mean ± standard deviation (median). Group comparisons were performed using the [a]Independent samples t-test or the [b]Mann-Whitney U test
SD: Standard deviation

These two primary findings—hematological and behavioral—may be interconnected. It is plausible that micronutrient deficiencies, such as folate deficiency observed in our patient group, could exacerbate disordered eating behaviors or the underlying temperamental traits. Conversely, specific eating patterns could contribute to inadequate micronutrient intake, creating a cyclical relationship that warrants further investigation. This study represents a pioneering effort to examine this intersection between feeding behaviors and BHS.

While our study focuses on factors present in early childhood, the long-term implications of these findings warrant consideration. A recent follow-up study by Polskaya and Aleksenko (17) examined the later outcomes of children with BHS, and future research could explore whether the nutritional and behavioral patterns we identified persist or resolve over time.

Study Limitations

Our study has several limitations that should be acknowledged. The primary limitation is the method of obtaining blood results for the control group, which was selected from the hospital's information system rather than being prospectively collected in the same manner as the patient group. This method introduces a potential for selection bias. Additionally, the single-center design and the relatively small sample size, although shown to be sufficient by power analysis, may limit the generalizability of our findings. A limitation, as noted by the reviewer, is that while the mean folate and Hb levels were statistically lower in the patient group, the mean values for both groups were within the normal clinical range. This issue raises important questions about the clinical significance of this statistical difference. However, the presence of a higher rate of folate deficiency in the patient group suggests that even subclinical variations may play a role. Our study was not designed to assess changes in eating behaviors after nutritional supplementation, and the reliance on a parental questionnaire carries an inherent risk of response bias. Another limitation of our study is the reliance on a single questionnaire to assess the complex nature of eating behaviors. Future studies could incorporate qualitative methods, such as clinical interviews or direct observation of feeding, to provide a richer understanding. Therefore, our findings on eating behaviors should be considered preliminary.

Despite these limitations, the study possesses significant strengths. Its prospective case-control design is a key strength. A key strength of our study is the rigorous diagnostic process used to ensure the integrity of our BHS cohort, which included EEG and ECG to exclude cardiac or epileptic etiologies. While a recent study by Hellström Schmidt et al. (18) has highlighted the potential for overuse of these tests in typical BHS cases, their application in our research context was crucial for diagnostic certainty and strengthening the validity of our findings. The use of the Denver Developmental Tests also ensured that developmental delays were not a confounding factor, thereby increasing the internal validity of our findings.

Conclusion

This study provides new insights into the pathophysiology of BHS by identifying two key findings. First, children with BHS have significantly lower Hb and folate levels compared to healthy controls. Furthermore, our findings suggest that impaired folate status may be a risk factor, a hypothesis that requires confirmation in larger studies. Second, this is the first study to demonstrate that children with BHS exhibit specific eating behaviors, namely, a tendency to eat rapidly, which may be linked to their underlying temperamental traits.

These findings carry notable clinical implications. Establishing standardized management approaches may benefit from incorporating routine screening for anemia and folate deficiency in children with BHS. In addition, providing families with guidance on managing the observed eating-related behavioral patterns may constitute an important component of a comprehensive therapeutic strategy.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University of Health Sciences Türkiye, Gaziosmanpasa Training and Research Hospital (approval no.: 20, date: 05.06.2024).

Informed Consent: Written informed consent was obtained from the parents or legal guardians of all participating children prior to their inclusion in the study.

Footnotes

Authorship Contributions

Design: O.C., S.I., E.E.I. Data Collection or Processing: O.C., E.E.I., Analysis or Interpretation: O.C., U.T., Literature Search: O.C., S.I., Writing: O.C., U.T.

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