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A PROSPECTIVE STUDY OF HEART RATE VARIABILITY IN SEVERELY MALNOURISHED CHILDREN AGED 6 -59 MONTHS

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ABSTRACT

Background: Severe malnutrition can significantly compromise the autonomic nervous system. As there is limited information about the cardiac autonomic activity in severely acute malnourished children, our intention in this study is to assess the effect of severe malnutrition on heart rate variability (HRV), a noninvasive tool to estimate cardiac autonomic activity. The aim is to compare autonomic functions in severely acute malnourished children and controls aged 6 - 59 months by heart rate variability (HRV) analysis. **Material and Methods:** The study was conducted in the Department of Physiology, postgraduate laboratory, Gajra Raja Medical College, Gwalior. A total of 60 children were enrolled and divided into two groups: severe acute malnutrition (SAM group) and normally nourished children (control group) as per the Z-score criteria based on the nutritional status for height and age. The Control group was selected from patients who came into Out Patient Department (OPD). To analyze the HRV indices, the heart rate of each child in the supine position was recorded for 5 minutes. These indices were analyzed using linear methods in the time and frequency domains. Student's t-test for unpaired data was used to compare variables between groups with a significance level of 5%. **Results:** In severely acute malnourished children, a decrease in systolic and diastolic blood pressure and an increase in heart rate were found compared to normally nourished children. HRV indices indicate that malnourished children exhibit sympathetic and parasympathetic autonomic nervous system activity alteration. RR Interval, SDNN, RMSSD, LF (nu)%, and LF/HF indices were higher in SAM children. **Conclusion:** SAM children show changes in cardiac autonomic functions, characterized by modulation in sympathetic and parasympathetic activity, as well as increased heart rate and decreased blood pressure.

Keywords: Severe acute malnutrition, heart rate variability, time domain, frequency domain, cardiac autonomic activity.

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INTRODUCTION

Malnutrition in children is considered a serious public health problem.[1] Child malnutrition permanently damages health and thus causes difficulties later in life.[2] SAM is one of the leading causes of mortality and morbidity in the pediatric population in developing countries.[3] The autonomic nervous system (ANS) is significantly impaired in malnourished children.[4] The brain and heart are the organs that have a high rate of oxidative metabolism

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and are soon affected by any mechanism that reduces oxidative efficiency. This leads to a chaotic state of the hypothalamic-autonomic-endocrine axis.[5] Children with severe malnutrition have smaller and thinner hearts and lower stroke volume. The cell membrane of the heart becomes leaky because of oxidative damage.[6] The number of Na+ K+ pumps in the cell membrane gets reduced to conserve energy and the remaining pumps also work slowly. Thus, intracellular sodium accumulation and potassium leakage occur, leading to electrolyte and fluid imbalance.[6]

Because of the close relationship between the ANS and sinoatrial node function, heart rate and its fluctuation reflect changes in cardiac autonomic control. HRV is a non-invasive electrocardiographic marker reflecting the activity of the ANS's sympathetic and vagal components at the heart's sinus node level. Increased efferent vagal activity is characterized by decreased heart rate and increased heart rate variability, whereas sympathetic stimulation increases heart rate and decreases heart rate variability.[7]

Krishnamurthy et al,[8] indicated the involvement of the parasympathetic nervous system in malnourished children when they studied the immediate reduction in the cardiac cycle duration in response to standing and lying down in normal and malnourished children. Belchior et al,[9] analyzed the effects of protein malnutrition in rats and found an increase in blood pressure, however, alterations in vascular reactivity were not found. Sawaya et al,[10] found a strong association between malnutrition and hypertension. These studies suggest possible changes in HRV. This correlation could be considered an important tool for determining prognosis and the need for special attention and care towards the autonomic nervous system and cardiovascular functions in malnourished children.

The evaluation of the modulation of the autonomic nervous system in malnutrition using HRV was found scarce in the literature. Srivastava et al,[11] compared the HRV of malnourished children with healthy children matched for sex and age. The author concluded that the cardiac autonomic functions are characterized by an increase in sympathetic modulation which occurs in malnourished children.

Therefore, this study was designed to investigate cardiac autonomic activity in children with severe acute malnutrition. The hypothesis was that cardiac autonomic tone shifts towards sympathetic dominance in severe malnourished children.

METHODOLOGY

This study was conducted in the post-graduate laboratory of the Department of Physiology, Gajra Raja Medical College, and J.A. group of Hospital, Gwalior (M.P.). The case group (SAM) consisted of 30 children of the age group 6 to 59 months (mean age: ± yrs), who were selected based on anthropometric parameters included in the study group admitted in SMTU-KRH, GRMC Gwalior. The control group included age & sex-matched, 30 normally nourished healthy subjects, who attended KRH, and OPD for cold and cough. Following approval from Institutional Research and Ethical Clearance committees, written informed consent was obtained from all guardians/parents of the children. A detailed history and complete clinical examination were done of all the subjects. Subjects were recruited after measuring body weight (kg) using a digital weighing machine while subjects wore light clothing and no shoes. Height (cms) was measured using a measuring tape with bare feet together. The mid-upper arm circumference (MUAC) in cms was measured with tape at the midpoint of the left upper arm. An aneroid infant sphygmomanometer with an arm diameter range of 10 to 18 cm (Premium®, China) on the child's left arm, by criteria established by the VI Brazilian Hypertension Guidelines. (12) Basal Heart Rate (RHR) was recorded.

SAM children were included in the study according to WHO classification i.e. 'severe acute malnutrition (SAM) as very low weight-for-height or a mid-upper arm circumference less than 115 mm, or by the presence of nutritional edema.[13] Children who were excluded from

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our study with any congenital anomalies, endocrinal disorders leading to short stature, Liver diseases, Central nervous system damage, Diabetes mellitus, and Other autonomic disorders.[14]

Instructions to patients: In the morning, we performed the test in a quiet room with an ambient temperature between 21 and 23 ◦C and humidity between 40% and 60%, to avoid circadian variations. Participants and their parents were explained in brief about the procedure. They were advised to remain free from any physical or mental stress.

Procedure-Lead II ECG recordings were done at (25 mm/s & voltage at 10 mm/mV) for 300 seconds to obtain HRV, using the data acquisition system, BIO PACK STUDENT LAB 4.1. For the recording of short-term HRV, the recommendation of the Task Force on HRV was followed.[15]

After acquiring the signal in the supine position, the data were checked for any artefacts or ectopic beats, and only those ECG signals that were free of any artefacts or ectopic beats were kept for further analysis. The data recorded was subjected to time domain and frequency domain analysis using the HRV analysis software (Kubios standards 3.5). It included time domain parameters: SDNN, RMSSD & PNN50. SDNN- Standard deviations of the averages of NN intervals in all 5 minutes segments of the entire recording; RMSSD- the square root of the mean of the sum of the squares of differences between adjacent NN intervals; PNN50- % of several instances in which two consecutive NN intervals differ by more than 50 msec. Frequency domain analysis was performed using the non-parametric method of Fast Fourier Transformation. The power frequency spectrum was subsequently quantified into standard frequency–domain measurements as low frequency (LF) component (0.04–0.15 Hz), high frequency (HF) component (0.15–0.4 Hz) in normalized units (nu) & LF-HF ratio.

For HRV analysis through geometrical methods, the following indices were used: triangular index, TINN, and the indices obtained from the Poincaré plot SD1, SD2, and SD1/SD2 ratio. All HRV indices were obtained through Kubios HRV, version 3.5 software (Kubios standards software 3.5 version).[16]

Statistical analysis - All data were expressed as Mean ± SD. Differences between the study group and controls were examined using the unpaired Student's t-test. The Chi-square test was used to evaluate differences in gender between the groups.

RESULTS

Table 1: Anthropometric and cardiovascular parameters in malnourished & control groups (n=30 in each group)

Parameters	Severe acute malnourished	Control	P-Value
	Mean ± SD	Mean ± SD	
Age	1.58 ± 0.91	1.85 ± 0.93	0.263
Gender(male/female)	14/16	17/13	0.438
Weight	6.40 ± 1.74	12.33 ± 2.20	0.000**
Height	68.33 ± 10.41	89.30 ± 11.47	0.000**
MUAC	10.74 ± 1.58	13.83 ± 1.41	0.000**
SBP	102.23 ± 2.75	113.20 ± 6.47	0.000**
DBP	64.00 ± 3.93	67.73 ± 4.45	0.001**
RHR	126.07 ± 24.14	91.43 ± 4.48	0.000**
Data presented are mean±SD; The analysis of data was done using unpaired student's t-test; **Significant Statistically RHR: Resting Heart Rate; BP: Blood Pressure and MUAC: Mid Upper -arm circumference			

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There was no significant difference in age and gender between the two groups. However, body weight, height, and MUAC were significantly lower (P<0.01) in severely acute malnourished children than in the control group [Table 1]. There were statistically significant differences between the systolic blood pressure (SBP), diastolic blood pressure (DBP), and (RHR) resting heart rates obtained from both groups [Table 1]. On HRV analysis, LFnu was found to be statistically increased (P=0.000) while HFnu was decreased (P=0.000) in the SAM (Case group). Also, the LF-HF ratio increase in the severely acute malnourished group was statistically significant (P=0.015) compared to the controls. RR interval, SDNN, NN50, and pNN50 have significantly differed between the groups [Table 2]. RMSSD did not differ significantly in both groups.

The values of SD1, SD2, SD1/SD2 ratio, triangular index, and TINN are depicted in Table 3. A significant change was observed in TINN in the severe acute malnourished group. For the SD1, SD2, SD1/SD2 ratio and triangular index, there were no differences between the two groups. The autonomic system indexes can be observed in [Figure 1].

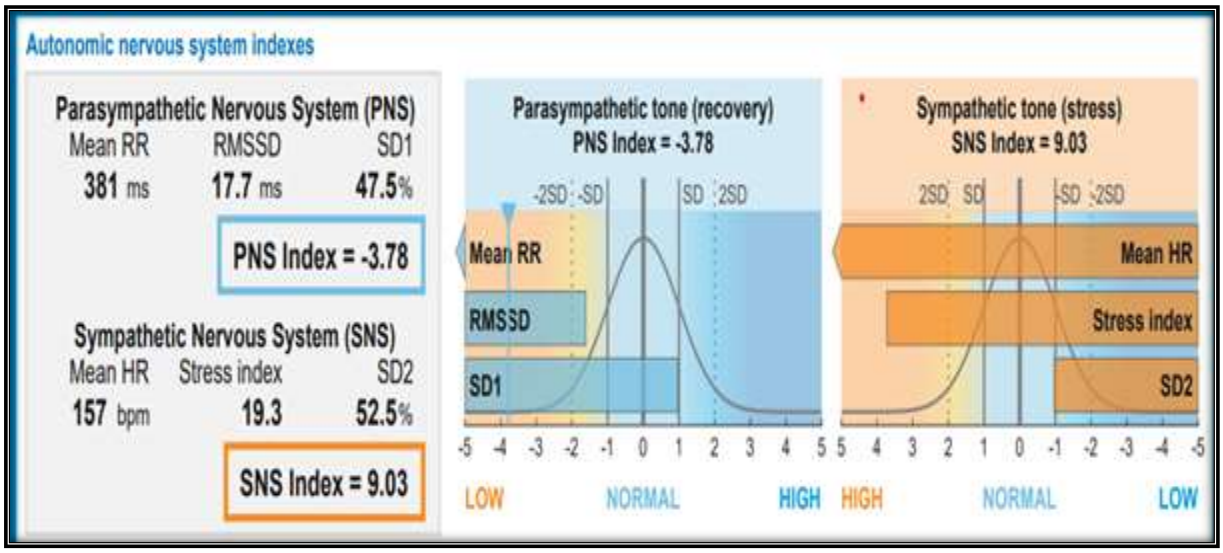

Figure 1: Report of severe acute malnourished children (age 2.7yrs) showing autonomic nervous system index

Table 2: Time domain and frequency domain indices of spectral HRV analysis in case and control groups (n=30 in each group)

Parameters	Severe Acute Malnourished (Mean ± SD)	Control (Mean ± SD)	P-Value
RR Interval(ms)	493.70 ± 105.83	779.93±167.58	0.000**
SDNN (ms)	192.53 ± 178.25	103.86±87.17	0.019**
RMSDD (ms)	240.22 ± 235.61	148.94±129.11	0.069
NN50 (ms)	48.97 ± 51.78	131.97±65.43	0.000**
PNN50(%)	10.34 ± 12.29	36.74±25.80	0.000**
Lf (nu) (%)	59.27 ± 23.22	35.43 ± 22.13	0.000**
Hf (nu) (%)	40.76 ± 23.13	62.94 ± 22.72	0.000**
LF/HF	3.66 ± 5.27	1.07 ± 1.74	0.015**
Values are expressed as mean±SD; ** Significant Statistically SDNN: Standard deviations of the averages of NN intervals in all 5 min segments of the entire recording; RMSSD: the square root of the mean of the sum of the squares of differences between adjacent NN intervals; pNN50: % of a number of instances in which two consecutive NN intervals differ by more than 50 msec; LF: low-frequency component & HF: high-frequency component			

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(expressed as nu.: normalized unit) and LF-HF ratio: the ratio between low frequency and high-frequency components.

Table 3: Mean values followed by standard deviations for SD1, SD2, SD1/SD2 ratio, triangular index, and TINN obtained from severe acute malnourished and normal children(n=30 in each group)

Parameters	Severe Acute Malnourished	Control	P-value
	Mean± SD	Mean±SD	
SD1	166.72±167.58	186.97±301.24	0.749
SD2	202.24±195.18	182.24±318.00	0.770
SD1/SD2	1.335±0.68	1.18±0.39	0.320
Triangular index	8.715±7.28	6.33±2.69	0.098
TINN(ms)	1791.03±1427.88	241.70±127.25	0.000

SD1, the standard deviation of the instantaneous variability of beat-to-beat; SD2, the standard deviation of long-term continuous RR intervals; TINN, the triangular interpolation of RR intervals

DISCUSSION

Severe acute malnutrition (SAM) affects tissue proteins throughout the body and causes significant skeletal muscle wasting. The heart is also affected by this general atrophy of the muscle tissues, but not to a very great extent. Although cardiomegaly has been found in nonedematous SAM infants.[17] Other changes include atrophy of myocardial fibres with variations in the fibre size, vacuolization in the cells, fading of sulci, and changes in nuclei. These changes are mostly found in the left ventricle and the conducting tissues. All these pathological changes lead to the disturbance in the cardiac functions of the heart's electrical activity which may be reflected in the electrocardiogram (ECG).[18] Malnutrition during the crucial period of brain growth (till 2 years of age) can lead to autonomic imbalance through morphological changes in several areas of the central nervous system involved in the modulation of sympathetic activity, such as the hypothalamus.[19] Singh et al,[20] related vitamin D and vitamin E deficiency with modifications in HRV and Mann et al,[21] associated vitamin D with changes in autonomic modulation in humans. Thus, it can also be said that the reduction in nutrients in malnourished children should be a factor to be taken into account to explain the alterations in cardiac autonomic modulation. The present study extends the observation of an earlier study by Bedi et al,[4] who reported that resting heart rate was significantly higher in the malnourished group (P=0.000). The HRV analysis in the present study revealed significantly increased LFnu (P=0.000), decreased HFnu (P=0.000), and increased LF-HF ratio (P=0.015) in the case group. These changes may indicate a shift of autonomic balance toward a sympathetic predominance and a reduced vagal tone. Blood pressure is related to body weight during the growth phase; therefore, malnourished children tend to have lower SBP and DBP since their body mass is smaller. During the last two decades, a decreased HRV has been recognized as a factor related to cardiovascular mortality. An increase in the LF-HF ratio, the most sensitive indicator of sympathovagal balance, has been implicated in the pathophysiology of arrhythmogenesis and sudden cardiac death.[7,15,22] In the present study the pNN50, NN50, and HF (ms2), which reflect parasympathetic modulation of the autonomic nervous system, showed a reduction in the severe acute malnourished group compared to the normal nourished group, suggesting that these children may be more vulnerable to adverse cardiac events due to immaturity in autonomic control of the heart. We concluded that impaired cardiac autonomic nerve function characterized by sympathetic overactivity may occur in severely acute malnourished children.

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CONCLUSION

In conclusion, our results suggest that severe acute malnourished children had lower HRV compared to the normal nourished control group. The reduced HRV, characterized by a reduction in parasympathetic modulation is a potential indicator of increased mortality risk and impaired autonomic nervous system in SAM patients. However, further research is needed to fully understand the mechanisms underlying this relationship and to determine, if HRV monitoring could be a useful tool in the management of severe acute malnutrition in children.

WHAT DOES THE PURPOSE OF THE STUDY

Malnutrition leads to significant changes in cardiac autonomic functions, and data on the analysis of this behaviour are rare. Thus, to add elements to the literature related to the above issue, this study aimed to compare the autonomic behaviour between SAM and normally nourished healthy children aged 6-59 months, based on the analysis of HRV indices.

LIMITATIONS

24–hour assessment of HRV (Holter monitoring), echocardiography, and complex evaluation of the autonomic nervous system including baroreceptor sensitivity as well as a follow-up study on a larger sample size are warranted to further elucidate the impact and mechanism of adverse effects of severe acute malnutrition.

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