Original Article

Frequency of Anemia Among Children Presenting with Breath Holding Spells

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ABSTRACT

Objective: To determine the frequency of anemia among children presenting with breath holding spells.
Study Design: Descriptive / cross-sectional study
Place and Duration of Study: This study was conducted at the Pediatrics Department, Postgraduate Medical Institute, Hayatabad Medical Complex Peshawar from March 2015-August 2015.
Materials and Methods: All children meeting the inclusion criteria and presenting with Breath-holding spells(BHS) were included in the study. All information was recorded in a pre-designed proforma and strictly exclusion criteria was followed to control confounders and bias in the study results. Data was stored and analyzed in SPSS version 20. Anemia was stratified among age and gender to see the effect modifications. Post stratification was done through chi-square test keeping p-value ≤ 0.05 was taken significant. All results were presented in the form of table and graphs.
Results: The mean age group of our sample was 2.6 $\pm$ 1.4 years of which 63.5% were male and 36.5% were female children. The mean hemoglobin concentration was 8.6 $\pm$ 1.9 gm/dl of blood and 39.9% of children were confirmed to have anemia.
Conclusion: There is a high incidence of anemia associated with breath holding spells. A full blood count and where possible serum ferritin level would therefore be warranted in the work up of children presenting with breath holding spells.

Key Words: Breath holding spells, hemoglobin, anemia, ferritin.

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INTRODUCTION

Breath-holding spells (BHS) are among the common benign paroxysmal non-epileptic disorders occurring in healthy otherwise normal children[1]. The prevalence has been estimated between 0.1% and 4.6% in the general population[2]. These episodes are often precipitated by emotional stimuli like anger, frustration, sudden fright, or minor trauma[3].Iron therapy, piracetam, levetiracetam, and atropine are considered as treatment and have shown variable efficacy[4].

The spells most commonly begin in the first 6 to 12 months of life and almost always by 2 years of age. In 90% of children the spells got remission by school age[5].

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The presence of autonomic imbalance with cerebral anoxia, anemia and genetic disorders may be responsible in these spells[6].

A study showed complete resolution of spells in 50% patients on iron therapy and 50% reduction in another 36.4%[7].

It has been documented that iron deficiency anemia may lead to adverse effects on oxygen uptake in the lungs and reduce available oxygen to the tissues, including central nervous system tissues[8]. In one study, association of breath holding spells with iron deficiency anemia in children revealed as 56.67% anemia in cases with BHS and 3.33% in controls without BHS (P value 0.0001)[9]. In another study, 7.5% of anemic children had history of BHS[10].

A study at start of therapy, 25 patients were having more than 10 episodes per week while no patient was having such episodes at 12 weeks of therapy (p-value=0.000)[11].

The present study is designed to determine the frequency of anemia among children presenting with BHS. Since, very rare work has been done on this issue throughout Pakistan. So, this study will be an attempt to establish the local magnitude of the anemia among children with BHS

MATERIALS AND METHODS

This was a Cross sectional, descriptive study and conducted through Non-probability consecutive

sampling. Duration of study was six months and it was conducted in pediatric department Hayatabad medical complex Peshawar (EPI) center. Sample Size Was 148, keeping frequency of 56.6%[9] proportion of anemia among children with Breath-holding spells (BHS), with 95% confidence interval & 8% margin of error using World Health Organization (WHO) sample size calculator.

Data Collection Procedure: The study was conducted after approval from hospitals ethical and research committee. All children meeting the inclusion criteria (Age: 6 Months- 5Years, both gender and presenting with BHS) were included in the study. The purpose and benefits of the study was explained to the patient's attendants and a written informed consent was obtained. All patients were subjected to complete history and clinical examination. From all the children, a 5cc of blood was obtained and sent to hospital laboratory. All the laboratory investigations were done under supervision of same consultant pathologist. All the above-mentioned information was recorded in a pre-designed proforma and strictly exclusion criteria (Children with thalassemia, Congenital malformations of throat, malnutrition) was followed to control confounders and bias in the study results.

Data Analysis Procedure: Data was stored and analyzed in SPSS version 20. Mean $\pm$ SD was calculated for quantitative variables like age and hemoglobin level. Frequencies and percentages were calculated for categorical variables like gender and anemia. Anemia was stratified among age and gender to see the effect modifications. Post stratification was done through chi-square test keeping p-value ≤ 0.05 was taken significant. All results were presented in the form of table and graphs.

RESULTS

The study was conducted on 148 children presenting with breath holding spells. We analyzed their serum hemoglobin concentration to determine the presence or absence of anemia. The mean age of the sample was 2.6 $\pm$ 1.4 years. The range of age in our study was 4.20 years with minimum age of 0.8 years and maximum age of 5.00 years. On grouping the sample in different age groups, we observed that 30.4% of patients were in the age group between 6 months and 1.5 years, 27.7% were in the age group 1.51 to 3.00 years and 41.9% of patients were in the age group 3.01 to 5.00 years.

While distributing the patients with regards to gender, we observed that in our study 63.5% of the sample was male and 36.5% were female gender.

The mean hemoglobin concentration was 8.6 $\pm$ 1.9 gm/dl of blood. As per operational definitions, we observed that 39.9% of children were confirmed to have Anemia. (Table 1)

While we stratified Anemia with regards to age groups, we observed that the difference was statistically significant after applying chi-square test with a p value of 0.035 (Table 2)

While we stratified Anemia with regards to gender, we observed that the difference was statistically significant after applying chi-square test with a p value of 0.023 (Table 3)

Table No.1: Frequency of Anemia (n=148)

Anemia		Frequency	Percent
	Yes	59	39.9
	No	89	60.1
	Total	148	100.0

Table No.2: Age group wise stratification of anemia (n=148)

		Anemia		Total
		Yes	No	
Age Groups	6.00 months to 1.5 years	25	20	45
		55.6%	44.4%	100.0%
	>1.5 to 3 years	13	28	41
		31.7%	68.3%	100.0%
	>3 years to 5 years	21	41	62
		33.9%	66.1%	100.0%
Total		59	89	148
		39.9%	60.1%	100.0%

P Value: 0.035

Table No.3: Gender group wise stratification of anemia (n=148)

		Anemia		Total
		Yes	No	
Gender of the Child	Male	44	50	94
		46.8%	53.2%	100.0%
	Female	15	39	54
		27.8%	72.2%	100.0%
Total		59	89	148
		39.9%	60.1%	100.0%

P Value: 0.023

DISCUSSION

Breath Holding Spells usually begin between the ages of 6 and 24 months of life, peaking in frequency by around 2 to 3 years, and 90% or more of patients have their initial spells by age 2 years.[12-15] It may begin as early as during neonatal period, and almost never after the age of 5 years.[16,17,18] About half of the children stops experiencing spells by age 4 years, and almost all by age 6 years[41], beyond which their occurrence is extremely uncommon.[12,19,20]

Episodes are described as infants crying, for up to a minute, and while crying excessively they will hold their breath to a point at which they might lose consciousness. Soon thereafter, the infant will usually regain consciousness and breathe normally. Breath-holding spells are not harmful and pose no long-term risks for the infant.[12]

Many episodes of breath holding are associated with an inciting incident in which the infant is irritated, is being disciplined, or is angry. Examples include when infants are having their hair splashed in the bath, when they

insist on holding a toy, or when they experience a minor injury.[19,20]

In a recent study from Turkey, children with breath-holding spells and a matched control group were subjected to a brainstem auditory evoked potentials test, and the inter-peak latencies were significantly prolonged in the breath-holding spells group compared with the control group (P = .009 and P = .03, respectively, for type III–V and type I–V interpeak latencies). This might mean that maturation delay in myelination of the brainstem could be the cause of breath-holding spells in children.[21]

Several studies, suggest an association between breath-holding spells and anemia in young infants. Among 91 children 6 to 40 months of age who were followed prospectively for an average of 2 years, 63 (69%) were found to have iron deficiency anemia.[22] About half (47.9%) of 165 children in another group from Turkey with breath-holding spells were found to have iron deficiency anemia.[23] and a recent larger Turkish study also confirms these findings.[24]

Two studies established the benefit of treatment with iron. In one group treated with iron (6 mg/kg daily) for 3 months, a significant reduction in cyanotic spells was recorded, compared with those not treated (84% vs 21%).[22] In the second study, mean levels of hemoglobin and total iron-binding capacity were predictive of a substantial reduction in the frequency of spells (88% vs 6%) for iron-treated versus untreated children, respectively.[18] Owing to the high frequency of anemia among children with breath-holding spells, testing for anemia or treating empirically for iron deficiency anemia is recommended.[18]

Iron deficiency anemia has also been shown to play a role in the pathophysiology of breath holding spells.[25-26,27] A study showed complete resolution of spells in 50% patients on iron therapy and 50% reduction in another 36.4%.[18] A recent study has also suggested a possible relationship between maternal iron deficiency anemia and children with breath holding spells.[28] Iron's role is thought to be due to it being a cofactor in catecholamine metabolism and neurotransmitter function.[18]

Although the pathogenesis and the triggering factors of the disease are not quite understood, there are studies indicating that iron deficiency anemia is frequently observed in children with spells which respond well to iron therapy.[18,29] Piracetam treatment has been demonstrated to be effective in children without anemia.[30] It is well known that children with iron deficiency cry more frequently, become easily depressed, and are more irritable.[12]

Similarly, the present study also documented that anemia was observed with higher frequency in patients with breath-holding spells. In another study association of breath holding spells with iron deficiency anemia in children revealed as 56.67% (n=17) in cases and 3.33% (n=1) in control group while remaining 43.33% (n=13) in cases and 96.67% (n=29) in control group had no findings of this association. P value was calculated as 0.0001 and Odds Ratio was 37.92 which show a significant difference between the two groups.[9]

In another study, a total of 165 children with BHS comprised the study group. A matched group of 200 children with febrile convulsions served as controls. Among the first-degree relatives, 13.3% had BHS, 1.8% had febrile convulsions and 12.1% had epilepsy. The spells were cyanotic in 140 (84.8%) children and pallid or mixed in the remainder. Eighteen patients had abnormalities in electroencephalography, however only one patient was diagnosed with epilepsy. Sixty nine (47.9%) patients were found to have iron deficiency anemia.[23].

Iron deficiency is implicated in conditions other than anemia and BHS. It is increasingly recognized to be a cause of restless legs, febrile seizures, thrombosis, impaired immunity and poor behavior.[31]

It is not known how iron deficiency leads to BHS. It may involve the role of iron in catecholamine metabolism and the functioning of enzymes and neurotransmitters in the central nervous system.[32,33]

In another study, anger and pain were the most common triggering factors (65.1 %) for BHS. A positive family history of BHS was identified in 51% and parental consanguinity was found in 30% of cases. The spells were cyanotic in 79.1% (34 children). 78% of cases were iron deficient and 53% of cases had iron deficiency anemia.[34]

Infancy and childhood is the critical period for brain growth, and nutrient deficiencies during this time may affect psychomotor development and neurocognition.[35] It is less well known that long-term neurocognitive impairment may persist. Young children with iron deficiency anemia have been found to score 12 to 15 points lower on the Bayley infant development scale than their iron sufficient peers.[36]

CONCLUSION

There is a high incidence of anemia associated with breath holding spells. A full blood count and where possible serum ferritin level would therefore be warranted in the work up of these children. Treatment of BHS is more likely to be successful when there is concomitant treatment of associated anemia.

Author's Contribution:

Concept & Design of Study:	Sami ul Haq
Drafting:	Jalil khan
Data Analysis:	Hazrat Bilal Khan
Revisiting Critically:	Sami ul Haq
Final Approval of version:	Sami ul Haq

Conflict of Interest: The study has no conflict of interest to declare by any author.

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