

## Autonomic dysfunction in children with cerebral palsy

Rajkumar G<sup>1</sup>, Anbarasi M<sup>2</sup>

<sup>1</sup> Associate Professor of Paediatrics, <sup>2</sup> Professor, Department of Physiology, Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur, Tamil Nadu, India.

### Abstract

**Background:** Cerebral palsy is a group of disorder that affects the motor function. Some children with cerebral palsy (CP) were also found to have symptoms of autonomic dysfunction like high heart rate, bowel and bladder disturbances, hyperhidrosis, altered salivary parameters and others. This study is done to investigate the specific degree and type of autonomic dysfunction (AD) in the children with cerebral palsy and correlate with their clinical symptoms. **Methods:** The study is done after getting approval from Institutional Ethics Committee and written consent from the parents. 20 children with CP (age, 5 – 12 years and of both genders) were included. Children with known history of cardiac diseases were excluded. A detailed history regarding the antenatal, perinatal and postnatal period were elicited from the mother and autonomic symptom scoring was done. After recording the baseline vital signs, the children were subjected to resting Heart Rate Variability (HRV) analysis. Time domain and frequency domain parameters were analyzed and correlated with autonomic symptom scores. Statistical analysis was done using SPSS version 17.0. **Results:** Out of 20 children with CP, 65% had mild autonomic dysfunction and 15% had moderate AD. Time domain parameters of HRV were reduced in comparison with the standards. Frequency domain analysis showed increased Low Frequency (LF), decreased High Frequency (HF) and increased LF/HF ratio. A positive correlation was observed between absolute power of LF and autonomic symptom scores ( $\rho = 0.484$ ,  $p = 0.03$ ). **Conclusion:** This study has brought out the subjective and objective evidences of autonomic dysfunction in children with cerebral palsy.

**Keywords :** autonomic dysfunction, cerebral palsy, heart rate.

### Corresponding Author

Dr. M. Anbarasi, Professor, Department of Physiology, Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur, Tamil Nadu, India.

Telephone: +91 9790542244 E-mail: anbarasi.physio@gmail.com

### Introduction

Cerebral palsy (CP) is a group of disorder that affects the motor function resulting in abnormal movement and posture which is caused by a non-progressive lesion in the immature brain during the prenatal, perinatal or postnatal period.<sup>1</sup> Children with cerebral palsy were found to have symptoms suggestive of autonomic imbalance like high heart rate, bowel and bladder disturbances, hyperhidrosis, altered salivary parameters and others as associative conditions. Most children with cerebral palsy suffer from poor nourishment because of the co-existing oral-motor

dysfunction. Swallowing difficulties, Intestinal dysmotility, delayed gastric emptying and reflux may lead to food aspiration, choking and increase the risk of pneumonia.<sup>2</sup> Temperature regulation is also affected in a majority of children with cerebral palsy. Hyperhidrosis was one of the common findings among them. Problems with bowel and bladder functions like urinary incontinence and constipation are not uncommon but are seldom complained by the care givers. Symptoms of circulatory system like flushing of face and increased heart rate was also observed frequently.<sup>3</sup>

Autonomic dysfunction can be assessed by various techniques of which heart rate variability analysis is the reliable, simplest and noninvasive bedside method. HRV analysis in cerebral palsy patients in previous studies have shown sympatho-vagal imbalance as evidenced by increased LF/HF ratio.<sup>4,5</sup> Electrocardiographic finding showed increase in heart rate in CP patients when compared to normal children.<sup>6</sup>

In spite of the frequency and different presentations of autonomic abnormalities in cerebral palsy, much of research has been done only in the area of motor compromise and its sequelae. This study was done with the objective of assessing autonomic dysfunction with autonomic symptom scoring and HRV analysis.

### Methodology

This was a cross-sectional study done in 20 children of both genders diagnosed with cerebral palsy of age group 5-12 years. The study was initiated after getting clearance from Institutional Ethics Committee and written consent from the parents of the children. Patients with known history of cardiac diseases and with paralysis due to post-meningitis/post-encephalitis sequelae, were excluded based on history and other investigations done previously, if any. After getting the demographic details about the child, a detailed history regarding the antenatal, perinatal and postnatal period were elicited from the mother. Details regarding the age at diagnosis, duration of illness, history of high-risk pregnancy, history of exposure to radiation or infection during pregnancy, mother's age at delivery, history of multiple pregnancies in the mother, nature of delivery, history of birth asphyxia, history of neonatal infection, any other co-morbid diseases, history of treatment and rehabilitation were asked elaborately. The children were then examined for the presence of any other observable congenital malformations. Vital signs were recorded and the type of cerebral palsy was diagnosed by the pediatrician. The motor disability was assessed and classified according to Gross Motor Function Classification System [GMFCS].<sup>7</sup>

The primary care giver was then questioned about the child's autonomic symptoms in their native language. Based on the responses autonomic

symptoms were classified system-wise and scored. The minimum score is 0 and the maximum score is 15. Patients having scores less than 3 were considered to be without autonomic dysfunction (AD) as those symptoms would have occurred by chance. Scores between 3 and 7 were categorized into mild AD, between 8 to 12 as moderate AD and more than 12 as severe AD.

After recording the baseline vital signs, the children were subjected to resting HRV analysis. The children were asked to remain in the supine position for 5 minutes and continuous recording of ECG signals in lead II was done in Physiopac. The raw data were then analyzed for HRV using the software Kubios HRV 2.1. Time domain parameters included were mean R to R interval (RRI), NN50 count divided by the total number of all NN intervals (pNN50), the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD) and standard deviation of the averages of NN intervals in all 5 min segments of the entire recording (SDANN). Among these, RMSSD and pNN50 represents the short-term components of HRV while SDANN represents the long-term components of HRV. Frequency domain parameters that were studied include Low Frequency (LF) and High Frequency (HF) – in absolute power (msec<sup>2</sup>) and in normalised units (nu). The representation of LF and HF in n.u. emphasizes the controlled and balanced behaviour of the two branches of the autonomic nervous system.<sup>8</sup>

Time domain and frequency domain parameters were retrieved and correlated with autonomic symptom scores. The continuous data were represented as Mean  $\pm$  Standard Deviation. Qualitative data were expressed as percentages. Correlation between HRV variables and autonomic symptom scores were done using Spearman Rank Correlation test. Statistical analysis was done using SPSS version 17.0. A p value of less than 0.05 was considered significant.

### Results

Descriptive characteristics of the 20 study participants with CP and related maternal factors were depicted in the table 1. The average birth weight of the study participants in grams was 2366  $\pm$  34 (1800 to 3000) which comes under low birthweight according to WHO. Another notable

feature is that 55% of the study participants were premature babies.

Table 2 explains the different types of CP and their percentage among study participants. Percentage of children in different grades of motor deficit, according to GMFCS was shown. Mean values of vital signs were also mentioned. Time domain and frequency domain parameters of HRV analysis done from the ECG signals were depicted in the table 3. Correlation of HRV parameters with the autonomic symptom scores done using Spearman Rank Correlation test (Figure 1) showed a moderately positive correlation of low frequency component, LF (AP) with autonomic symptom scores (Rho = 0.484, p value = 0.03)

### Discussion

The autonomic system involvement in cerebral palsy was studied in 20 children with CP, based on symptom scoring and HRV analysis. The fact that the average birthweight of the children is 2366 grams and 55 % of children were born as preterm babies fits well into the risk factors of cerebral palsy. A review on cerebral palsy clearly states that birth after fewer than 32 weeks' gestation, birth weight of less than 2,500 g were the strong risk factors for CP.<sup>7</sup> The APGAR scores could not be recollected by history from the mothers. In majority of cases in this study, there was no history of infection during antenatal period and neonatal period. Hence, this points to the fact that most cases of CP would have resulted from birth asphyxia.

The grading of motor deficit based on GMFCS in this study showed that majority of patients belonged to Grade I and II which means that the children could walk but with limitations. Hence it was feasible for us to subject them to HRV analysis.

The scoring of autonomic dysfunction was done based on conventional scoring of symptoms. 10% of children had no AD, 65% of children had mild AD and 25% had moderate AD. Similar study by Susan Agarwal also showed that majority of children with CP had mild AD.<sup>3</sup> Majority of the symptoms in this study were urological, followed by neurological and gastrointestinal. Susan et al in their study, presented that, majority of their subjects were suffering from significant gastrointestinal (49%) and temperature regulation problems (neurological) (26%).<sup>3</sup> This

categorization is based on the caregiver's history and may be having subjective bias due to exaggeration or underestimation.

Systolic Blood Pressure was found to be in the higher range for children in this group while normal for diastolic BP when compared with the published data on BP in South Indian children.<sup>9</sup> This may be related to enhanced sympathetic activation yet, it may not be significant as this variable is not compared with the normal children of the same age group.

Objective analysis of autonomic dysfunction was done by HRV analysis. Analysis of the four major time domain parameters, viz. mean RR interval, pNN50, RMSSD and SDANN were found to be lower when compared with the published Indian standard values for this age group.<sup>10</sup> Zamecznik et al. showed in their study that the time domain variables were smaller in children who were born as small-for-gestational age and have impaired autonomic function where their autonomic balance moved towards sympathetic component.<sup>11</sup> Another study by Aziz et al also showed similar results.<sup>12</sup> Similar study by Panju et al in their comparative study, showed no significant difference in time domain parameters in children with CP compared to healthy normal children.<sup>13</sup>

Frequency domain analysis done in this study showed increased Low frequency components, LF(nu) and absolute power of LF (LF msec<sup>2</sup>) and an increase LF/HF ratio all pointing towards sympathetic dominance. Eun Sook Park et al, in a similar study among CP patients showed similar increase in absolute and normalized LF component and decreased HF component when the patients were subjected to 70 degrees tilt.<sup>1</sup> Zamenur et al also reported increased LF and decreased HF values in CP patients.<sup>14</sup> They also add that the effect on the autonomic system in children with cerebral palsy may be due to the hemispherical influence over the autonomic centres. Yang et al. showed no significant differences in Frequency domain patterns between children with CP and healthy children in supine position.<sup>4</sup> Another study by Panju et al. also showed similar results.<sup>13</sup> Our study concludes that increased sympathetic parameters could pose a threat as a cardiovascular risk factor in children with CP.

Correlation was sought between subjective autonomic symptom scoring and the HRV parameters. It showed moderate positive correlation between the symptom scores and LF component which clearly signifies that autonomic dysfunction do

exists in a measurable quantity in children with CP and hence they need to be evaluated appropriately.

### Conclusion

Autonomic symptom scores and sympathovagal imbalance elicited by HRV studies concludes that autonomic dysfunction do exist in children with cerebral palsy at a significant level and hence cannot be ignored.

### Limitations

Autonomic symptom scoring is devised exclusively for this study and has to be validated for a large sample. There was no control group in this study to pinpoint exact differences. Considering the physical disability, only resting HRV in supine position was done in this study. Other provocative autonomic function tests like deep breathing test, cold pressor, Valsalva maneuver and others could not be done. Further studies including larger sample and control groups is needed to extrapolate the results.

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**Conflict of interest:** Nil

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**Table 1. Descriptive characteristics and related maternal factors of children with CP**

<b>Descriptive parameter</b>	
Average age in years (Mean $\pm$ SD)	8.55 $\pm$ 2.25
Male: female	12:8
Nature of delivery, Number (percentage)	
Normal vaginal	9 (45)
C-section	6(30)
Assisted vaginal	5 (25)
Average age of mother during pregnancy (Mean $\pm$ SD)	24.6 $\pm$ 4.59
Single/multiparous pregnancy, Number (percentage)	
Single	3 (15)
Two	2 (10)
Multiple	15 (75)
Illness during pregnancy, Number (percentage)	
Yes	4 (20)
No	16 (80)
Average birth weight in grams (Mean $\pm$ SD)	2366 $\pm$ 34
Gestational age, Number (percentage)	
Term	9 (45)
Preterm	11 (55)
Significant illness during neonatal period, Number (percentage)	
Fever	5 (25)
Jaundice	3 (15)
Seizures	2 (10)
Acute watery diarrhoea	1 (5)
Nil	9 (45)

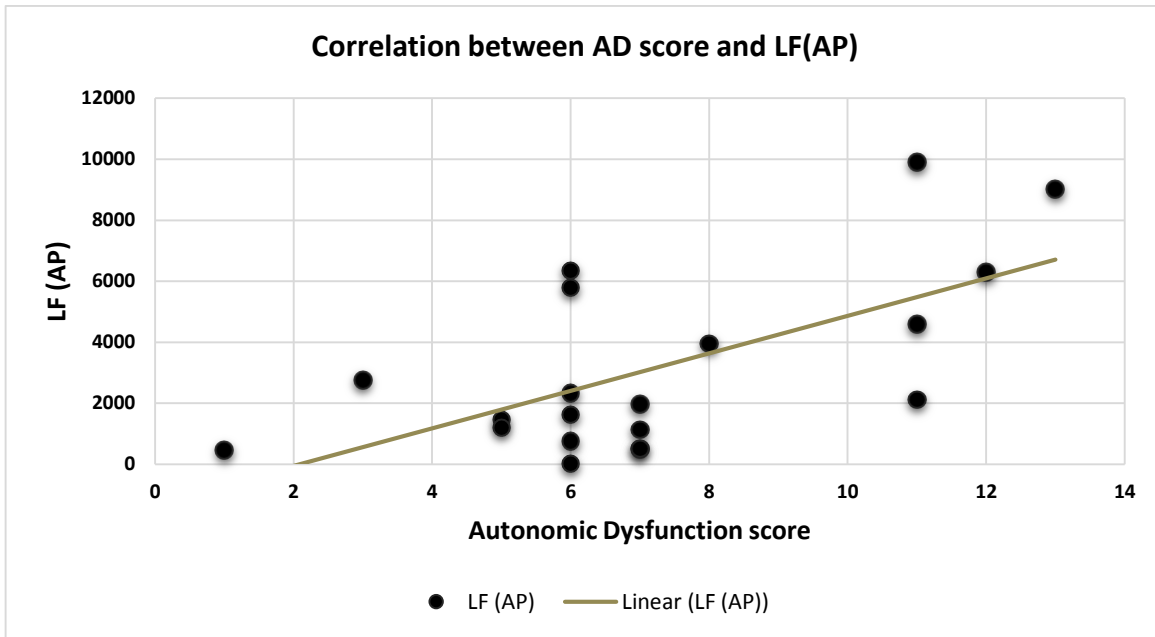
**Table 3. HRV parameters of children with CP**

<b>Time domain parameters (Mean <math>\pm</math> SD)</b>	
Mean RRI	520.67 $\pm$ 154.84
pNN50	14.43 $\pm$ 12.27
RMSSD	32.23 $\pm$ 14.86
SDANN	28.31 $\pm$ 42.52
<b>Frequency domain parameters (Mean <math>\pm</math> SD)</b>	
LF(msec <sup>2</sup> )	2299 $\pm$ 2419.7
LF (nu)	62.87 $\pm$ 17.48
HF(msec <sup>2</sup> )	1780.56 $\pm$ 2496.50
HF (nu)	36.90 $\pm$ 17.51
LF/HF Ratio	2.74 $\pm$ 2.87

**Table 2. History and Examination findings of children with CP**

	Number (percentage)
<b>Type of CP</b>	
Spastic diplegia	5 (25)
Spastic quadriparesis	1 (5)
Spastic quadriplegia	14 (70)
<b>Level of Physical functioning by GMFCS</b>	
I	6 (30)
II	8 (40)
III	4 (20)
IV	2 (10)
V	0
<b>Autonomic dysfunction scores</b>	
Average score	7.2
Median score	6.5
No AD	2 (10)
Mild AD	13 (65)
Moderate AD	5 (25)
Severe AD	0
Pulse rate in beats per minute (Mean ± SD)	92 ± 7.98
Respiratory rate in breaths per minute (Mean ± SD)	17 ± 2.63
Systolic BP in mm Hg (Mean ± SD)	112 ± 8.59
Diastolic BP in mm Hg (Mean ± SD)	72 ± 5.25

Figure 1. Correlation of Autonomic Dysfunction symptom scores and LF(AP) of HRV



LF(AP) – Low Frequency (Absolute power) in  $mSec^2$  ; Spearman's rho – 0.484,  $p=0.03$ .