



## IRON DEFICIENCY ANEMIA;

Association of breath holding spells with in children with iron deficiency anemia.

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### INTRODUCTION

Breath holding spell (BHS), a stereo typed sequence of clinical events, is not an uncommon clinical presentation and is a frightening experience for the parents. During the spell, the child cries excessively because of frustration, pain, or both. At the end of prolonged expiration, they become apneic for several seconds and become either blue [cyanotic spells] or pale [pallid spells] and some children can experience both. Sometime they go in for tonic spasms and occasionally develop clonic movements.

**ABSTRACT... Objective:** To determine the association of breath holding spells with iron deficiency anemia in children. **Study Design:** Case control study. **Place and Duration of Study:** Military Hospital Rawalpindi from Jun 2012 to Dec 2012. **Study Population:** Sixty children of either gender meeting inclusion criteria aged 6 months to 5 years with 30 of breath holding spells in case group and 30 in control group as healthy children were included in the study after informed consent from parents. **Method:** Complete blood picture and serum ferritin levels were performed of all children in both case and control groups. Tests were carried out at AFIP Rawalpindi. All data was entered and analyzed using SPSS version 10. Frequencies and percentages were calculated for categorical (qualitative) variables like sex and children having iron deficiency anemia in cases and controls. Mean and Standard Deviation (SD) was calculated for numerical (quantitative) variable like Age. Odds ratio was calculated from the data of cases and controls. Regarding iron deficiency anemia p value <0.05 was considered as significant. **Results:** In this study, we recorded 43.33% (n=13) cases were between 0.6-3 years and 56.67% (n=17) were between 4-5 years while 53.33% (n=16) controls were between 0.6-3 years and 46.67% (n=14) were between 4-5 years. Mean±SD was calculated as 3.3+1.46 years in cases and 2.93+1.48 years in control group. Male children were 60% (n=18) in patient group and 46.67% (n=14) in controls group. Female children were 40% (n=12) in patient and 53.33% (n=16) in control group respectively. 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 shows a significant difference between the two groups. **Conclusions:** The association of breath holding spells with iron deficiency anemia in children is significantly higher than healthy controls. So, it is recommended that every child who present with breath holding spells should be evaluated for iron deficiency anemia.

**Key words:** Children, breath holding spells, iron deficiency anemia, association

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Breath-holding spells can take one of two forms. The cyanotic form of breath-holding, which is most common, is initiated subconsciously by young children often as a component of a temper tantrum or in response to a scolding or other upsetting event. Episodes peak at about 2 years and are rare after 5 years. The pallid form typically follows a painful experience, such as falling and banging the head or being suddenly startled. The child stops breathing, rapidly loses consciousness, and becomes pale and limp. A seizure and incontinence may occur. Because this form is rare, further diagnostic evaluation and treatment may

be needed if the spells occur frequently<sup>1</sup>.

A large epidemiological study in Karnataka, initiated by Indian Council of Medical Research, found that the prevalence of breath holding spells was 5.9% among 0 to 3 years age group, more common than other developmental disorders. Majority of these breath holders (88.9%) had hemoglobin level between 7 and 11 g%, while 7.4% of cases showed hemoglobin level less than 7 g%. Only one child had hemoglobin (Hb) value above 11 g%. For three children, value was not available<sup>2</sup>. Yilmaz U et al studied and showed that sixty nine (47.9%) patients with breath holding spells were found to have iron deficiency anemia<sup>3</sup>.

Although breath-holding spells are not harmful, they can sometimes be a sign of an underlying medical condition like a seizure disorder, cardiac arrhythmia, or iron deficiency anemia. Treating these conditions may help reduce the frequency of breath-holding spells. Association of iron deficiency with breath holding spells is increasingly being recognized<sup>4</sup>.

The prevalence rates of iron depletion (ID) and Iron Deficiency Anemia (IDA) were 32.5% and 7.8% respectively in children 7 months to 7 years in China. ID was more prevalent than IDA in each age group in children, suggesting that latent iron deficiency was currently one of the major nutritional problems for Chinese children. The present study also showed that infants were still at higher risk for iron deficiency in spite of rapid socioeconomic development in the last two decades<sup>5</sup>.

Long term prognosis of children with BHS, there is a predisposition to fainting spells. It is also found that 29.4% of children with BHS had concentration problems. Further follow-up studies are needed to confirm this trend<sup>6,7,8</sup>. Carman KB et al reported that positive family history for BHS, birth sequence, parents' education status and fathers' age were identified as risk factors associated with BHS<sup>9</sup>.

This study is being planned to explore the association of iron deficiency anemia with breath

holding spells in children. If association is found than these children can be diagnosed easily and timely treated with iron therapy which is very cheap and readily available.

## PATIENTS AND METHODS

The present case control study was carried out at Paediatrics Department of Military Hospital Rawalpindi, which is a 1200 bedded tertiary care hospital with Paediatrics Department of 300 beds from Jun 2012 to Dec 2012. The study population consisted of children of army personnel and civilians reporting to MH Rawalpindi for medical treatment or those referred from primary or secondary care hospitals for management. Sample size was 60 as calculated using world health organization (WHO) Calculator. All children of either gender from 6 months to 5 years of age presenting with breath holding spells meeting the inclusion criteria in case group and healthy children in control group were included in the study by consecutive (Non Probability) sampling technique. Children with congenital heart disease diagnosed by echocardiography, febrile or non febrile seizures, on anticonvulsant therapy, mental disability and severe malnutrition evaluated by weight, OFC, height/ length meeting exclusion criteria were not included in case group. Children with any chronic illness (history and record based) were not included in control group.

Administrative permission from the concerned authorities and ethical committee was sought to conduct the study. Parents were explained about the risk and benefits of the study and informed written consent was obtained for their children examination and intervention according to the guidelines of Helsinki Declaration. Permission was also obtained regarding use of data for research and publication. Demographic data was collected regarding age and sex. Complete blood picture and serum ferritin levels were performed of all children in both case and control groups. Tests were carried out at Armed Forces Institute of Pathology. Appropriate entries were made in the structured study performa by the trainee researcher. Data was collected through a structured performa (Annex A).

All data was entered and analyzed using SPSS version 10. Descriptive statistics were used to analyze and describe data. Frequency and percentage were calculated for categorical (qualitative) variables like sex and children having iron deficiency anemia in cases and controls. Mean and Standard Deviation (SD) was calculated for numerical (quantitative) variable like Age. Qualitative variables were presented in the form of tables and charts (bar and pie charts). Odds ratio was calculated from the data of cases and controls. Chi square test was used to determine the difference in cases and controls. Regarding iron deficiency anemia p value <0.05 was considered as significant.

## RESULTS

A total of 60 cases (30 in each group) fulfilling the inclusion/exclusion criteria were enrolled to determine the association of breath holding spells with iron deficiency anemia in children.

Age distribution of the patients was done which shows that 43.33%(n=13) in cases were between 0.6-3 years and 56.67%(n=17) were between 4-5 years while 53.33%(n=16) in controls were between 0.6-3 years and 46.67%(n=14) were between 4-5 years, mean±SD was calculated as 3.3±1.46 years in cases and 2.93±1.48 years in control group. (Table No. I)

Age (in years)	Cases (n=30)		Controls (n=30)	
	No. of patients	%	No. of patients	%
0.6-3	13	43.33	16	53.33
4-5	17	56.67	14	46.67
Total	30	100	30	100
Mean±SD	3.3±1.46		2.93±1.48	

**Table-I. Age distribution (n=60)**

Gender distribution of the patients was done which shows 60% (n=18) males in cases group and 46.67% (n=14) in control group while female children were recorded 40%(n=12) in cases and 53.33% (n=16) in control group. (Table No. II) Association of breath holding spells with iron

Gender	Cases (n=30)		Controls (n=30)	
	No. of patients	%	No. of patients	%
Male	18	60	14	46.67
Female	12	40	16	53.33
Total	30	100	30	100

**Table-II. Gender distribution (n=60)**

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 shows a significant difference between the two groups. (Table No. III)

Association	Cases (n=30)		Controls (n=30)	
	No. of patients	%	No. of patients	%
Yes	17	56.67	01	3.33
No	13	43.33	29	96.67
Total	30	100	30	100

**Table-III. Association of breath holding spells with iron deficiency anemia in children (n=60)**  
P value=<0.0001 Odds Ratio: 37.92

Stratification for association of breath holding spells with iron deficiency anemia in children with regards to age was done which shows that out of 17 children in cases group, 76.47%(n=13) were recorded between 0.6-3 years and 23.53%(n=4) were between 4-5 years while in control group 100%(n=1) children was recorded in between 0.6-3 years of age.

Stratification for association of breath holding spells with iron deficiency anemia in children with regards to gender was done which shows that out of 17 children in cases group, 41.18%(n=7) were male and 58.82%(n=10) were females while in control group 100%(n=1) children were female.

## DISCUSSION

Breath-holding attacks (BHA) are paroxysmal events affecting approximately 5% of healthy children. Breath-holding attacks are also called breath-holding spells by some<sup>10</sup>. They occur most commonly within the first 12 months of life and virtually all breath-holders experience their initial spell by the age of 2 years<sup>11,12</sup>. In the prior researches about these spells, pathophysiologic mechanisms are emphasized on autonomic nervous system dysregulation<sup>11-13</sup>. Holowach and Thurston reported that different degrees of the anemia were detected in patients with breath-holding spells<sup>14</sup>.

The present study was planned to explore the association of iron deficiency anemia with breath holding spells in children as no local literature is available and hypothesized that if association is found then these children can be diagnosed easily and timely treated with iron therapy which is very cheap and readily available.

Anil BG et al reported that 60% of cases were found in the age group of 1-2 years. Male to female ratio was 3:2 and the male predominance was seen in all the age groups. Most common age of onset of BHS was between the ages 7-12 months<sup>15</sup>. The present study also showed that 43.33% in cases were between 6 months to 3 years and 56.67% were between 4-5 years while 53.33% in controls were between 6 months to 3 years and 46.67% were between 4-5 years. Male children were 60% in cases group and 46.67% in control group while female children were recorded 40% in cases and 53.33% in control group.

Iron deficiency may have an impact on autonomic dysregulation in patients with breath holding spells<sup>16</sup>. In this study of breath-holders, iron-deficiency anemia was detected in 56% of patients<sup>17</sup>. Association of breath holding spells with iron deficiency anemia in children revealed as 56.67% in cases and 3.33% in control group in the present study. P value was calculated as <0.0001 and Odds Ratio was 37.92 which shows a significant difference between the two groups in the present study.

The findings of the study are consistent with a large epidemiological study in Karnataka, initiated by Indian Council of Medical Research, found that the prevalence of breath holding spells was 5.9% among 0 to 3 years age group, more common than other developmental disorders. Majority of these breath holders (88.9%) had hemoglobin level between 7 and 11 g%, while 7.4% of cases showed hemoglobin level less than 7 g%. Only one child had hemoglobin (Hb) value above 11 g%. For three children, value was not available<sup>2</sup>.

Holowach et al<sup>18</sup> demonstrated that children with severe BHS had significantly lower hemoglobin and serum iron values, a lower percentage of transferrin saturation, and higher TIBC than those of controls. Colina and Abelson<sup>19</sup> reported the resolution of BHS in 2 children with correction of anemia. Daoud et al demonstrated that iron therapy is effective in the treatment of BHS especially those with iron deficiency.

In recent years, however, studies have noted a high incidence of iron-deficiency anemia in children with breath-holding spells, with improvement or resolution of the spells after treatment with ferrous sulfate. It is not clear how iron deficiency may predispose to breath-holding spells. Anemia may increase a child's vulnerability to hypoxia. Iron also appears to play a role in catecholamine metabolism and neurotransmitter function, and thus the deficiency may directly affect autonomic regulation of cardiac and respiratory function<sup>20</sup>.

In this study, we did not give trial of the management of iron deficiency anemia and also did not check response to treatment which may be done in further trials. However, we suggest that children with BHS require investigations for iron deficiency anemia and treatment with iron where appropriate.

## CONCLUSIONS

The association of breath holding spells with iron deficiency anemia in children is significantly higher than healthy controls. So, it is

recommended that every child who present with breath holding spells should be evaluated for iron deficiency anemia. However, it is also required that every setup should have their surveillance in order to know the frequency of the problem.

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