



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**

SJIF Impact Factor: 7.187

Available online at: <http://www.iajps.com>

Research Article

**A CROSS SECTIONAL STUDY ON THE FREQUENCY OF
ANEMIA AMONG CHILDREN PRESENTING WITH BREATH
HOLDING SPELLS****Muhammad Bilal Alim, Asad Maqbol, Abrar Maqbool
DHQ Hospital Sargodha****Article Received:** October 2020 **Accepted:** November 2020 **Published:** December 2020**Abstract:**

Objective: The aim of this study was to determine the frequency of anemia among children presenting with breath holding spells.

Material and Methods: The design of this study was Cross-sectional descriptive study. This study was conducted at DHQ Hospital Sargodha and the duration of this study was from June 2020 to September 2020. 100 patients of Breath-holding spells were selected in a consecutive manner OPD and their hemoglobin level was determined.

Results: The mean age group of our sample was 2.6 ± 1.4 years of which 61.3% were male and 34.3% were female children. The mean hemoglobin concentration was 8.6 ± 1.9 gm/dl of blood and 37.9% of children were confirmed to have anemia.

Conclusion: There is a high incidence of iron deficiency 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.

KEYWORDS: Breath holding spells, iron, hemoglobin, anemia, ferritin

Corresponding author:**Muhammad Bilal Alim,
DHQ Hospital Sargodha**

QR code



Please cite this article in press Muhammad Bilal Alim et al., A Cross Sectional Study On The Frequency Of Anemia Among Children Presenting With Breath Holding Spells., Indo Am. J. P. Sci, 2020; 07(12).

INTRODUCTION:

Breath-holding spells (BHS) are among the common benign paroxysmal non-epileptic disorders occurring in healthy otherwise normal children. The prevalence has been estimated between 0.1% and 4.6% in the general population [1]. These were first described in 1737 by Nicholas Culpepper and were thought to be voluntary breath holding. These episodes are often precipitated by emotional stimuli like anger, frustration, sudden fright, or minor trauma. A detailed history and exam are important to diagnose these spells and help distinguish from epileptic seizures and other causes of syncope [2]. The cornerstone of therapy is reassuring the parents and educating them about the condition. Iron therapy, piracetam, levetiracetam, and atropine are considered as treatment and have shown variable efficacy. 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 and the persistence is extremely rare. The mechanism of Breath-holding spells (BHS) yet remains controversial [3]. The presence of autonomic imbalance with cerebral anoxia, anemia and genetic disorders may be responsible in these spells.

Iron deficiency anemia has also been shown to play a role in the pathophysiology of breath holding spells [4]. A study showed complete resolution of spells in 50% patients on iron therapy and 50% reduction in another 36.4%. A recent Cochrane Systematic Review suggests that iron supplementation reduces the frequency and severity of breath-holding attacks, particularly in children with iron deficiency (OR 76.48; 95% CI 15.65 to 373.72; $P < 0.00001$) [5]. 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. In one study [6], association of breath holding spells with iron deficiency anemia in children revealed as 56.67% anemia in patients with Breath-holding spells and 3.33% in controls without BHS (P value 0.0001) [7]. In another study, 7.5% of anemic children had history of BHS. In a study by Khan, I et al, there was a statistically significant fall in the frequency of breath holding spells with 12 weeks of iron therapy. 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) [8]. The present study is designed to determine the frequency of anemia among children presenting with Breath-holding spells (BHS) [9]. The results of this study will be shared with other local pediatricians to make them aware of the problem and to develop future

recommendations for preventing and treating Breath-holding spells (BHS) [10].

MATERIAL AND METHODS:

This study was conducted at DHQ Hospital Sargodha and the duration of this study was from June 2020 to September 2020. 100 patients, keeping frequency of 54.4% proportion of anemia among children with Breath-holding spells (BHS), with 93% confidence interval & 6% margin of error using World Health Organization (WHO) sample size calculator. The inclusion criteria for this study were, all children presenting breath holding spells as history given by mother, both genders (male & females) were included and age of the children in this study was between 6 months to 5 years. The Exclusion Criteria for this study was Children with thalassemia as detected on medical records, Children with congenital malformations of the throat on physical examination, Children with malnutrition as detected by physical examination and growth chart and Children with history of multivitamin supplementation in the last two weeks. The study was conducted after approval from hospitals ethical and research committee. All children meeting the inclusion criteria and presenting with Breath-holding spells (BHS) was included in the study. The purpose and benefits of the study was explained to the patient 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 under aseptic technique and sent to hospital laboratory to detect anemia. All the laboratory investigations were done under supervision of same consultant pathologist having minimum of five years of experience. All the above-mentioned information including name, age, sex was recorded in a pre-designed Performa and strictly exclusion criteria were followed to control confounders and bias in the study results. 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 100 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 ± 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 26.0% of patients were in the age group between 6 months and 1.5 years, 23.3% were in the age group 1.51 to 3.00 years and 39.7% of patients were in the age group 3.01 to 5.00 years. (Table 1) While distributing the patients with regards to gender, we observed that in our study 61.3% of the sample was male and 34.3% were female gender. (Table 2). The mean hemoglobin concentration was 8.6 ± 1.9 gm/dl of blood. As per

operational definitions, we observed that 37.9% of children were confirmed to have Anemia. (Table 3) 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 4) 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 5)

Table 1: Age-Wise Distribution of Sample (n=100)

	N	Range	Minimum	Maximum	Mean \pm SD
Age of the Child	100	4.20	.80	5.00	2.6669 \pm 1.41942

Table 2: Gender-Wise Distribution of Sample (n=100)

Age Groups	Frequency	Percent
6.00 months to 1.5 years	23	26.0
>1.5 to 3 years	20	23.3
>3 years to 5 years	57	39.7
Total	100	100.0

Table 3: Frequency of Anemia (n=100)

Gender	Frequency	Percent
Male	60	61.3
Female	40	34.3
Total	100	100.0

Table 4: Age Group Wise Stratification of Anemia (n=100)

Anemia	Frequency	Percent
Yes	39	37.9
No	61	58.1
Total	100	100.0

Table 5: Gender Group Wise Stratification of Anemia (n=100)

		Anemia		Total
		Yes	No	
Age Groups	6.00 months to 1.5 years	20	20	23
		33.4%	22.2%	100.0%
>1.5 to 3 years		13	26	20
		29.5%	66.1%	100.0%
>3 years to 5 years		11	20	57
		11.7%	66.1%	100.0%
Total		44	66	100
		37.9%	58.1%	100.0%

P VALUE: 0.035

DISCUSSION:

Breath-holding spells represent an age-limited disorder. It usually begins 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 [11,12]. It may begin as early as during neonatal period, and almost never after the age of 5 years. About half of the children stops experiencing spells by age 4 years, and almost all by age 6 years, beyond which their occurrence is extremely uncommon [13]. A genetic causative factor may be responsible for the disease, and autosomal-dominant inheritance is suggested. A positive family history of BHS has been reported in up to 30% of children with BHS. Breath-holding spells are extremely frightening to parents. 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. On rare occasions a seizure might be witnessed immediately after the infant loses 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. Many episodes of breath holding are associated with an inciting incident in which the infant is irritated, is being disciplined, or is angry [14]. 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. While considered by many to be "attention seeking" behavior, these spells are not intentional; they result from an involuntary reflex, and the child has no ability to control them. 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 interpeak 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 [15].

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. About half (47.9%) of 165 children in another group from Turkey with breath-holding spells were found to have iron deficiency anemia, and a recent larger Turkish study confirms these findings. 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%). 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. 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. Iron deficiency anemia has also been shown to play a role in the pathophysiology of breath

holding spells [16]. A study showed complete resolution of spells in 50% patients on iron therapy and 50% reduction in another 36.4%. A recent study has also suggested a possible relationship between maternal iron deficiency anemia and children with breath holding spells. Iron's role is thought to be due to it being a cofactor in catecholamine metabolism and neurotransmitter function.

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. Piracetam treatment has been demonstrated to be effective in children without anemia. It is well known that children with iron deficiency cry more frequently, become easily depressed, and are more irritable [17]. Similarly, the present study also documented that iron deficiency 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 34.45% in patients and 1.11% in control group while remaining 21.11% in patients and 74.45% in control group had no findings of this association. P value was calculated as 0.0001 and Odds Ratio was 15.70% which show a significant difference between the two groups. 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. 18 patients had abnormalities in electroencephalography, however only one patient was diagnosed with epilepsy [18]. 69 (47.9%) patients were found to have iron deficiency anemia. Iron deficiency is implicated in conditions other than anemia (a late manifestation) and Breath-holding spells. It is increasingly recognized to be a cause of restless legs, febrile seizures, thrombosis, impaired immunity and poor behaviour. It is known that children who have experienced BHS may become adolescents with syncopal episodes. A recent retrospective cohort study of largely non-iron deficient children with BHS showed a 29.4% incidence of concentration problems. It is not known how iron deficiency leads to BHS [19]. It may involve the role of iron in catecholamine metabolism and the functioning of enzymes and neurotransmitters in the central nervous system. Increased brain erythropoietin production may have a protective effect. The correction of spells during treatment with iron may be related to the functional restoration of these

neurotransmitters. 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 patients. The spells were cyanotic in 79.1% (34 children). 78% of patients were iron deficient and 53% of patients had iron deficiency anemia.

CONCLUSION:

There is a high incidence of iron deficiency 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 is more likely to be successful when there is concomitant iron deficiency anemia. Length of iron therapy can vary between 4 and 16 weeks. A course of 8 weeks would seem reasonable, long enough to improve anemia.

REFERENCES:

1. Zehetner AA, Orr N, Buckmaster A. Iron supplementation for breath-holding attacks in children [Systematic Review] Cochrane Database Syst Rev. 2010;5CD008132.
2. Rathore G, Larsen P, Fernandez C, Parakh M. Diverse Presentation of Breath Holding Spells: Two Case Reports with Literature Review. Case reports in neurological medicine 2013. Available at <http://dx.doi.org/10.1155/2013/603190>. (Accessed June 5, 2015).
3. Zehetner A. Iron supplementation reduces the frequency and severity of breath-holding attacks in non-anaemic children. Clinics and Practice. 2011;1(4): e98.
4. Zaman SQ, Mahmood A, Ahmed S, Mahmud S. Iron deficiency anemia; Association of breath holding spells with in children with iron deficiency anemia. Prof Med J 2014;21(4):29-33.
5. Sajid A, Ikram MA, Shahid HM, Saeed SM. Iron Deficiency Anemia in Children; Common But Commonly Missed Pak Paed J 2014;38(2):91-5.
6. Khan I, Muhammad T, Khan MA. Effectiveness of oral iron supplement on breath-holding spells in children J Med Sci 2012;20(3):138-41.
7. Chen MH, Su TP, Chen YS, Hsu JW, Huang KL, Chang WH, et al. Association between psychiatric disorders and iron deficiency anemia among children and adolescents: a nationwide population-based study. BMC Psychiatry. 2013 Jun 4. 13:161.
8. Mateos Gonzalez ME, de la Cruz Bertolo J, Lopez Laso E, Valdes Sanchez MD, Nogales Espert A. [Review of haematology and biochemistry parameters to identify iron deficiency] [Spanish]. An Pediatr (Barc). 2009 Aug. 71(2):95-102.

9. Goddard AF, James MW, McIntyre AS, Scott BB. Guidelines for the management of iron deficiency anaemia. *Gut*. 2011 Oct. 60(10):1309-16.
10. DeLoughery TG. Microcytic anemia. *N Engl J Med*. 2014 Oct 2. 371(14):1324-31.
11. Koutroubakis IE, Oustamanolakis P, Karakoidas C, Mantzaris GJ, Kouroumalis EA. Safety and efficacy of total-dose infusion of low molecular weight iron dextran for iron deficiency anemia in patients with inflammatory bowel disease. *Dig Dis Sci*. 2010 Aug. 55(8):2327-31.
12. Onken JE, Bregman DB, Harrington RA, Morris D, Buerkert J, Hamerski D, et al. Ferric carboxymaltose in patients with iron-deficiency anemia and impaired renal function: the REPAIR-IDA trial. *Nephrol Dial Transplant*. 2013 Aug 20.
13. Brooks M. FDA Approves Injectafer for Iron Deficiency Anemia. *Medscape Medical News*. Available at <http://www.medscape.com/viewarticle/808800>. Accessed: August 3, 2015.
14. Grogan K. Vifor gets FDA approval for Injectafer. *PharmaTimes*. Available at http://www.pharmatimes.com/Article/13-07-26/Vifor_gets_FDA_approval_for_Injectafer.aspx. Accessed: July 3, 2015.
15. Fernandez-Gaxiola AC, De-Regil LM. Intermittent iron supplementation for reducing anaemia and its associated impairments in menstruating women. *Cochrane Database Syst Rev*. 2011 Dec 7. 12:CD009218.
16. De-Regil LM, Jefferds ME, Sylvetsky AC, Dowswell T. Intermittent iron supplementation for improving nutrition and development in children under 12 years of age. *Cochrane Database Syst Rev*. 2011 Dec 7. 12:CD009085.
17. Araki T, Takaai M, Miyazaki A, Ohshima S, Shibamiya T, Nakamura T, et al. Clinical efficacy of two forms of intravenous iron--saccharated ferric oxide and cideferron--for iron deficiency anemia. *Pharmazie*. 2012 Dec. 67(12):1030-2.
18. Beutler E, Lichtman MA, Coller BS. *Williams Hematology*. 6th ed. New York, NY: McGraw-Hill Book Co; 2001. 295-304, 447-70.
19. Boggs W. Ferric Carboxymaltose Improves Iron-Deficiency Anemia in Renal Impairment. *Medscape Medical News*. Available at <http://www.medscape.com/viewarticle/810657>. Accessed: June 16, 2016.