Original Research Article

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Electroencephalographic Study in Children with Breath-Holding Spells in a Tertiary Care Hospital in South India

Ravi L.A.[1], D. Shyam Anand[2]

Abstract

Breath holding spells, otherwise called as "Infantile syncope", are well recognized, common clinical entity characteristically seen in infants and younger children aged 6 months to 5 years. Breath holding spells are non-epileptic paroxysmal event that occur in otherwise healthy children. The attacks are benign but may cause fearfulness and anxiety to parents, until the condition is "defused" by explanation and reassurance. The events are self limited and gradually disappear before child reaches 5 years of age . It is important to differentiate breath holding spells from epileptic seizures so that inappropriate treatment with antiepileptics can be avoided. To differentiate from closely resembling epilepsy, one hundred children with breath holding spells in this study, were examined electroencephalographically during sleep between the intervals of the spells. Our study found that all of the children in the study group had normal EEG findings except for one child, which showed slow waves but no epileptic form discharges. Hence it is concluded that EEG study in combination with detailed history and clinical observation is of value in differentiating breath holding spells from convulsive disorders.

Keywords: Breath Holding Spells; EEG; Children; South India.

Introduction

Breath holding spells are common clinical problem affecting five percent of healthy children. The onset of BHS usually occur between 6 months and 18 months of age. In approximately 80% of affected children, the spells commence before 18 months of age and in all cases they begin before 3 years of age. Less than 10 percent have onset more than 2 years of age. The last episode usually occurs by 4 years of age no later than 8 years of age.

Cyanotic spells are three times more common than pallid spells. Most children experience only one or other, but 20% have both type. The frequency of episodes ranges from once a year to several times daily. The spells are varied individually from child to child and even in the same child at different periods. The spells are gradually started to decrease in frequency after 24 months of age [11]. The spells were thought to be a manifestation of disturbances in relationship between child and parents and It was documented that behavioural problems like temper tantrums, hyperactivity and stubbornness, seen in thirty percent of breath holding children [11].

The diagnosis of breath holding spells is usually made clinically based on typical sequence of events initiated by a provocative event such as emotional upset or trauma, followed by crying, cessation of breathing in expiration, developed cyanosis or pallor with or without loss of consciousness.

Although Breath-Holding spells is known to be a benign condition, it should be differentiated from epilepsy by doing EEG,as it is considered to be one among the conditions that mimic seizure.

Olgu Hallioglu et. al. [13], done a study in 2000, at University of Mersin, Turkey "Electroeccephalographic abnormalities in children with breath holding spells"The study reported that interval EEGs

Author's Affiliation: [1]Assistant Professor, Department of Neurology, Institute of Child Health & Hospital for children, Halls road, Egmore Chennai, Tamil Nadu 600008, India. [2]Assistant Professor, Paediatrician, Government Sivagangai Medical College, Sivagangai, Tamil Nadu 630561, India.

Corresponding Author: D. Shyam Anand, Assistant Professor, Government Sivagangai Medical College, Sivagangai, Tamil Nadu 630561, India.
E-mail: shyam1107@gmail.com, laravi92@gmail.com

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showed significant abnormalities in breath holding spells, as in benign rolandic epilepsy of Childhood.

Niels L.Low et. al. [21], conducted a study, "To determine the Electroencephalographic findings in breath holding spells", at Illinois Neuropsychiatric institute, Chicago. All these children but one had normal EEG. One tracing taken during a BHS which showed slow wave but no seizure activity.

Not many studies have been published in the recent years especially in south India. Hence the present study was designed to study EEG abnormalities in the intervals of Breath-Holding Spells in children from 6 months to 5 yrs.

Methods

Experimental Design

All children aged 6 months to 5 years presented with typical Breath-Holding spells in OPD and those who admitted in medical Ward in institute of child health & hospital for children chennai-600008 between May 2016 to October 2016 were included in the study. Children with a haemoglobin level of ≤ 7 gm/dl, H/o febrile convulsions or seizure disorder, known case of cyanotic CHD, developmental delay, or any chronic systemic disease were excluded from the study. Sex matched healthy volunteers were considered as control subjects (N=100). The study was approved by institution ethical committee.

Study Design

Prospective observational study

Study Manoeuvre

1. All children meeting the inclusion criteria were included in the study after getting informed written consent from parents. Detailed history of spells and clinical examination were done. Important clinical findings including anthropometry and vitals signs were noted down in the data collection form.
2. Investigations like Complete Blood Count, C-Reactive Protein, Non Enteric blood Culture, urine analysis, urine culture & sensitivity, Chest X-Ray were performed. CBC was analysed using automated cell counter. Under strict aseptic precautions, One ml of blood was collected by venepuncture into bottles containing Ethylene Diamine Tetra Acetic acid (EDTA) solution and transported immediately to laboratory. In this study, MINDRAY BC-5300, type of automated cell counter was used. The following parameters were measured in this cell counter and were documented.

a. Hemoglobin
b. PCV
c. MCV (Mean corpuscular volume)
d. MCH (Mean corpuscular Hemoglobin)
e. MCHC (Mean corpuscular Hemoglobin concentration)
f. RDW (Red cell distribution width) Type equation here.
g. RBC count
h. Total WBC count, Differential leucocyte count.
i. Platelet count.

6. Electrocardiography :

   The 12 lead surface ECG of the entire case group were obtained using a Bionet cardiocare electrocardiography machine, RR and corrected QT intervals were measured and interpreted by paediatric cardiologist. QT interval was measured as the interval between QRS complex and the end of T wave. The Bazett formula was used for the calculation of corrected QT (QTC =√), which was recorded in milliseconds (ms) or on a normal / abnormal scale on the patient's record.

Echocardiography

Echocardiography was done by paediatric cardiologist in all children with BHS in this study using ATL Philips machine, to rule out congenital heart disease.

Electroencephalogram

All children meeting the inclusion criteria were subjected to undergo Electroencephalogram (EEG) study, to detect abnormalities related to electrical activity of the brain. EEG study was done in neurology ward, ICH, after getting consent from parents. It usually took 30 to 60 minutes to complete. EEG was taken during sleep or on sedation of the child using oral Tricofos in age appropriate dosage. Interpretations of EEG was done as normal or abnormal waves and noted down in the record.

Statistics

- Data was entered in excel sheet. Statistical analysis of data was performed by statistical software SPSS. Outcome variables were categorized as normal or abnormal and their prevalence was expressed as percentage. The primary outcome was expressed as proportion. Chi Square test was used to determine the association between outcome variable an

dependent variable. Independent t test was used to determine the difference between unpaired samples.

If the P value is 0.000 to0.010, it implies Significant at 1% level (Highly Significant) If the P value is 0.011 to 0.050, it implies Significant at 5% level (Significant) If the P value is 0.051 to 1.000, then it is not significant.

Observation

The Table 10,10a and Figure 10 showed that Among 100 children in the studygroup, Mild anemia was noted in 29% of cases, moderate anemia was noted in 53% of cases and in total 82% of cases had low haemoglobin levels (Hb <11 gm/dl), as compared to control group, mild anemia was noted in 40% and moderate anemia in 36% of controls.

Table 1: Frequency distribution of patients based on age in months

Age in months	Group					
	Cases		Controls		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
6-12	33	33.0	40	40.0	73	36.5
13-24	53	53.0	39	39.0	92	46.0
>24	14	14.0	21	21.0	35	17.5
Total	100	100.0	100	100.0	200	100.0

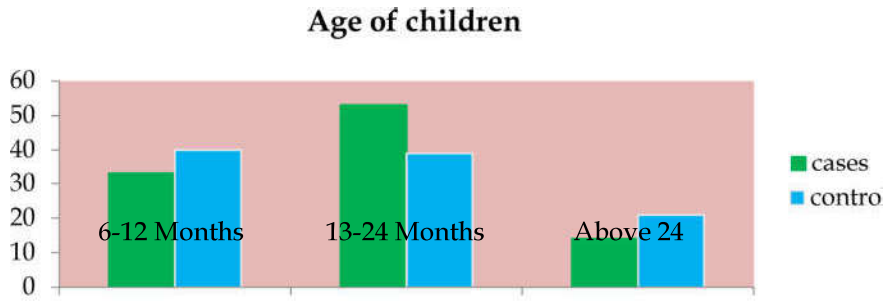

Fig. 1: Frequency distribution of patients based on age in months

The above Table 1 and Figure 1 shows thatAmong 100 children in the study group, around 33% of children were between 6 and 12 months of age, 53% between 13 and 24 months, and 14% above 24 months of age. Maximum cases were seen in the age group of 13-24 months as against in the control group of 6-12 months.

Table 2: Frequency distribution based on Sex

Sex	Group				Total	
	Cases		Controls			
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Male	63	63	60	60	123	61.5
Female	37	37	40	40	77	37.5
Total	100	100	100	100	200	100

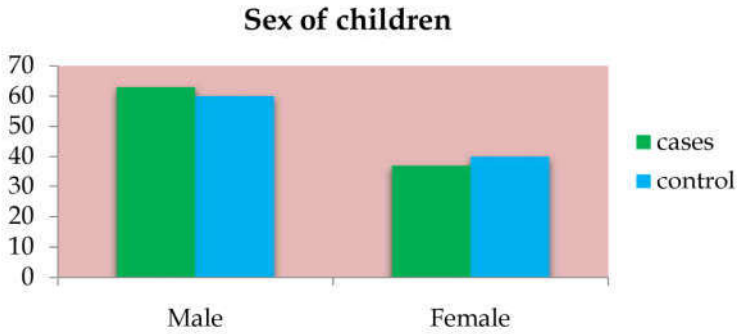

Fig. 2: Frequency distribution based on Sex

The above Table 2 and Figure 2 shows that Among 100 children in the cases group, 63 % were male and 37% were female. With Male : Female is 1.7 : 1.0 in cases group as compared to 1.5 : 1 in control group.

Table 3: Frequency distribution of patients based on age of onset in months

Age onset in months	Group				Total	
	Cases		Controls			
	Frequency	Percent	Frequency	Percent	Frequency	Percent
6-12	68	68	45	45	113	56.5
13-24	31	31	48	48	79	39.5
>24	1	1	7	7	8	4
total	100	100	100	100	200	100

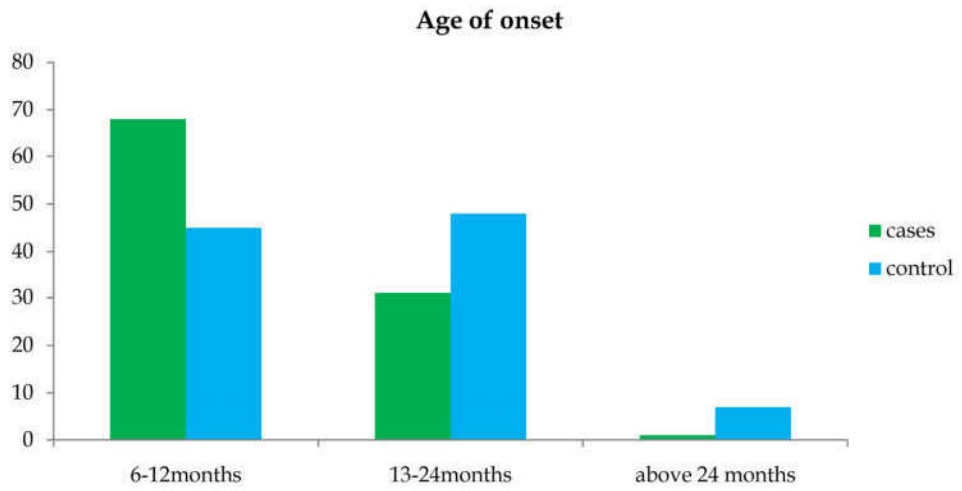

Fig. 3: Frequency distribution of patients based on age of onset in months

The above Table 3 and Figure 3 showed that age of onset of cases was more common in 6 – 12 months of age. Mean age of onset in cases was 12.17 months as compared to controls was 15.96 months There was significant relationship between cases and controls, and was statistically significant, as p-Value was 0.002.

Table 4: Frequency distribution of patients based on Consanguinity history

Consanguinity H/o	Group				Total	
	Cases		Controls			
	Frequency	Percent	Frequency	Percent	Frequency	Percent
No	87	87	86	86	173	86.5
Yes	14	14	13	13	27	13.5
Total	100	100	100	100	200	100

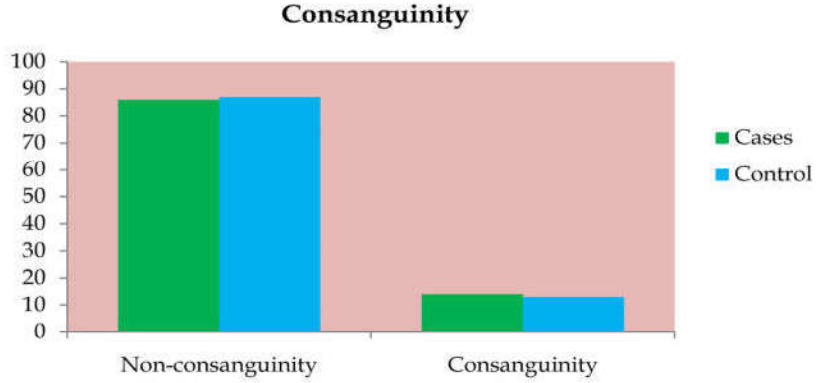

Fig. 4: Frequency distribution of patients based on Consanguinity history

The above Table 4 and Figure 4 showed that Among 100 children in the study group, parental consanguinity was present in 14 % of cases as compared to 13 % of control group.

Table 5: Frequency distribution of patients based on Family history

Family H/o	Group				Total	
	Cases		Controls			
	Frequency	Percent	Frequency	Percent	Frequency	Percent
No	74	74	89	89	163	81.5
Yes	26	26	11	11	37	18.5
Total	100	100	100	100	200	100

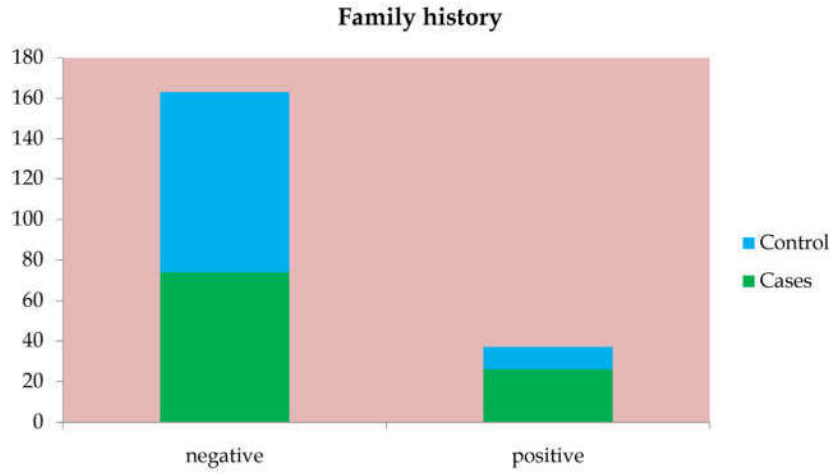

Fig. 5: Frequency distribution of patients based on Family history

The above Table 5 and Figure 5 showed that family history was present in 26% of cases as against 11% of control group. There was significant relationship between cases and controls, and was highly statistically significant, as p-Value was 0.006.

Table 6: Provocative event

	Frequency	Percent	Valid Percent	Cumulative Percent
Emotional	72	72.0	72.0	72.0
Painful stimulus	28	28.0	28.0	100.0
Total	100	100.0	100.0	

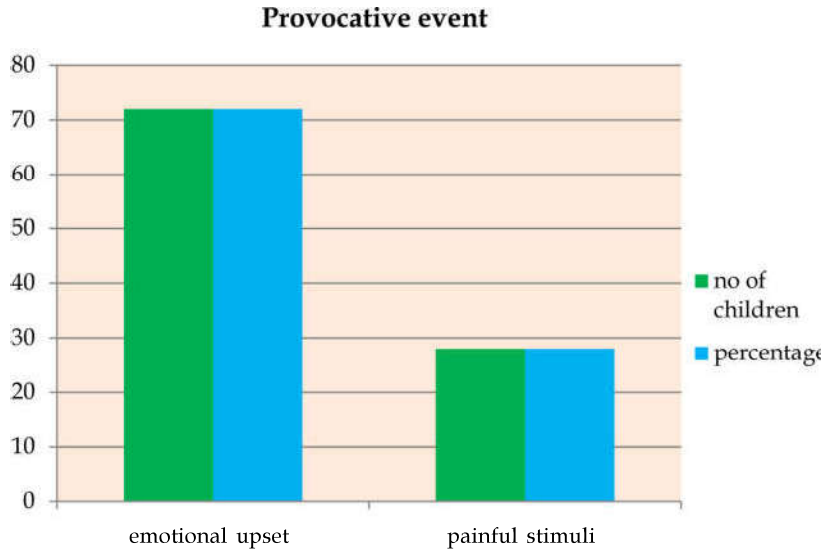

Fig. 6: Frequency distribution based on clinical events

The above Table 6 and Figure 6 showed that Among children with BHS, 72 % cases were initiated by emotional upset and 28% cases by painful stimuli.

Table 7: Frequency distribution based on Type of spells

	Frequency	Percent	Valid Percent	Cumulative Percent
Cyanotic	62	62.0	62.0	62.0
Pallid	26	26.0	26.0	88.0
Mixed	12	12.0	12.0	100.0
Total	100	100.0	100.0	

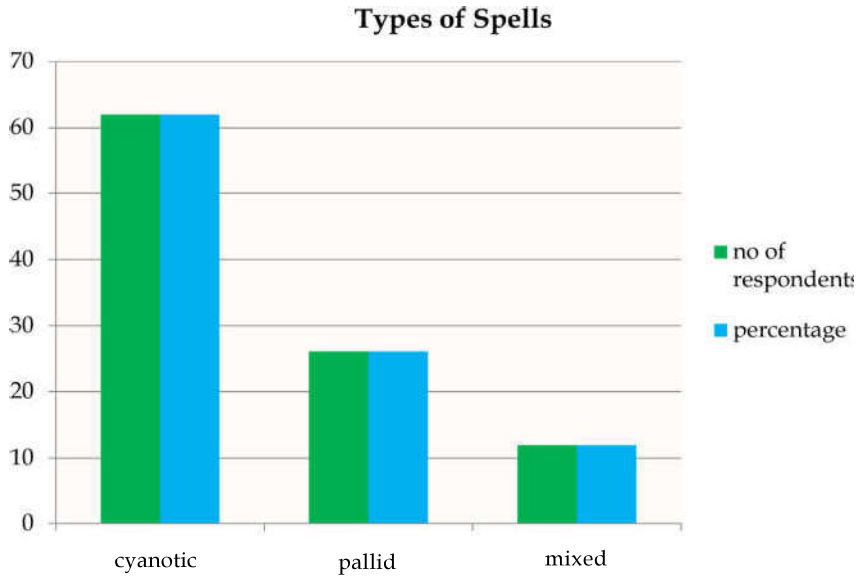

Fig. 7: Frequency of distribution based on type of spells

The above Table 7 and Figure 7 showed that In this study of children with BHS, cyanotic spells were occured in(62%) , pallid spells (26%) and mixed spells (12%).

Table 8: Frequency distribution based on posturing/seizures associated with BHS

	Frequency	Percent	Valid Percent	Cumulative Percent
Nil	56	56.0	56.0	56.0
Posturing	40	40.0	40.0	96.0
Anoxic seizures	4	4.0	4.0	100.0
Total	100	100.0	100.0	

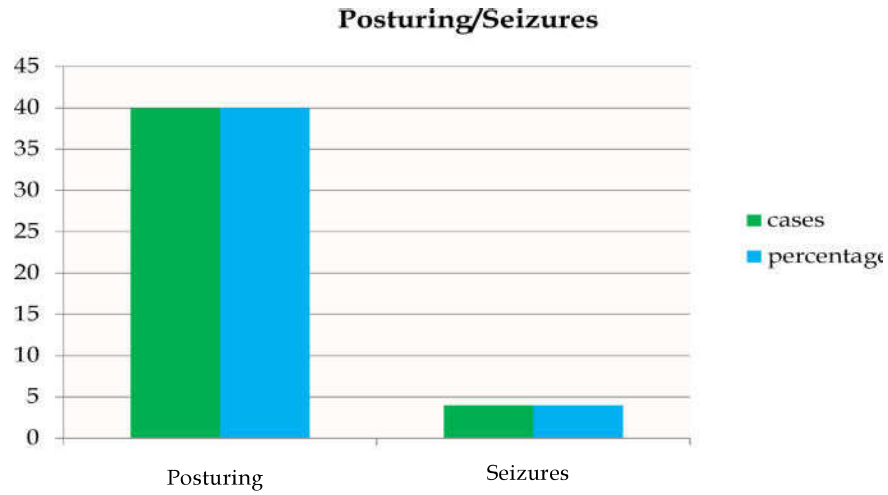

Fig. 8: Frequency distribution based on posturing/seizures associated with BHS

The above Table 8 and Figure 8 showed that Among 100 children with BHS, 40% of cases associated with posturing and 4% of cases developed seizures.

Table 9: Frequency distribution based on frequency of spells per month

Frequency of spells	Cases	Percentage
<5	72	72.0
5-10	24	24.0
10<	4	4.0
Total	100	100

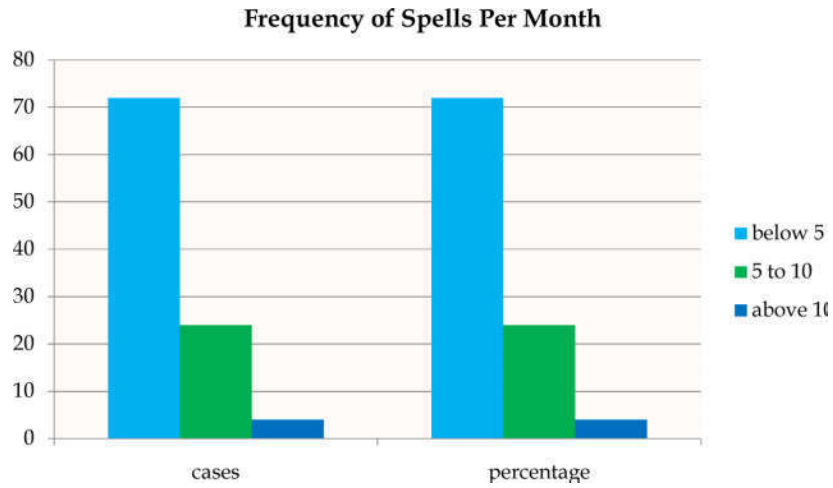

Fig. 9: Frequency distribution based on frequency of spells per month

The above Table 9 and Figure 9 showed that Higher frequency of spells per month > 10 spells seen in 4%, while lower frequency <5 spells per month in 72% of cases.

Table 10: Comparison of haemoglobin levels between cases and controls

Haemoglobin (%)	Cases		Control	
	Number	Percent	Number	Percent
7-9.9 (moderate anemia)	53	53.0	36	36.0
10-10.9 (mild anemia)	29	29.0	40	40.0
≥ 11 (normal)	18	18.0	24	24.0
total	100	100.0	100	100.0

Table 10a: Comparison of mean Hemoglobin levels between cases and controls

	Group	Number	Mean ± 2 SD	Std. Error Mean	P -value
Haemoglobin (%)	Cases	100	9.978 ± 0.925	0.0925	0.026
	Control	100	10.276 ± 0.947	0.0947	

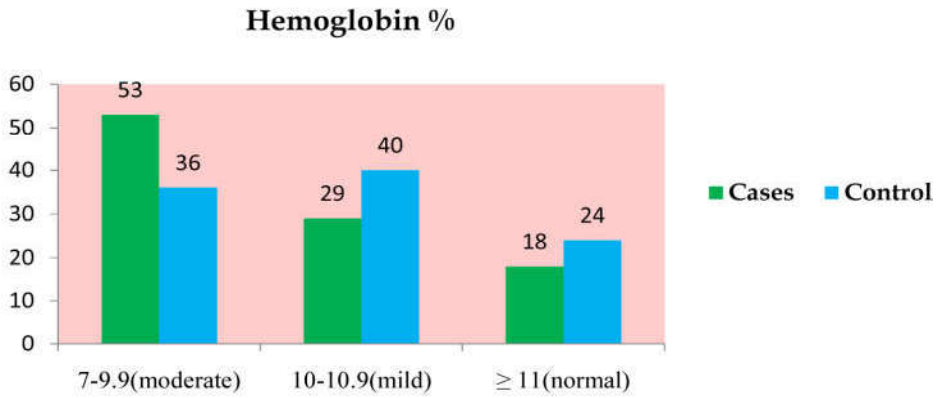

Fig. 10: Comparison of haemoglobin levels between cases and controls

Mean Hemoglobin value of cases was 9.978 ± 0.925 as compared to control of 10.276 ± 0.947. There was

Result

In this prospective observational study, which included 100 children with breath holding spells aged between 6 months and 60 months, were compared with 100 children of simple febrile convulsions in similar age and sex group.

Age parameter revealed that 63% of children with BHS was seen in the age group of 13-24 months. Male to female ratio was 1.7 : 1 and the male preponderance was seen in all age groups. Most common age of onset

Table 11: Comparison of MCV values between cases and controls

	Group	Number	Mean	Std. Deviation	Std. Error Mean
MCV	Cases	100	70.02	3.693	.369
	Control	100	71.14	3.280	.328

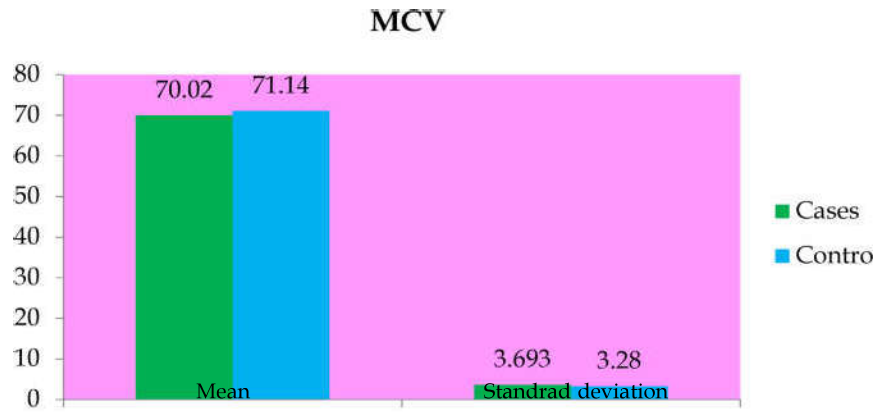

Fig. 11: Comparison of MCV values between cases and controls

The above Table 11 and Figure 11 showed that MCV was significantly lower in children with BHS as compared to controls (70.02 ± 3.693 in patients with BHS, 71.14 ± 3.280 in controls, $p < 0.024$) and 90% cases had low MCV value < 75 fl.

Table 12: Comparison of Haemoglobin and MCV mean values in Cyanotic and Pallid BHS

	Cyanotic BHS (N=62)	Pallid BHS (N=26)	p value
Hemoglobin	10.87 ± 0.93	9.98 ± 0.92	0.56
MCV	70.092 ± 3.679	69.306 ± 3.646	0.14

The above Table 12 that There was no statistically significant difference between cyanotic BHS and pallid BHS in haemoglobin and MCV values.

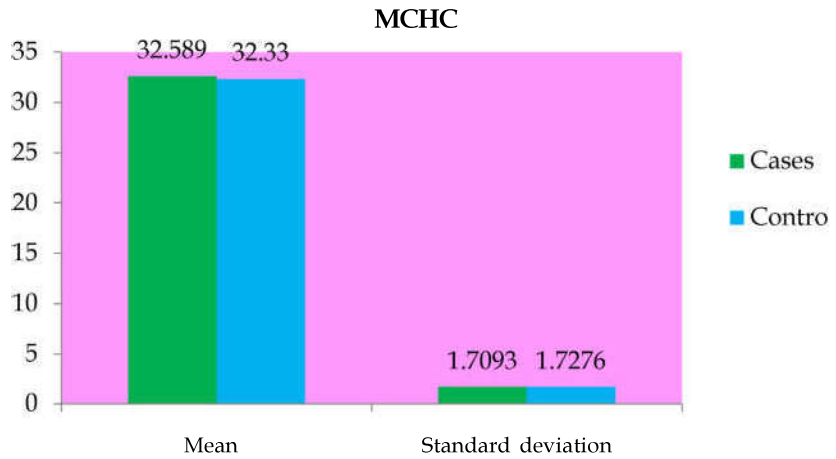

Fig. 12: Comparison of MCHC values between cases and controls

Table 12a: Comparison of MCHC values between cases and controls

	Group	Number	Mean	Std. Deviation	Std. Error Mean
MCHC	Cases	100	32.589	1.7093	.1709
	Control	100	32.330	1.7276	.1728

The above Table 12a and Figure 12 showed that There was no statistical difference between cases and controls, as p-value=0.288. 16% cases had low MCHC value < 31 as compared to controls 18%.

Table 13: EEG between cases and controls

EEG	Group				Total	
	Cases		Controls			
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Normal	99	99	96	96	195	97.5
Abnormal	1	1	4	4	5	2.5
Total	100	100	100	100	200	100

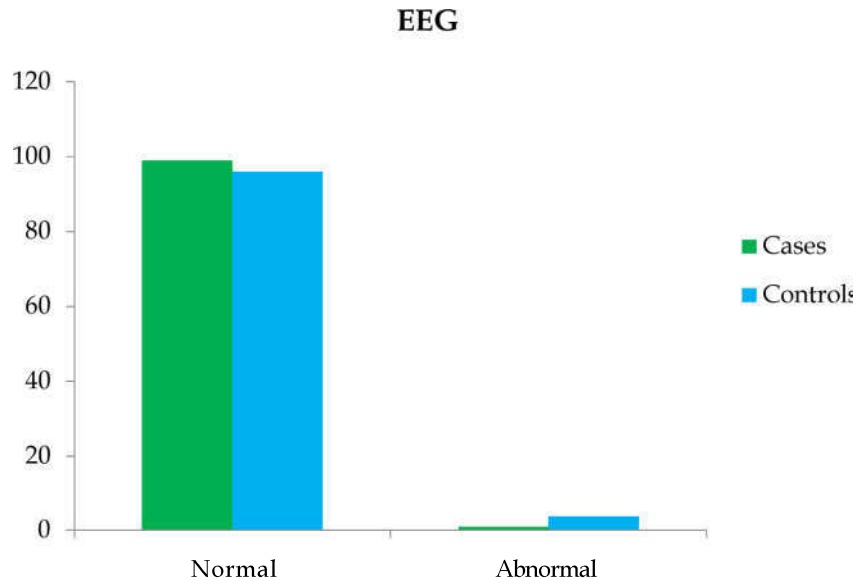

Fig. 13: Comparison of EEG between cases and controls

The above Table 13 and Figure 13 showed that Electroencephalographic study done in all children in the study group were found to have one percent abnormality when compared to control group 4 percent. There was no statistically significant difference between cases and controls, as p-value=0.604.

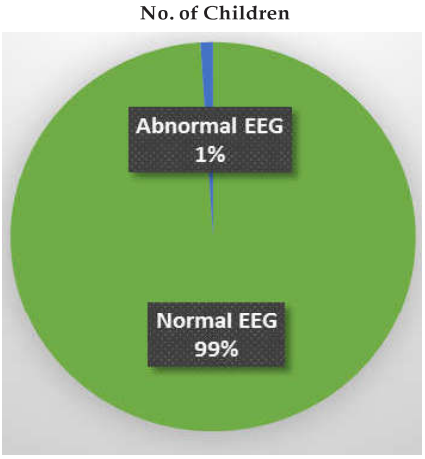

Fig. 14: EEG findings in Breath holding spells cases

Figure 14 showed that electroencephalography done was normal in all children with BHS in this study group except one patient.

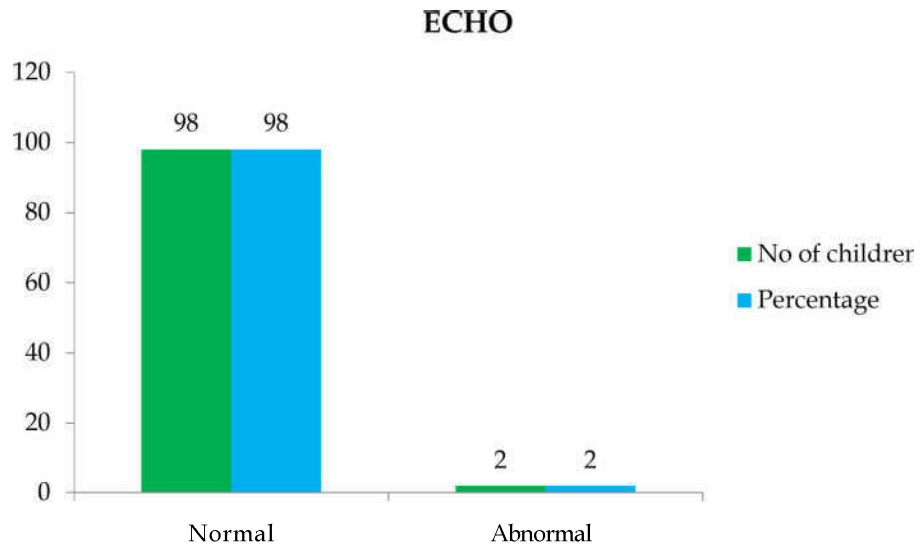

Fig. 15: ECHO in study group

Figure 15 showed that Echocardiography revealed two percent abnormalities in the study group.

of BHS was between 6 and 12 months of age (68%). By 17 months, about 86% cases had their first episode of BHS and by 24 months, 96% cases had their first episode. The mean age of onset was 12.17 months (range 7 to 32 months).

Parental consanguinity was positive in 13 percent of children with BHS. Twenty six percent had a positive family history for occurrence of BHS while 11% positivity was seen in control groups.

Out of these 100 patients with BHS, Cyanotic spells (62%) were more common than pallid (26%) and mixed (12%) spells. The spells were provoked by emotional events such as anger and frustration in 72 % of cases and by painful stimulus in 28 % of cases. Fifty percent cases were associated with posturing and only 5% of cases developed anoxic seizures at the end of the spells. The frequency of spells per month was less than 5 in 72%, 5-10 in 24%, and higher frequency >10 in 4% of cases. There was no significant relationship between the haemoglobin concentration and frequency of occurrence of BHS.

Mean haemoglobin level was significantly lower in children with BHS (9.978 ± 0.925 g/dl) when compared to the controls (10.276 ± 0.947 g/dl) with p value=0.026. Similarly MCV was significantly lower in children with BHS (70.02 ± 3.693) as compared to controls (71.14 ± 3.280) with p value < 0.024. Eighty two percent cases had low haemoglobin value < 11g/dl, 90% cases had low MCV value < 75 fl, and 16 % cases had low MCHC value < 31. Mean haemoglobin values of cyanotic BHS and pallid BHS were 10.87±0.934 and 9.98±0.926 respectively (p = 0.56), Mean MCV values of cyanotic BHS and pallid BHS were 70.092±3.679 and 69.306±3.646 respectively (p=0.14). There were no significant differences for haematological parameters between cyanotic and pallid BHS.

In our study, Electrocardiography was found to be normal in all enrolled children, the mean corrected QT interval (QTc) measured was 398 ± 19.7 msec. Echocardiography revealed atrial septal defect in one patient and patent foramen ovale in another patient.

Table 14: Demographic profile of children with BHS and controls with febrile convulsions

Parameters		BHS (n=100)	Controls (n=100)	p Value
Sex	Male	63	60	
	Female	37	40	
Age of onset	6-12	68	45	0.002
(months)	13-24	31	48	
	>24	1	7	
Parental consanguinity		14	13	
Family history		26	11	

Electroencephalographic study done in all children in the study group were found to have normal study except for one child, which showed slow wave but no epileptic form dicharges. There was no statistically significant difference between cases and controls (p=0.174).

Table 15:

	BHS	Controls	p Value
Haemoglobin (mg/dl), ±S.D	9.978 ±	10.276 ±	0.026*
MCV (fl), ±S.D	70.02 ±	71.14 ±	

Table 16: Clinical characteristics of Breath Holding Spells

Blood Indices	Parameters		N=100
Provocative event	Emotional upset		72
	Painful stimuli		28
Type of spells	Cyanotic		62
	Pallid		26
	Mixed		12
Frequency of spells per month	<5		72
	5-10		24
	>10		4
Severity of spells	Simple		45
	Complicated	Posturing	50
		Seizures	5

Discussion

Breath holding spells are benign and self limited clinical phenomena, observed in early childhood, which terminate in nearly all children by preschool years. These episodes are dramatic, paroxysmal, involuntary events and are quite worrisome for parents. BHS are the common conditions, that closely resemble the epilepsy and also at times they may cause anoxic seizures at the end of the prolonged apnoea. So it is important to differentiate breath holding spells from the epilepsy by doing EEG. Hence this study was planned to determine the EEG abnormalities in children with BHS.

The total number of cases analyzed were 100, out of which 63% were males and 37% were females. This showed greater incidence of BHS in boys as compared to girls (M:F=1.7:1) and it is consistent with Unsal Yilmaz et. al.[28] and Hilal mocan et. al.[19] study.

In our study, the mean age of onset in cases (12.17 months) was significantly lower when compared to controls (15.96 months) (p=). It was found that maximum percentage of children(96%) had their first episode of BHS below 24 months of age, which is consistent with findings of Cesare T. Lombroso et. al.[17], and Unsal Yimaz et. al. [28] study.

Consanguinity among parents was positive in 13% of children with BHS which is consistent with Unsal Yilmaz et. al.[28] study (13.4%). Family history of breath holding spells was seen in 26% of cases as against 11% of control groups and there was significant relationship between occurrence of BHS and family historyof spells (p-Value = 0.006). It is consistent with Cesare T. Lombroso et. al. [17] (23%) , Shabbir Hussain et. al. [14] (29%) and Abdul kerim kolkiran et. al. [16] (27%). Dimario et. al. [6] explained this considerable positive family history by the autosomal-dominant inheritance with incomplete penetrance of BHS.

In this study, Cyanotic spells(62%) were found to be more common than pallid(26%) and mixed (12%) spells , which is similar to the study demonstrated by Cesare T. Lombroso [17] (62%) and Hilal mocan [19] (63%), but contrast to the study shown by Unsal Yilmaz [28] (84.8%).

In our study, frequency of spells per month were graded as <5, 5-10 and >10spells and occurence was 72%, 24%, and 4% of cases respectively, whereas Unsal Yilmaz et. al. [28] and Hilal mocan et. al. [19] studies graded the frequency of spells as <10, 10-30, and >30 spells per month due to higher frequency of the spells in their population. We do not find any plausible explanation for these differences, even though mean haemoglobin values of our study population is lower than their population.

Among 100 children in the study group, Mean haemoglobin values was found to be significantly lower than that of controls (9.978±1.180 g/dl in BHS group, 10.276±1.895 in controls, p=0.026). Mild anemia was noted in 29% of cases, moderate anemia

was noted in 53% of cases and in total 82% of cases had low haemoglobin levels (Hb<11 gm/dl).

Similarly MCV and MCHC were significantly lower in children with BHS as compared to controls. The above results are accepted the proven hypothesis, that there was association between anemia and occurrence of breath holding spells and this is in accordance with results of the studies done by Hilal Mocan et. al.[19], Adulkerim kolkiran et. al. [16] and Abdelrahim[24] et. al.

Electrocardiography was done in all children with BHS in this study for assessing the repolarization of ventricular myocardium to rule out Long QTsyndrome. It was analysed by measuring corrected QT interval, which was found to be normal in all cases. These results are in accordance with study of Unsal Yilmaz et. al.[28], and Abdelrahim et. al.[24], but in contradictory to the study of Movahedian et. al.[20].

To differentiate from closely resembling epilepsy, one hundred children with breath holding spells in this study, were examined electroencephalographically during sleep between the intervals of the spells. Our study found that all of the children in the study group had normal EEG findings except for one child, which showed slow waves but no epileptic form discharges. These results are consistent with studies of Ashrafi et. al.[3]., Niels L. Low et. al.[21], and Anne Lise Olsen et. al. [22].

But our study results are contradictory to the following studies :

- Egyptian study done by Abdelrahim et. al. [24], reported focal mild epileptic discharges in 62.5% cases and generalized dysrhythmia in 3.13% case.
- Turkish study done by Hilal mocan et. al.[19], showed abnormalities in EEGs in 20% of the studied patients in the form of slight or moderate EEG abnormalities
- Another Turkish study done by Hudagolu et. al. [13], observed, 37.5% cases had epileptogenic abnormalities and 12.5% cases had benign EEG variants. There was no statistically significant difference between patients with epileptiform EEG changes and patients with normal EEGs.

The reason for this disparity is not known, may be attributed to genetic, racial and social factors. Limitation of our study was small sample of 100 children. Association between severe anemia (Hb < 7g / dl) and occurrence of BHS is not evaluated in our study. Serum iron studies and response to oral iron therapy was not included in the scope of the study.

Conclusion

To the best of our knowledge, our study is the first to be done in south Indian children, to study the EEG findings in children with breath holding spells. In our study, EEG done in all children with breath holding spells have not shown any significant abnormality except for one which showed slow wave but no epileptiform discharges . And also our study accepted the hypothesis that association of anemia with breath holding spells Hence it is concluded that EEG study in combination with detailed history and clinical observation is of value in differentiating breath holding spells from convulsive disorders.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Akalin F, Turan S, Gu, Ayabakan C, Yilmaz Y. Increased QT dispersion in breath holding spells. Acta Pediatr. 2004;(8):770-774.
2. Anil.B.G, Nedunchezian, Jayanthini.V et. al, Breath Holding Spells: Evaluation of autonomic nervous system function, Indian Pediatr 2005;42:923-927.
3. Ashrafi MR, Mohammed M, Shervin Badve R. Efficacy of piracetam in treatment of breath holding spells Iran. J Pediatr. 2002;12(4):33-6.
4. Bhatia MS, Singhal PK, Dhar NK, Nigam VR. Breath holding spells: an analysis of 50 cases. Indian paediatr 1990;27(10):1073-9.
5. Daoud AS, Batieha A, al-Sheyyab M, Abukteish F, Hijazi S. Effectiveness of iron therapy on breath-holding spells. J pediatr 1997;130:547-550.
6. DiMario FJ. Breath holding spells in childhood. Ame J Dis child (1960), 1992;146(1):125-131.
7. DiMario FJ, Sarfarazi M. Family pedigree analysis of children with severe breath holding spells. J Pediatr. 1997;130(4):647-651.
8. DiMario FJ Jr. Prospective study of children with cyanotic and palli breath holding spells. Paediatrics 2001;107:265-9.
9. DiMario FJ, Burleson JA. Autonomic nervous system function in severe breath holding spells. Pediatr. Neurol. 1993;9(4):268-274
10. Galen N, Breningstal MD, Breath holding spells. Pediatr Neurol 19h96;14:91-7.
11. Garza, J.E., Fenichel's Clinical Pediatric Neurology. 7th edition. Elsevier health sciences publication, Page 15-18.

12. Gauk EW, Kidd L, Prichard JS. Mechanism of seizures associated with breath holding spells. N Eng J Med 1963;268:1436-41.

13. Hallliogl O, Ozge A, Yilgor E, Topaloglu AK, Canim A. Electroencephalographic abnormalities in children with Breath holding. Mersin universetesi tip fakultesi dergisi, 2000;2:148-152.

14. Hussain S, Afzal M, Imam SM, Sabir MU et. al. Demographic profile and efficacy of iron supplementation in children with breath holding spells and anemia on reduction in frequency of these spells. Pak Armed Forces Med J2016;66(suppl-1): S26-30.

15. Kliegman RM, Stanton, St Geme JS Schor NF, Behrman RE., Nelson text book of paediatrics 20th edition, Elsevier health sciences publication; Vol (2); Page 2800-2862.

16. Kolkiran A, Tutar A, Atalay S, Deda G, Cin S. Autonomic nervous system functions in patients with breath holding spells and effects of iron deficiency. Acta paediatr. 2005;94:1227-1231.

17. Lombroso CT, Lerman P. Breath holding spells (cyanotic and pallid infantile syncope). Paediatrics. 1967;39(4):563-581.

18. Mclntosh, N, Helms, P. Smyth,R.L., Forfar and Arneil's textbook of pediatrics. 7th edition. Churchill Livingstone publishers, Page 841-870.

19. Mocan H, Yildiran A, Orhan F, Erduran E. Breath holding spells in 91 children and response to treatment with iron. Arch Dis child 1999;81(3)261-2.

20. Movahedian AH, Heidarzadeh Arani M, Motaharizad M et. al., Evaluation of Q dispersion in children with Breath holding spells, Iran J Child Neurol. Winter 2016;10(1):2-30.

21. Niels L.Low, Erna L Gibbs, Frederic A. Gibbs, Electroencephalographic findings in breath holding spells, Newyork neuro J child Neurol. 1954.

22. Olsen AL, Mathiasen R, Rasmusen NH, Knudsen FU. Long term prognosis for children with breath holding spells. Dan Med Bull 2010;57(11):A4217.

23. Orii KE, Kato Z, Osamu F, Funato M, Kubodero U, Inoue R et. al. Changes of autonomic nervous system function in patients with breath holding spells treaed with iron. J Child Neurol. 2002;17:333-40.

24.Sadek AA, Mohamed MM, Ahmed sharaf MM et al, Clinic laboratory profile of breath holding spells in children in Sohag University Hospital, Upper Egypt, Egyptian pediatr 2016;8(2):222-31.

25.Seham F.A.Azab, Ahmed G.siam, Safaa H saleh et al, Novel findings in Breath holding spells in Zagzig university, Egypt. J med 2015;94(25).

26.Swaiman, K.F. and Ashwal, S. and Ferriero, D.M. and Schor, N.F., Swaiman's Pediatric Neurology: Principles and Practice, 5th editon; Elsevier Health Sciences: Vol (1); pp.900-904.

27. World Health Organization. Iron Deficiency Anaemia. Assessment, Prevention and control. A Guide for Progra Managers. WHO/NHD/013; Geneva: 2001.

28.Yilmaz U, Doksoz O, Celik T, Akinci G, Mese T, Yilmaz TS. The value of neurologic and cardiologic assessment in breath holding spells. Pak J Med sci 2014;30(1);59-64.