ORIGINAL ARTICLE

Iron Deficiency and Breath Holding Spells in Children - A Descriptive Cross Sectional Study at Children Hospital Faisalabad

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ABSTRACT

Objective: To determine the frequency of iron deficiency in children presenting with breath-holding spells.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: OPD of Pediatric Medicine unit of Children Hospital & Institute of Child Health, Faisalabad. Six months, from: 1st January 2024 to 30th June 2024.

Material and Methods: Ninty six patients from age 6 months to 5 years of of either gender with breath holding spells were included in the study. Patients with epilepsy, cardiac diseases, lung pathology, metabolic disorders and patients on anticonvulsants and antidepressant were excluded. Venous blood samples were taken for iron deficiency anemia. Data was analyzed through SPSS version 20.0. Descriptive statistics were applied to calculate the mean and standard deviation for numerical data and frequencies and percentages for categorical data.

Results: Out of 96 patients, 59.4% of patients were aged 6-36 months and 40.6% aged 37-60 months (mean age 32.52 months ±SD of 16.15 months). Males comprised 63.5%, and females 36.5%. The mean weight is 13.29 kg. Mean spell duration was 37.80 seconds ±SD of 13.72 seconds. Mean hemoglibin was 8.6 ±SD 1.9. Mean ferritin level was 14.42 µg/dL ±SD of 6.55 µg/dL, and mean iron level was 54.11 µg/dL ±SD of 18.95 µg/dL. Fifty-one percent (n=96) of patients had iron deficiency.

Conclusion: There was a significant prevelance of iron deficiency and breath-holding spells, highlighting the need for routine screening and iron supplementation to reduce the frequency and severity of these spells.

Key Words: *Breath-holding spells, Children, Ferritin levels, Iron deficiency*.

INTRODUCTION

The breath-holding spell is described as a nonepileptic benign event that is paroxysmal with loss of consciousness. Infants and children between 6 months to 60 months of age are the most common age group involved. Onset usually occurs between 6 to 18 months of age.[1] It nearly

affects 0.1% to 4.6% of the pediatric population worldwide. Children with breath-holding spells have positive family history in about 30% of cases. Breath-holding spells trigger by crying and pain that lead the child to in the apneic state with or without tonic posturing for less than 1 minute. Upon change of color of body breath-holding spells have three types first is cyanotic type, second is pallid, and third mixed variety.[2]

WHO states that most common micronutrient deficiency is iron and primarily children under 5 years are the main sufferers. In Pakistan more than half of children under the age of 5 are anemic. About 45% of children in the world and about 30% in Pakistan suffering from iron deficiency and in developing countries it is the major cause of iron deficiency anemia.[3] Breath holding spells etiology is unclear but it is likely due to multiple factors which include autonomic dysregulation, iron deficiency, over-vagal stimulation, and delayed demyelination of brain tissue. Some antioxidant agents such as selenium or glutathione deficiency have an association with breath-holding spells. Most of the cyanotic type of breath-holding spells have an association with autonomic dysregulation and pallid type with over-vagal stimulation.[4] The most common micronutrient deficiency between the age group of 6 to 24 months is iron deficiency and this age also correlates with the onset of breath-holding spells. Iron being a cofactor for various enzymes and neurotransmitters and myelin formation in the central nervous system has an important role in autonomic dysregulation. Iron deficiency decreases oxygen carrying capacity and hence aggravate breath-holding spells. Children with iron deficiency have irritable behavior and this also precipitates the breath-holding spells.[5]

In the world multiple studies were done in which patients with breath-holding spells have iron deficiency and clinical trial of iron supplementation therapy have resulted in a decrease in the frequency of spells in both pallid and cyanotic types. Shamaoon et al found in their study a strong association of iron deficiency with breath holding spells. According to their study, children with iron deficiency anemia having breath holding spells were 51.58%. Their study concluded that Iron deficiency anemia is higher in breath holding children and cheap iron preparation is the easily available and the most effective treatment for these children.[6]

As no study has been conducted in Children Hospital Faisalabad with breath holding spells and iron deficiency. This study will find the frequency of iron deficiency in children with breath holding spells. It will also help to treat these children effectively with readily available and cheap iron supplement. There will be reduction in parent anxiety and number of unnecessary investigations will also decrease. There will also be a decrease in number of hospital visits leading to decrease burden of hospital resources and less morbidity.

The objective of this study is to find association between iron deficiency anemia and breath holding spells in children.

MATERIAL AND METHODS

Study was conducted at OPD of Pediatric Medicine Department of Children Hospital & Institute of Child Health, Faisalabad from 1st January 2024 to 30th June 2024. It was descriptive cross sectional study. Ninty six patients were included in the study by non-probability consecutive sampling technique.

Inclusion Criteria:

- Age group: 6 months to 5 years and of either gender
- Patient having breath-holding spells as per operational definition

Exclusion Criteria:

Following patients were excluded based on history and medical records.

- Patients with epilepsy or other central nervous system pathology
- Patients with congenital heart diseases
- Patients with any lung pathology
- Patients with metabolic disorder
- Patients taking anticonvulsant or antidepressant drugs

Operational definitions

Iron deficiency: It is serum iron level less than 50 microgram/dl and serum ferritin level less than 12 microgram/L in children 6 months to 5 years of age.[10]

Breath holding spell: It is an episode in which a child involuntarily stops breathing during expiration after a deep inspiration while crying for less than 1 min. with or without bluish discoloration of the skin.

Data collection procedure: After approval from the Institutional Ethical Review Committee (IRB no. 25 dated 04/04/2023), study was started. Informed written consent was obtained from each participant's parents, who were briefed about the objectives of the study, ensuring confidentiality of the information. After obtaining history, a venous blood sample (3cc) was collected in a serum vial by trained staff and sent for analysis to the hospital laboratory. Serum iron was measured by spectrophotometry using Beckman Coulter (DXC 700AU). Serum ferritin was measured by spectrophotometry/Elisa (Elisys Uno, Human). Iron deficiency was diagnosed by serum iron level of less than 50 micrograms/dL and a serum ferritin level of less than 12 micrograms/L. Patients age, gender, weight and duration of spells were entered into a pre-designed proforma.

Data analysis: Data was entered into and analyzed through SPSS version 20.0. Descriptive statistics were applied to calculate the mean and standard deviation of age, weight, duration of spells, serum iron, and ferritin levels. Frequencies and percentages were calculated for gender and iron deficiency. Effect modifiers such as age, gender, weight, and duration of spells were controlled by stratification. A post-stratification Chi-square test was applied to determine their effect on iron deficiency. A p-value of ≤0.05 was considered significant.

RESULTS

The age distribution of the 96 patients was categorized into two groups: aged 6 to 36 months and 37 to 60 months. There were 57 patients (59.4%) in the 6-36 months group and 39 patients (40.6%) in the 37-60 months group. The mean age of the patients was 32.52 ±16.15 months (**table 1**). The gender distribution of the patients showed that out of the 96 children, 61 (63.5%) were male, and 35 (36.5%) were female (**table 1**).

The duration of spell was also categorized into two groups: those lasting up to 30 seconds and those lasting more than 30 seconds. There were 27 patients (28.1%) whose spells lasted up to 30 seconds and 69 patients (71.9%) whose spells lasted more than 30 seconds. The mean duration of the spells was 37.80 ±13.72 seconds (**table 1**).

TABLE 1: Demographic Data.

Variable		Number of patients	Percentage
Age (in months)	(6-36)	57	59.4
	(37-60)	39	40.6
	Total	**96**	**100**
	Mean±SD	**32.52±16.15**	
Gender	Male	61	63.5
	Female	35	36.5
	Total	**96**	**100**
Weight (kg)	Upto 10kgs	27	28.1
	>10kgs	69	71.9
	Total	**96**	**100**
	Mean±SD	**13.29±3.94**	
Duration of spells (in seconds)	Upto 30	27	28.1
	>30	69	71.9
	Total	**96**	**100**
	Mean±SD	**37.80±13.72**	

The mean ferritin level was 14.42 µg/dL ±6.55 µg/dL **(table 2).**

TABLE 2: Mean hemoglobin, ferritin, iron & iron deficiency data.

Paramete rs		Mean	SD
Mean hemoglobin		**8.6**	**1.9**
Ferritin levels (µg/dL)		14.42	6.55
Iron levels (µg/dL)		54.11	18.95
Iron deficiency	Yes	49	51
	No	47	49
	Total	**96**	**100**

The mean iron level was 54.11 µg/dL ±18.95 µg/dL. The frequency of iron deficiency in the study population showed that 49 patients (51%) were diagnosed with iron deficiency, while 47 patients (49%) were not.

Among the 57 patients aged 6-36 months, 28 (49.1%) had iron deficiency, while 29 (50.9%) had no deficiency. In the 37-60 months age group, 21 out of 39 patients (53.8%) had iron deficiency and 18 (46.2%) had no deficiency. The p-value for the difference between the age groups was 0.649.

Table 3 presents the iron deficiency distribution among male and female patients. Out of 61 male patients, 30 (49.2%) had iron deficiency, while 31

(50.8%) had no deficiency. Among 35 female patients, 19 (54.3%) had iron deficiency, and 16 (45.7%) had not. The p-value for the difference between genders was 0.630.

TABLE 3: Descriptive statistics of iron deficiency of the patients by age, gender, weight and duration of spells (n=96)

Veriable		Iron Deficiency		Total	P-Value
		Yes	No.		
Age (in months)	6-36	28(49.1%)	29(50.9%)	57(100%)	0.649
	37-60	21(53.8%)	18(46.2%)	39(100%)	
Gender	Male	30(49.2%)	31(50.8%)	61(100%)	0.630
	Female	19(54.3%)	16(45.7%)	35(100%)	
Weight (kg)	Upto 10kgs	17(63%)	10(37%)	27(100%)	0.144
	>10kgs	32(46.4%)	37(53.6%)	69(100%)	
Duration of spells (in seconds)	Upto 30	16(59.3%)	11(40.7%)	27(100%)	0.314
	>30	33(47.8%)	36(52.2%)	69(100%)	

*chi-square test

Among the 27 patients weighing up to 10 kg, 17 (63%) had iron deficiency, while 10 (37%) had not. In the group of 69 patients weighing more than 10 kg, 32 (46.4%) had iron deficiency, and 37 (53.6%) had not. The p-value for the difference between these weight categories was 0.144.

Among the 27 patients with spells lasting up to 30 seconds, 16 (59.3%) had iron deficiency, while 11 (40.7%) had not. For the 69 patients with spells lasting more than 30 seconds, 33 (47.8%) had iron deficiency, and 36 (52.2%) did not. The p-value for the difference based on spell duration was 0.314 **(Table 3)**.

DISCUSSION

Iron deficiency anemia and breath-holding spells (BHS) association in children has been a topic of significant interest in pediatric research. Our findings corroborate with existing literature and provide local data to support the global understanding of this association.

Out of 96 children included in this study with BHS, 63.5% were male, 36.5% were female and the mean age group was 2.6 ± 1.4 years. 51% of children were diagnosed with IDA with mean hemoglobin concentration of 8.6 ± 1.9 gm/dl. These results are compatible with study of Shamaoon et al. Who reported a 51.58% prevalence of IDA among children with BHS. Their study concluded that IDA is higher in children with BHS and that effective treatment with affordable iron preparations is readily available.[6] This high prevalence highlights the critical need for routine screening of iron levels in children presenting with BHS.

In another study, Hamed and colleagues[7] evaluated children with BHS in which 180 children were included and mean age group was 1.82 ± 0.53 years. Children were divided into 3 categories. 1st one includes children with iron deficiency, 2nd one includes children with iron deficiency anemia, and 3rd one includes children without iron deficiency. The frequency of spell was not significantly different between the two groups. However, after 3 and 6 months of iron therapy (p=0.0001), spell frequency was reduced significantly and there was an increase in hemoglobin, ferritin, and iron levels. There is an inverse relation between spell frequency and patient serum iron levels (p=.001), hemoglobin (p=.001) and ferritin (p=.0001) levels. It means higher the hemoglobin and iron levels the body lesser the chance of BHS. Our study did not include follow-up data on the impact of iron therapy, but the high prevalence of IDA we observed supports the notion that iron deficiency is a common underlying factor in children with BHS.

In another study done by Chesti in India, clearly mentioned the effectiveness of iron supplements in reducing the frequency of BHS. This study was prospective and interventional, it was conducted at GMC Baramulla. Seventy patients aged between 6 months and 5 years with BHS, iron

deficiency, and iron deficiency anemia were included in this study. They found a significant increase in hemoglobin levels, serum ferritin, and serum iron after 6 and 12 weeks of iron therapy ($p<0.001$). There was a significant decrease in the frequency of BHS ($p<0.001$). Our study's identification of a high frequency of IDA among children with BHS underscores the potential benefits of iron supplementation as a therapeutic intervention. Chesti's findings support the hypothesis that iron therapy can effectively reduce the frequency of BHS, providing a rationale for early diagnosis and treatment of iron deficiency in these patients. They assessed the role of iron in BHS and established the effectiveness of iron therapy in reducing their frequency.[8]

In a study done by El-Din *et al,* in Egypt showed frequency of iron deficiency with breath holding spells to be 44% and Saleh et al. in (sukkhar) Pakistan showed (46%) asssociation between iron defeciency and breath holding spells which are consistent with our results.[9,10]

The mean ferritin level in our study was 14.42 µg/dL, and the mean iron level was 54.11 µg/dL, indicating a substantial variation in iron storage and serum iron among the study population. These values are crucial for diagnosing iron deficiency and tailoring appropriate treatment strategies. The significant presence of iron deficiency anemia in our study population aligns with the global data reported by the World Health Organization, which highlights iron deficiency as the most common micronutrient deficiency affecting children. [11,2,5]

Arslan et al. in their study showed prevalencwe of Iron deficiency in breath holding spells tp be (27%) and improvement in symptoms of patients with oral iron therapy.[12,13] Multiple studies across the globe showed remission of symptoms of breath holding spells with iron therapy, which indicates a strong association between them.[14,15]

In summary, our study's findings are in line with previous research demonstrating a high prevalence of iron deficiency among children with breath-holding spells[16,17] High prevelance of iron deficiency suggests that routine screening for iron levels should be an integral part of the clinical evaluation of children presenting with BHS. Iron supplementation therapy effectively reduces the frequency of BHS.[18-20]

Limitations: Our study provides local evidence supporting the global understanding of association of iron deficiency with BHS and underscores the importance of early diagnosis and treatment to improve clinical outcomes and reduce the burden on healthcare resources.

CONCLUSION

We found a significant prevalence of iron deficiency with breath-holding spells, highlighting the need for routine screening and iron supplementation to reduce the severity and frequency of spells. Future research should focus on long-term follow-up and the impact of iron supplementation on the quality of life in children with BHS.

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Author's Contribution

MAS: Data collection and writing
ZMA: Study planning, desiging and manuscript
J**M:** Data collection
M**IK:** Data collection
AI: Data analysis and proof reading
AM: Data analysis and proof reading

All the authors have approved the final manuscript draft and accept the responsibility of research integrity.