



Original Article

## Study of Qt Interval Abnormalities in Electrocardiogram in Children with Breath Holding Spells

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### ABSTRACT

**Aim:** The aim of the present study was to assess QT interval abnormalities in ECG among children with breath-holding spells.

**Methods:** This study was conducted in the Department of Paediatrics, National Institute of Medical Sciences and Research (NIMS), Jaipur, Rajasthan for the period of 18 months. All patients >6 months to <5 Years of age with diagnosis of breath holding spells attending Department of Paediatrics, National Institute of Medical Sciences and Research (NIMS), Jaipur, Rajasthan.

**Results:** The mean age of children in the breath-holding spells group was  $3.03 \pm 1.16$  years, while in the healthy group it was  $2.99 \pm 1.23$  years. Regarding sex distribution, 19 (63.3%) children in the breath-holding spells group were males and 11 (36.7%) were females, whereas in the healthy group, 18 (60.0%) were males and 12 (40.0%) were females. 21 (70.0%) children in the breath-holding spells group had normal nutritional status compared to 25 (83.3%) in the healthy group. Malnutrition was observed in 9 (30%) children in the breath-holding spells group and 5 (16.7%) in the healthy group. The mean height of children in the breath-holding spells group was  $93.39 \pm 11.50$  cm compared to  $91.93 \pm 12.31$  cm in the healthy group ( $p=0.64$ ). The mean weight was  $12.85 \pm 2.56$  kg in the breath-holding spells group and  $11.51 \pm 2.40$  kg in the healthy group ( $p=0.07$ ). The mean PR interval was  $155.95 \pm 24.26$  ms in the breath-holding spells group and  $158.27 \pm 24.42$  ms in the healthy group, with no significant difference ( $p=0.70$ ). All 30 (100%) children in the breath-holding spells group were symptomatic, presenting with crying spells or loss of consciousness, whereas all 30 (100%) children in the healthy group were asymptomatic.

**Conclusion:** These findings highlight the importance of integrated clinical, electrocardiographic, and hematological evaluation for early identification of children at potential risk of arrhythmias.

**Keywords:** Breath-holding spells; QT interval; ECG; Iron deficiency; Pediatric arrhythmia.

### INTRODUCTION

Breath-holding spells (BHS) are a form of paroxysmal disorder commonly observed in infancy and early childhood. They are characterized by involuntary episodes of apnea, changes in skin coloration, and in some cases, transient loss of consciousness. Breath-holding spells typically occur in otherwise healthy children and are triggered by emotional or painful stimuli, including frustration, fear, anger, or minor trauma. Although BHS are considered benign and self-limiting, they frequently generate considerable concern among caregivers due to their dramatic clinical presentation, which may resemble seizure activity or cardiac events.<sup>1,2</sup>

The prevalence of BHS varies across populations but is generally reported to affect approximately 1% to 5% of all children, with a slight male predominance. The onset of BHS most commonly occurs between 6 months and 2 years of age, peaking around 18 months, and episodes usually resolve spontaneously by the age of 5 to 6 years.<sup>3,4</sup> Epidemiological studies have shown that familial clustering is frequent, suggesting a potential genetic predisposition. Several researchers have reported that up to 30% of children with BHS have a positive family history, indicating the likelihood of an inherited susceptibility.<sup>5</sup>

Clinically, BHS are classified into two primary types based on the predominant colour change during the episode: cyanotic and pallid. Cyanotic BHS are triggered predominantly by anger or frustration and are characterized by prolonged expiration, apnea, and a bluish discoloration of the lips and skin secondary to hypoxia. In contrast, pallid BHS are typically precipitated by a sudden fright or minor trauma, leading to a transient loss of consciousness accompanied by pallor, bradycardia, or even asystole in severe cases. A mixed type, combining features of both cyanotic and pallid spells, has also been described, although it is less common.<sup>6,7</sup>

The natural history of BHS suggests a favourable prognosis, with most children experiencing spontaneous resolution by early school age. However, the episodic nature of BHS, combined with its dramatic presentation, often leads to repeated medical consultations and anxiety among families. Early recognition, education, and reassurance are therefore central components of management. Identifying children at risk for associated complications, such as prolonged QT intervals or underlying cardiac pathology, is equally important to prevent adverse outcomes.<sup>8,9</sup> Emerging research has begun to elucidate the molecular and genetic underpinnings of BHS. Studies suggest that mutations in genes regulating autonomic nervous system function, catecholamine metabolism, and cardiac ion channels may contribute to susceptibility. Genetic investigations have demonstrated associations between BHS and variants in genes such as SCN5A, which encodes a sodium channel implicated in cardiac conduction, highlighting potential overlap with inherited arrhythmogenic disorders.<sup>10,11</sup>

The aim of the present study was to assess QT interval abnormalities in ECG among children with breath-holding spells.

## **MATERIALS AND METHODS**

This study was conducted in the Department of Paediatrics, National Institute of Medical Sciences and Research (NIMS), Jaipur, Rajasthan for the period of 18 months. All patients >6 months to <5 Years of age with diagnosis of breath holding spells attending Department of Paediatrics, National Institute of Medical Sciences and Research (NIMS), Jaipur, Rajasthan.

### **INCLUSION CRITERIA:**

1. Children of all sexes aged >6months to <5 years with typical history of breath-holding spells or those who have typical spell during examination (witnessed) will be included as cases.
2. Healthy children of all sexes >6months to <5years coming for routine check vaccination in well-baby clinic will be included as controls.
3. Children for whom consent has been given by parents to participate in this study.

### **EXCLUSION CRITERIA**

1. Children <6months and >5years of age.
2. Children with:
  - Cardiac diseases
  - Central nervous system diseases
  - Endocrinal disorders
  - Metabolic disease
  - Those receiving drugs such as anti-histamines, macrolide, quinolone, ondansetron and furosemide.

## **METHODOLOGY**

After obtaining permission from the Scientific and Ethics Committee of National Institute of Medical Sciences & Research, Jaipur, children fulfilling the inclusion criteria were enrolled in the study. Written informed consent was obtained from the parents or guardians after explaining the purpose and procedures of the study. Clinical diagnosis of breath-holding spells was made based on detailed history and physical examination, and corroborated with parental description. Socio-demographic and clinical data, including age, gender, type of breath-holding spells (cyanotic, pallid, or mixed), frequency, duration, and family history, were recorded on a specially designed semi-structured proforma.

All enrolled children underwent a standard 12-lead electrocardiogram (ECG). The QT interval, corrected QT interval (QTc calculated using Bazett's formula), were measured and recorded. Abnormalities were defined according to age-appropriate pediatric reference values. Additional investigations, including complete blood count, serum iron, and ferritin levels, were performed to identify associated iron deficiency anemia. Following data collection, appropriate statistical methods were applied to assess the prevalence and correlation of QT interval abnormalities with clinical and demographic parameters under the supervision of a statistician.

### **TECHNIQUE:**

- Clinical diagnosis based on detailed history and parental report.
- Semi-structured proforma designed for demographic and clinical details.
- 12-lead Electrocardiogram (ECG) for measurement of QT and QTc.
- Iron profile to assess associated iron deficiency.
- Statistical analysis using SPSS and Microsoft Excel for correlation and prevalence assessment.

**RESULTS**

**Table 1: Demographic Profile of Study Participants**

Variable	Breath-Holding Spells (n=30)	Healthy (n=30)
Age (years)	3.03 ± 1.16	2.99 ± 1.23
Sex		
Male	19 (63.3%)	18 (60.0%)
Female	11 (36.7%)	12 (40.0%)

The mean age of children in the breath-holding spells group was 3.03 ± 1.16 years, while in the healthy group it was 2.99 ± 1.23 years. Regarding sex distribution, 19 (63.3%) children in the breath-holding spells group were males and 11 (36.7%) were females, whereas in the healthy group, 18 (60.0%) were males and 12 (40.0%) were females.

**Table 2: Nutritional Status, Anthropometric Measurements and ECG Parameters**

Category	Breath-Holding Spells	Healthy	p- value
Normal	21 (70.0%)	25 (83.3%)	
Malnutrition	9(30%)	5 (16.7%)	0.41
<b>Anthropometric Measurements</b>			
Height (cm)	93.39 ± 11.50	91.93 ± 12.31	0.64
Weight (kg)	12.85 ± 2.56	11.51 ± 2.40	0.07
Head Circumference (cm)	48.81 ± 1.98	48.42 ± 2.22	0.46
<b>ECG Parameters</b>			
Heart Rate (bpm)	80.17 ± 7.20	76.37 ± 10.54	0.13
PR Interval (ms)	155.95 ± 24.26	158.27 ± 24.42	0.70
QT Interval (ms)	404.18 ± 46.25	371.23 ± 41.59	0.005*
QTc Interval (ms)	426.56 ± 48.47	413.49 ± 41.56	0.04*

21 (70.0%) children in the breath-holding spells group had normal nutritional status compared to 25 (83.3%) in the healthy group. Malnutrition was observed in 9 (30%) children in the breath-holding spells group and 5 (16.7%) in the healthy group. The mean height of children in the breath-holding spells group was 93.39 ± 11.50 cm compared to 91.93 ± 12.31 cm in the healthy group (p=0.64). The mean weight was 12.85 ± 2.56 kg in the breath-holding spells group and 11.51 ± 2.40 kg in the healthy group (p=0.07). The mean head circumference was 48.81 ± 1.98 cm in the breath-holding spells group compared to 48.42 ± 2.22 cm in the healthy group (p=0.46). The mean heart rate in the breath-holding spells group was 80.17 ± 7.20 bpm compared to 76.37 ± 10.54 bpm in the healthy group, not statistically significant (p=0.13). The mean PR interval was 155.95± 24.26 ms in the breath-holding spells group and 158.27 ± 24.42 ms in the healthy group, with no significant difference (p=0.70). The mean QT interval was significantly higher in the breath-holding spells group (404.18± 46.25 ms) compared to the healthy group (371.23 ± 41.59 ms) (p=0.005). Similarly, the mean QTc interval was also significantly higher in the breath-holding spells group (426.56 ± 48.47 ms) compared to the healthy group (413.49 ± 41.56 ms) (p=0.04).

**Table 3: Hematological Parameters and Anemia status**

Hematological Parameters	Breath-Holding Spells (Mean ± SD)	Healthy (Mean ± SD)	p-value
Hemoglobin (g/dL)	11.69 ± 1.27	12.27 ± 1.12	0.06
Serum Iron (mcg/dL)	74.89 ± 21.29	81.25 ± 25.02	0.03
TIBC (mcg/dL)	365.63 ± 63.73	330.29 ± 62.34	0.04
<b>Anemia status</b>			
Normal	20 (66.7%)	26 (86.7%)	
Anemia	10 (33.3%)	4 (13.3%)	0.04*

The mean hemoglobin level in the breath-holding spells group was 11.69 ± 1.27 g/dL, compared to 12.27 ± 1.12 g/dL in the healthy group, with the difference not reaching statistical significance (p= 0.06). The mean serum iron level was 74.89 ± 21.29 mcg/dL in the breath-holding spells group and 81.25 ± 25.02 mcg/dL in the healthy group, demonstrating a statistically significant difference (p = 0.03). Additionally, the mean total iron-binding capacity (TIBC) was higher in the breath-holding spells group (365.63 ± 63.73 mcg/dL) compared to the healthy group (330.29 ± 62.34 mcg/dL), and this difference was also statistically significant (p = 0.04). 20 (66.7%) children in the breath-holding spells group had normal hemoglobin levels, while 10 (33.3%) were anemic. In contrast, 26 (86.7%) children in the healthy group were normal and 4 (13.3%) were anemic. This difference was statistically significant (p=0.04), indicating a higher prevalence of anemia among children with breath-holding spells.

**Table 4: Clinical presentation, diagnosis & outcome**

Variable	Breath-Holding Spells	Healthy
Symptomatic	30 (100%)	0

Asymptomatic	0	30 (100%)
<b>Diagnosis and Outcome</b>		
Final Diagnosis	30 (100%)	0
BHS		
Healthy Diagnosis	0	30 (100%)
Improved Outcome	30 (100%)	NA

All 30 (100%) children in the breath-holding spells group were symptomatic, presenting with crying spells or loss of consciousness, whereas all 30 (100%) children in the healthy group were asymptomatic. All children in the breath-holding spells group were diagnosed with breath-holding spells, while all children in the healthy group were categorized as healthy. All cases in the breath-holding spells group showed improvement in outcome.

**Table 5: Types of Breath-Holding Spells**

Type	Frequency (%)
Pallid	16 (53.3%)
Cyanotic	14 (46.7%)

Among children with breath-holding spells, 16 (53.3%) had pallid type spells, while 14 (46.7%) had cyanotic type spells, indicating a slightly higher prevalence of pallid type. No statistical comparison was applicable as this analysis was confined to a single group.

**Table 6: QT Interval Classification**

Category	Breath-Holding Spells	Healthy	p-value
Normal QT	23 (76.7%)	30 (100.0%)	
Prolonged QT	7 (23.3%)	0 (0.0%)	0.01

23 (76.7%) children in the breath-holding spells group had normal QT intervals, while 7 (23.3%) exhibited prolonged QT intervals. In contrast, all 30 (100.0%) children in the healthy group had normal QT intervals, and none showed QT prolongation. QT prolongation was notably more frequent among children with breath-holding spells, and this difference was found to be statistically significant ( $p = 0.01$ ).

## DISCUSSION

The present study was undertaken to evaluate the clinical, hematological, and electrocardiographic profile of children presenting with breath-holding spells (BHS) and to compare them with healthy controls. The findings provide meaningful insights into the interplay between autonomic function, iron metabolism, and cardiac electrophysiology in pediatric BHS. The discussion below critically interprets each table in light of existing literature.

The present study demonstrated that the mean age of children with BHS ( $3.03 \pm 1.16$  years) was comparable to that of healthy controls ( $2.99 \pm 1.23$  years). This finding reinforces that BHS is primarily an age-dependent phenomenon. The peak incidence around 2–4 years aligns with the developmental stage of autonomic nervous system maturation. These findings are consistent with DiMario et al. (2001), who reported that BHS commonly occurs in early childhood with no strong gender predilection.<sup>12</sup> Similarly, Colina et al. (2010) observed comparable demographic distributions between cases and controls.<sup>13</sup> However, some studies have reported a stronger male predominance. For instance, Daoud et al. (1997) noted a higher prevalence in males, suggesting possible hormonal or behavioral influences.<sup>14</sup> The lack of such difference in the present study may reflect sample size or regional variations. Although a higher proportion of malnutrition was observed in the BHS group (30%) compared to controls (16.6%), the difference was not statistically significant ( $p=0.41$ ). This suggests that while malnutrition may coexist with BHS, it may not be an independent determinant. However, the trend toward poorer nutritional status in BHS children cannot be ignored, as nutritional deficiencies—especially micronutrients—may influence neurological and autonomic stability.

Idro et al. (2008) similarly found no statistically significant association between general nutritional status and BHS.<sup>15</sup> In contrast, Hartfield et al. (2002) emphasized that micronutrient deficiencies, particularly iron deficiency, play a more critical role than overall nutritional status.<sup>16</sup> Thus, the findings indicate that gross nutritional assessment may underestimate subtle deficiencies relevant to BHS pathophysiology. No significant differences were observed in height, weight, or head circumference between the two groups, indicating comparable growth parameters. This suggests that BHS does not adversely affect physical growth and is not associated with chronic developmental compromise. These findings are consistent with Stephenson (1978), who reported normal growth patterns in children with BHS.<sup>17</sup> Similarly, Leung et al. (2005) found no anthropometric differences between affected children and controls.<sup>18</sup>

However, some authors have suggested that recurrent episodes may indirectly affect feeding behaviour. Singhi et al. (2003) noted subtle growth delays in severe cases.<sup>19</sup> The absence of such findings in the present study may reflect early diagnosis and management. A significant increase in QT interval ( $p=0.005$ ), and QTc interval ( $p=0.04$ ) was observed in the BHS group. These findings highlight underlying autonomic dysregulation and altered cardiac repolarization in children with BHS. Prolongation of QT and QTc intervals suggests increased vulnerability to arrhythmogenic events, although clinically

significant arrhythmias are rare. DiMario (2001) reported similar findings of prolonged QT intervals in children with BHS, attributing it to autonomic imbalance.<sup>12</sup> Additionally, Southall et al. (1985) demonstrated abnormal cardiac repolarization in pediatric syncope-related conditions.<sup>20</sup>

Conversely, McWilliam et al. (2003) found no significant QT prolongation in their cohort, suggesting that ECG changes may not be universal.<sup>21</sup> This discrepancy may be due to methodological differences or population variability. All children exhibited normal sinus rhythm, but QT prolongation was significantly higher in the BHS group (23.3%) compared to controls (0%) ( $p=0.01$ ). This indicates that while baseline rhythm remains normal, repolarization abnormalities are more frequent in BHS. Lombroso and Lerman (1967) described similar electrophysiological findings, suggesting that BHS may involve vagally mediated cardiac inhibition.<sup>22</sup> Likewise, DiMario et al. (1990) observed increased QT prolongation among affected children.<sup>23</sup> However, some studies report lower prevalence rates. Kahn et al. (1996) found minimal ECG abnormalities, indicating that QT prolongation may not be consistently present.<sup>24</sup> The study revealed significantly lower serum iron ( $p=0.03$ ) and higher TIBC ( $p=0.04$ ) in the BHS group, while hemoglobin levels were lower but not statistically significant ( $p=0.06$ ). These findings strongly support the role of iron deficiency in BHS pathophysiology. Iron plays a crucial role in neurotransmitter synthesis and autonomic regulation.

Hartfield et al. (2002) demonstrated significant improvement in BHS following iron therapy, even in non-anemic children.<sup>16</sup> Similarly, Daoud et al. (1997) reported reduced iron stores in affected children.<sup>14</sup> In contrast, Colina et al. (2010) found no consistent association between hemoglobin levels and BHS<sup>13</sup>, suggesting that iron deficiency without overt anemia may be more relevant. A significantly higher prevalence of anemia was observed in the BHS group (33.3%) compared to controls (13.3%) ( $p=0.04$ ). This reinforces the association between anemia and BHS, possibly through impaired oxygen delivery and altered neuronal excitability. Daoud et al. (1997) reported similar findings, highlighting anemia as a key contributing factor.<sup>14</sup> Idro et al. (2008) also found a higher prevalence of anemia among affected children.<sup>15</sup> However, Stephenson (1978) suggested that anemia is not universally present in all cases<sup>17</sup>, indicating heterogeneity in disease mechanisms. All children in the BHS group were symptomatic, while all controls were asymptomatic ( $p<0.001$ ). This was expected given the study design but underscores the clear clinical distinction between affected and healthy populations.

DiMario (2001) described crying, cyanosis, and transient loss of consciousness as hallmark features.<sup>12</sup> Similarly, Lombroso (1967) emphasized stereotypical presentation patterns.<sup>25</sup> All cases were correctly diagnosed as BHS and showed improvement. This supports the benign and self-limiting nature of the condition, especially with appropriate reassurance and management. Colina et al. (2010) reported excellent prognosis in most children.<sup>13</sup> However, Southall et al. (1985) cautioned about rare severe cases with cardiac involvement.<sup>26</sup> Pallid spells (53.3%) were slightly more common than cyanotic spells (46.7%). This distribution aligns with autonomic imbalance, where pallid spells are often vagally mediated. Lombroso (1967) reported similar proportions.<sup>27</sup> However, DiMario (2001) found cyanotic spells to be more common<sup>12</sup>, suggesting population variability. A significantly higher proportion of QT prolongation was observed in the BHS group (23.3%) compared to controls (0%) ( $p=0.01$ ). This finding is clinically important, as it links BHS with altered cardiac repolarization and potential arrhythmic risk. Southall et al. (1985) reported similar associations between syncope-related conditions and QT prolongation.<sup>20</sup> DiMario et al. (1990) also highlighted prolonged QT intervals in BHS.<sup>27</sup> Conversely, McWilliam et al. (2003) did not observe significant QT abnormalities, indicating variability across studies.<sup>22</sup>

The findings of the present study collectively suggest that breath-holding spells are associated with underlying autonomic dysfunction, as evidenced by QT and QTc prolongation. In addition, a strong association with iron deficiency anemia was observed, indicating the role of hematological factors in the pathogenesis of the condition. Despite these physiological alterations, the overall clinical course of breath-holding spells was found to be benign, with a favorable prognosis in all cases. Taken together, these results support a biopsychophysiological model in which neurological immaturity, hematological deficiencies, and cardiac electrophysiological changes interact to produce the characteristic clinical manifestations of breath-holding spells.

## CONCLUSION

The study highlights the importance of integrated clinical, biochemical, and electrocardiographic evaluation rather than isolated interpretation. Certain limitations exist, including single-center design, relatively small sample size, and lack of long-term follow-up. Further large-scale, multicentric studies with extended follow-up are recommended to better understand the long-term cardiac implications of BHS.

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