

CLINICAL AND EPIDEMIOLOGICAL PROFILE OF BREATH HOLDING SPELLS (BHS)- AN ANALYSIS OF 115 CASES

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ABSTRACT

BACKGROUND

Breath holding spells are common in non-epileptic, repetitive, paroxysmal events in young infants and children often considered as seizure mimics/ confused with seizure disorder can be a frightening experience for parents and demands a good history of the sequence of events, because the diagnosis is made clinically.

Aims and Objectives- To study the disease spectrum of Breath holding spells in infants and children in terms of clinical and epidemiological profile (i.e. age, sex, family history, parental consanguinity, triggering factors, associated comorbidities such as anaemia etc.).

MATERIALS AND METHODS

This case series study was conducted in our Child health clinics. A total of 125 children below 6 years with Breath holding spells were enrolled between May 2012 and April 2017, out of which 10 children were excluded from the study due to various causes. Remaining 115 children diagnosed as Breath holding spells by typical history, clinical examination and after ruling out other causes which mimic Breath holding spells are included in the study.

RESULTS

In the present study, a total of 115 children aged between 6 months and below 6 years were diagnosed as having Breath holding spells. In 73 (63.41%) cases Breath holding spells began during the first 24 months of age. Most common triggering factor being anger (45.2%) and pain (41.7%). A positive family history was found in 27% and parental consanguinity was found in 30.43% of cases. The spells were cyanotic in 62.6% and 76.52% were anaemic.

CONCLUSION

The result of this study suggests a new data regarding the natural history of Breath holding spells and is important for identifying interventional strategies and parental counselling and could serve as baseline data for future approaches on this paediatric clinical entity.

KEYWORDS

Breath Holding Spells, Cyanotic, Pallid, Anaemia.

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BACKGROUND

Breath holding spells are common in non-epileptic, repetitive, reflexive events described under "behavioural disorders" of children and are initiated by provocative events that cause anger, frustration or pain causing the child to cry. The term Breath holding spells is actually a misnomer, as these are not self-induced but results from immaturity of autonomic system and occurs in two different forms. The first type is pallid Breath holding spells. The second type is the cyanotic or blue Breath holding spells. Episodes usually start with a cry (often in the case of pallid type, a silent cry with marked pallor) and progress to apnoea and cyanosis. Some authors have described third variety as mixed Breath holding spells,

wherein both pallor and cyanosis occur in same child during the spell. Spells usually begin between 6 and 18 months of age. Breath holding spells are rare below 6 months, peak by 2 years and abate by 5 years. Syncope, tonic posturing and reflex anoxic seizure may follow the more severe episode, particularly in Breath holding spells of pallid type. Injury, anger and frustration, particularly with surprise are common triggers. The prevalence of Breath holding spells described variously between 5% and 15%.¹ Many authors have proposed the prevalence of an underlying dysfunctional autonomic nervous system in children with Breath holding spells. Other reports suggested an association between anaemia and Breath holding spells. Breath holding spells usually mimic or are confused with seizure disorder and can be a frightening experience for parents. Since the diagnosis is made clinically it demands a good history of sequence of events, lack of incontinence and postictal phase helps to make an accurate diagnosis. Education and reassurance of the parents usually all that is needed as these episodes are as a rule self-limited and are outgrown within a few years or by school age. However, treatment of coexisting anaemia or iron deficiency is needed if it is present as the spells are made worse by iron deficiency anaemia.^{1,2,3,4} Hence, we analysed

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the clinical and epidemiological profile of children with Breath holding spells in our study.

MATERIALS AND METHODS

This case series study was conducted in our “Child health clinics.” A total of 125 children below 6 years with Breath holding spells were enrolled between May 2012 and April 2017, out of which 10 children were excluded from the study because these children had other associated problems (like one child had Atrial septal defect, two children had Ventricular septal defect, three children had history of febrile convulsions and four children were lost for follow-up in due course). All children diagnosed as Breath holding spells by typical history, clinical examination and after ruling out other causes which mimic Breath holding spells are included in the study. A structured interview was undertaken at the time of initial consultation to confirm Breath holding spells and its type, sex and age at initial spells, laboratory tests, (CBC, EEG, ECG, 2D Echo and neuroimaging studies etc.) were done depending upon the demand of clinical situation to exclude other causes and comorbidities such as epilepsy/ seizures, congenital cyanotic heart diseases, prolonged QT syndrome, Chiari crisis and Brain stem lesions.

RESULTS

In the present study, a total of 115 children were diagnosed as Breath holding spells between 6 months and 60 months. In our study, Breath holding spells are observed more frequently in boys than in girls (58.3% vs. 41.7%). Hence, M/F ratio is 1.4: 1 (Table 1) in agreement with Ashrafi et al study (1999) of M/ F ratio of 1.15: 1. A positive family history was found in 27% (31 out of 115) and parental consanguinity was found in 30.43% (35 out of 115) of cases. The spells were cyanotic in 62.6% (72 out of 115) and pallid in 30.4% (35 out of 115). In our study, none of the children had mixed form of Breath holding spells. Most common triggering factors in the present study being anger 45.2% (52 out of 115) and pain 41.7% (48 out of 115), in agreement with the previous studies (Table 1). In the present study, about 76.52% (88 children out of 115) had anaemia (Table 2). In 73 (63.41%) cases, Breath holding spells began during the first 24 months of age (Table 3). In our study family history of Breath holding spells were found in 27% of children, whereas in Daoud study (1997) 47.5% and in Ashrafi MR study (1999) 51.2% (Table 4). In our study about 30.43% (35 out of 115) cases have positive history of parental consanguinity in agreement with Ashrafi MR study (Table 5).

Parameters		Number (n= 115)	(%)
Sex	Boys	67	58.3
	Girls	48	41.7
Family History	Yes	31	27
	No	84	73
Parental Consanguinity	Yes	35	30.4
	No	80	69.6
Type of Attack	Cyanotic	76	66.1
	Pallid	39	33.9
Triggering Factor	Anger	52	45.2
	Pain	48	41.7
	Injection (vaccination)	11	9.5
	Frustration	4	3.4

Table 1. Clinical and Epidemiological Profile of Children with Breath Holding Spells (n= 115) in the Present Study

Haematological Classification according to Hb% and RBC Indices	Number
Number of BHS children with anaemia	88
Number of BHS children with normal Hb% and RBC indices	27

Table 2. Haematological Classification according to Hb% and RBC Indices in the Present Study (n= 115)

Age	Number of Cases	%	Boys n= 67	%	Girls n= 48	%
0-6 months	1	0.87	1	0.8	0	0
7-12 months	42	36.52	31	27	11	9.6
1-2 years	30	26.02	15	13.04	15	13.04
2-3 years	25	21.74	14	12.2	11	9.56
3-4 years	12	10.43	5	4.34	7	6.08
4-6 years	5	4.35	1	0.87	4	3.47

Table 3. Distribution of Breath Holding Spells in Children according to Age of Onset of First Spell in the Present Study (n= 115)

Study	% of Cases with Positive Family History of Breath Holding Spells
Daoud Study (1997)	47.5%
Ashrafi MR Study (1999)	51.2%
Present Study	27%

Table 4. Comparison among Different Studies regarding Percentage of Cases having Positive Family History of Breath Holding Spells

Study	% of Cases with Positive History of Parental Consanguinity among Children with Breath Holding Spells
Daoud Study (1997)	70%
Ashrafi MR Study (1999)	30%
Present Study	30.43%

Table 5. Comparison among Different Studies regarding Percentage of Children with Breath Holding Spells having Positive Parental Consanguinity

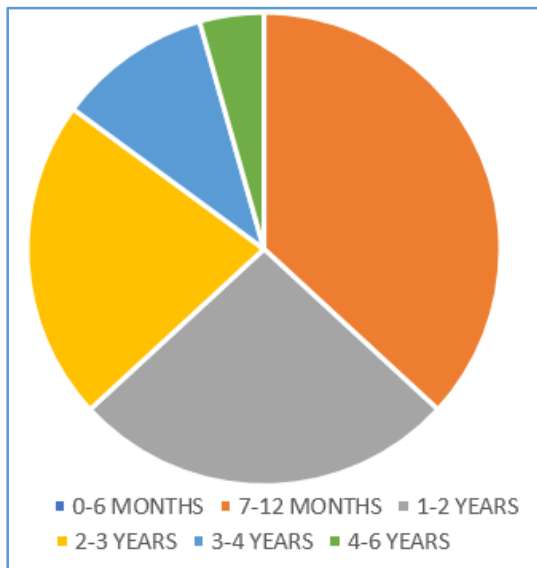


Figure 1. Pie Diagram showing Age Wise distribution of Children with Breath Holding Spells in the Present Study

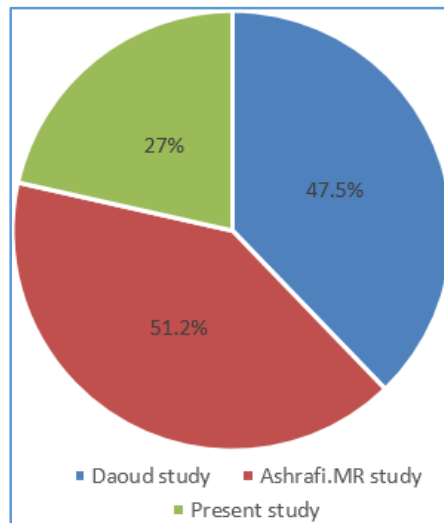


Figure 4. Pie Diagram showing Comparison of Positive Family History of Breath Holding Spells (in %) among Different Studies

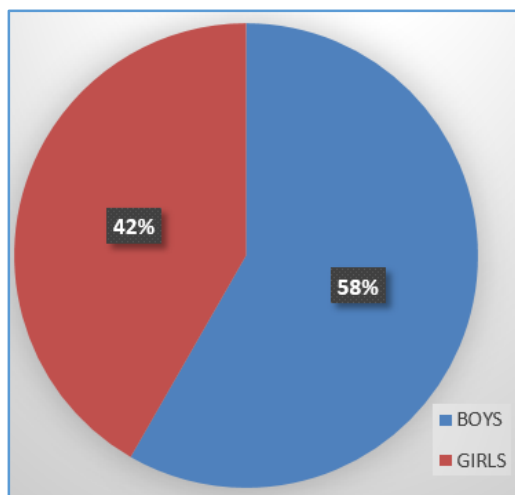


Figure 2. Sex Wise distribution of Breath Holding Spells in the Present Study

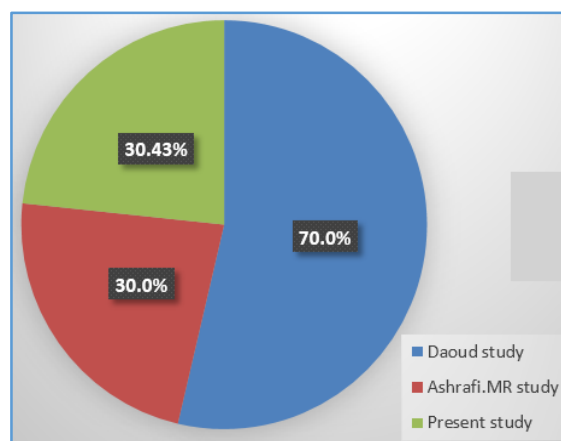


Figure 5. Pie Diagram showing Percentage of Cases with Positive History of Parental Consanguinity in Children with Breath Holding Spells among different Studies

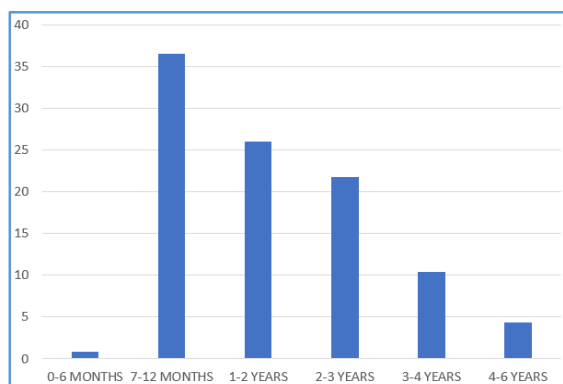


Figure 3. Age Wise distribution of Breath Holding Spells Cases in the Present Study

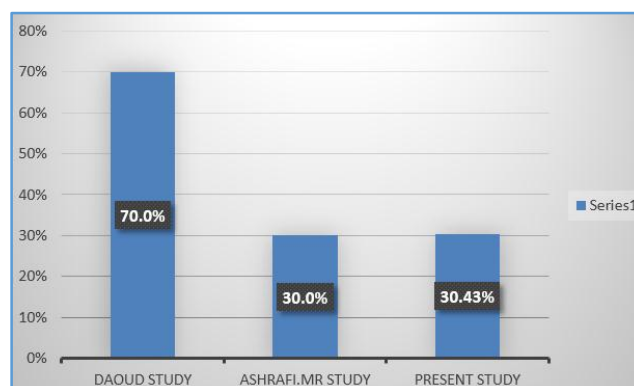


Figure 6. Bar Diagram showing Percentage of Cases with Positive History of Parental Consanguinity in Children with Breath Holding Spells among Different Studies

DISCUSSION

Breath holding spells is a common behavioural disorder of early childhood associated with a lot of parental anxiety, besides carrying a potential for misdiagnosis. The earliest reference to Breath holding spells, then referred to as infantile form of temper tantrums or infantile syncope was made by Rillet and Barthezin in 1843, and by Meigsin in 1848. Subsequently, various authors published their clinical viewpoints on its pathophysiology and prognostic significance. Based on the colour change demonstrated by the child during the spell, Breath holding spells were classified as cyanotic, pallid and mixed. Multiple factors like disturbed parent-child relationship, hereditary autonomic instability, self-asphyxiation, decreased cerebral blood flow secondary to increased intrathoracic pressure due to spontaneous Valsalva manoeuvre and altered cerebral mechanism secondary to various stimuli were implicated for cyanotic Breath holding spells.⁵ Breath holding spell occurs most commonly within the first 18 months of age and 90% or more of breath holders have their initial spell by age 2 years. In approximately half of all children with severe spells, the spells terminate by age 4 years. Virtually, all breath holders cease experiencing episodes by 7 - 8 years of age. A family history of Breath holding spells may be present.⁶ Some investigators found an increased incidence of syncope in later life in patients with a history of Breath holding spells. Aside from this, no lasting sequelae of Breath holding spells are anticipated of children who experience Breath holding spell, 54% - 62% are cyanotic, 19% - 22% pallid and 19% - 24% mixed or unclassifiable. In some children Breath holding spells at their apex occur many times a day. The peak frequency is generally present in the second-year life. Forms of anoxic seizures occurs in early childhood with considerable frequency. Anoxic seizures are dependent on the sudden depression of function of population of neurons due to ischaemia or asphyxia, in contrast to epileptic seizures which is simply the excessive discharge of a population of neurons. Two particularly common form of anoxic seizures in early childhood have been termed Breath holding spells. Breath holding spells have been subdivided as cyanotic or pallid based on the coloration of the child during the event.^{5,7,8} Despite ample literature regarding these two types of anoxic seizures, parents and practitioners continue to confuse these with epileptic seizures. Indeed, in some children Breath holding spells may be the precipitation of epileptic seizure or status epilepticus enhancing the confusion.⁹ The striking association of anaemia with Breath holding spells was first reported in 1963 by Halowach and Thurston.¹⁰ It was hypothesised that the low haemoglobin causes rapid cerebral anoxia due to decreased oxygen carrying capacity of blood that in turn leads to the Breath holding spells. It was also thought that the anaemic children being irritable may be more predisposed to Breath holding spells.

A vivid description of typical pallid Breath holding spells was given by Stephenson.¹¹ The precipitant for typical Breath holding spells is usually sudden, unexpected, unpleasant stimulus, frequently a mild injury to the head. Crying, if present, is not prominent. Generally, cyanosis is not present. Pallor and diaphoresis are common. The patient may be somnolent or go to sleep following the episode. In children experiencing Breath holding spells, whether pallid or cyanotic the first episode usually occurs by 18 months of

age.⁸ Breath holding per se with attendant cyanosis is the characteristic features of cyanotic Breath holding spells. Rouessen describes a cyanotic Breath holding spell which terminates, as frequently these do before syncope is reached.¹² The pathophysiology of cyanotic Breath holding spell is more complicated than that of pallid Breath holding spell. Cyanosis occurs in these patients with surprising rapidity. Cyanotic breath holding involves a diminished pulmonary oxygen reserve. Two infants with cyanotic Breath holding spells studied by Gauk et al¹³ were reported to experience pronounced oxygen desaturation with arterial hypertension and no significant alteration in pulse rate. Anoxic anoxia was deemed to be the mechanism for the loss of consciousness in these patients. A mechanism for cyanotic Breath holding spell was then advanced involving violent crying leading to hypocapnic cerebral ischaemia and respiratory spasm leading to increased intrathoracic pressure as well as apnoea proceeding to hypoxaemia.⁵ The hypocapnia and Valsalva manoeuvre combine to decrease arterial inflow and increase resistance to outflow in the cerebral circulation. It is proposed that interactions among central sympathetic activity, brain stem control of respiration and vasomotor activity, reflexes arising from around and within the respiratory tract and the matching of ventilation to perfusion account for the intrapulmonary shunting and expiratory apnoea occurring in these patients. A recent case control study from Turkey reported maturation delay in myelination of the brainstem as assessed from the interpeak latencies on brainstem auditory evoked potential, as the cause of Breath-holding spells.¹⁴ Pallid and cyanotic Breath holding spells both are frequent causes of syncope and anoxic seizures in early childhood. Both most generally occur in otherwise healthy children and both spontaneously resolve without sequel. History is the mainstay of diagnosis.⁹ Obtaining an accurate and detailed history of the episodes of concern is critical in the diagnosis of Breath holding spells. Pallid Breath holding spells occur in the context of an injury, frequently an unexpected blow to the head. Cyanotic Breath holding spells occur in the setting of anger and upset. Any losses of consciousness or seizure in early childhood that are provoked by either of these antecedents are primarily suspected to be anoxic in character. Epileptic seizures generally not provoked by anger or injury in the setting of a normal general and neurological examination. Laboratory testing usually adds little information. Difficulty in diagnosis may arise when certain of episodes are not witnessed from their initiation. Another diagnostic difficulty, to be discussed later, occurs when Breath holding spells in turn provoke epileptic seizures. Videotape documentation of typical episode may be considerable value.⁹ Patients with pallid Breath holding spells have frequently been studied with an electroencephalogram, during which ocular compression is performed. Patients with Breath holding spells may follow this EEG evolution without significant bradycardia or asystole. Spontaneously recorded Breath holding spells recapitulated this sequence of EEG alterations.^{8,9} Prolonged QT syndrome is rare, but potentially malignant cause of anoxic seizure. It is recommended that an ECG (Electrocardiogram) to screen for prolonged QT syndrome be performed.⁹ Anaemia may be a factor contributing to Breath holding spells in some children. Febrile illness may also be a precipitant of Breath holding spell in some children. Breath

holding spells were observed more frequently in boys than in girls. In our study the ratios were found to be 1.1: 1, 3: 1, 1.7:1 and 1.3: 1 in Ashrafi et al,¹⁵ Lombroso et al,⁵ Diamario et al⁸ and Goraya et al¹⁶ studies respectively. In a group of 384 children (3 months to 4 years) studied by Livingston, the mean age at onset of Breath holding spell was 12 months. In the present study, the minimum age at the onset of first spell was 6 months and upper age was 66 months. We found the mean age at the onset of Breath holding spells was 20.42 months in our study population (n= 115). Bhatia et al¹⁷ reported 80% of their cases experienced Breath holding spells during the first 18 months of age. In Ashrafi et al¹⁵ study, 76.8% of cases had their spells begun during their first year of age. But in the present study, about 63.41% of cases (73 out of 115) had their spells begun during the first 24 months of age. Data from more detailed analyses suggest an autosomal dominant pattern of inheritance in some cases of breath holding spells.^{5,8,9,18} A positive family history of Breath holding spells was found in 27% of our cases (31 out of 115), whereas positive family histories of Breath holding spells were found to be 51.2% and 47.5% in Ashrafi et al¹⁵ and Daoud et al studies respectively. Parental consanguinity was found in 30.43% of our cases, whereas it was 30% and 70% in Daoud et al studies respectively. The most common triggering factors for Breath holding spells in our study found to be anger (45.2%) and pain (41.7%). This finding was in agreement with previous studies. In our study, the most common type was cyanotic Breath holding spells (66.1%) which was in agreement with previous study reports.^{4,5,8,9,15,17} Based on number of previous studies, it is now well established that checking for iron deficiency or anaemia is probably worthwhile and also a trial of iron therapy is beneficial in reducing the frequency of Breath holding spells, especially in children with laboratory evidence of anaemia.¹⁹ Chandra et al study was carried out in Chandigarh with the objective of assessing the haemoglobin levels in children with Breath holding spells and determining the therapeutic role of iron in its management. It was also shown that iron therapy showed a more remarkable therapeutic benefit in controlling the spells in children with evidence of iron deficiency.²⁰

In the present study, anaemia was found in 76.52% (88 out of 115) of cases. After diagnosis of Breath holding spells is established, explanation and reassurance to families is the mainstay of therapy. The occurrence of Breath holding spells per se should not lead to any alteration in the general care of the child.⁸ Breath holding spells usually mimic or are confused with seizure disorder and can be a frightening experience for parents. Since the diagnosis is made clinically, it demands a good history of sequence of events. Lack of incontinence and postictal phase helps to make an accurate diagnosis.

Education and reassurance of the parents, usually all that is needed as these episodes are as a rule self-limited and are outgrown within a few years or by school age. However, treatment of co-existing iron deficiency is needed if it is present, as the spells are made worse by iron deficiency anaemia. It is neither feasible nor helpful to avoid circumstances which may provoke Breath holding spells.⁹ If Breath holding spells occur, placing the child in a lateral recumbent position is appropriate until recovery occurs. Cardiopulmonary resuscitation should generally be avoided. In the considerable minority of patients with particularly

severe Breath holding spells, treatment with atropine Sulphate or methonitrate has been utilised.²¹ Transdermal scopolamine²² or even pacemaker implantation has also been utilised.^{23,24} Recently, evidence for safe and effective use of piracetam, especially in hyperactive children to control Breath holding spells has emerged, but it still lacks FDA approval.^{19,25}

CONCLUSION

The result of this study suggests a new data regarding clinical and epidemiological profile of Breath holding spells and is important for identifying interventional strategies and parental counselling and could serve as baseline data for future approaches on this paediatric clinical entity.

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