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COMPARISON OF CARDIAC AUTONOMIC ACTIVITY BETWEEN MALNOURISHED AND HEALTHY CHILDREN

DIVYA SRIVASTAVA*[1], KIRAN SINGH[1], RAJESH MISRA[1] AND ASHISH PRAKASH[2]

Departments of [1]Physiology and [2]Pediatrics,
Subharti Medical College,
Meerut – 250 005

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Abstract : Severe malnutrition can significantly compromise autonomic nervous system. However, less is known about the cardiac autonomic activity in mild and moderate grades of malnutrition in children. Therefore, the objective of this study was to assess the effect of mild/moderate malnutrition on heart rate variability (HRV), a non invasive tool to estimate the cardiac autonomic activity. A cross sectional, community based study was conducted in which 35 malnourished children (mean age: 6.06±2.04 yrs), on the basis of anthropometric parameters, were enrolled in the study group by random samplings, who were the children of urban slum dwellers and 35 age and sex matched healthy children, were taken as controls. Grading of malnutrition was done according to Indian Academy of Pediatrics (IAP) classification. Anthropometry, basal heart rate (BHR), blood pressure were determined. Time domain and frequency domain indices of HRV were assessed using RMS Polyrite D (version 2.4). Weight, height, mid arm circumference (MAC) and body mass index (BMI) were found to be statistically lower in the study group. There was a strong negative correlation between MAC and LF component (P<0.01). BHR was found to be increased in the malnourished group (P=0.027). Low frequency (LFnu) & LF-HF ratio were found to be increased (P=0.000 & P=0.001 respectively) while high frequency (HFnu) component was decreased (P=0.000) in malnourished group. Our results suggested that impaired cardiac autonomic nerve function characterized by sympathetic over activity may occur in malnourished children. This study also enables us to compare, in future works, HRV in pediatric subjects with different grades of malnutrition.

Key words : mild, moderate, malnutrition, children, heart rate variability, mid arm circumference

INTRODUCTION

It has been demonstrated that autonomic nervous system (ANS) is significantly compromised in malnourished children (1). Apart from genetically and epigenetically

*Corresponding Author : Dr. Divya Srivastava, Associate Professor, Department Of Physiology, Subharti Medical College, NH-58, Delhi Haridwar Rd., Meerut – 250 005; Phone No.: 094560 88224; Email: divyaprabhat2000@yahoo.com

determined disease, evidence is presented that marginal high calorie malnutrition, particularly with reference to simple carbohydrates, is responsible for widespread dysautonomia. The brain and heart are the organs that have a fast rate of oxidative metabolism and are affected early by any mechanism that reduces oxidative efficiency. It is hypothesized that this results in a chaotic state of the hypothalamic/autonomic/endocrine axis (2). Due to close link between ANS and function of the sino-atrial node, heart rate and its fluctuations reflect changes in cardiac autonomic control. HRV is a noninvasive electrocardiographic marker reflecting the activity of the sympathetic and vagal components of the ANS on the sinus node of the heart. Increased efferent vagal activity is characterized by reduced heart rate and increased variability of heart rate, whereas sympathetic stimulation increases heart rate and decreases variability of heart rate (3).

Recent research indicates that 53% of child deaths, in developing countries, were attributable to malnutrition and 83% were linked to mild and moderate malnutrition, as opposed to severe malnutrition (4). Information on relationship between cardiac autonomic function and mild/moderate grade of malnutrition is scant. Therefore, this study was designed to investigate the cardiac autonomic activity in children with mild/moderate grades of malnutrition. The hypothesis was that cardiac autonomic tone would shift towards sympathetic dominance in malnourished children.

MATERIALS AND METHODS

This community based study was conducted in research laboratory of department of Physiology in collaboration with department of Pediatrics, Subharti Medical College and associated C.S.S. Hospital, Meerut. A total of 35 malnourished children in age group (mean age: 6.06±2.04 yrs), selected on the basis of anthropometric parameters comprised the study group which consisted of the children of labourers, residing in temporary accommodations and working at construction sites in Subharti Campus. The control group consisted of age & sex matched, 35 healthy subjects, who were wards of the faculty members residing in the Subharti campus. Following approval from Institutional Research and Ethical Clearance committees, written informed consent was obtained from all guardians of the subjects. A thorough history and complete clinical examination was done of all the subjects. BHR was recorded. Mercury sphygmomanometer with appropriate cuff size was used for recording basal blood pressure.

Anthropometric measurements

Subjects were screened after measuring body weight (kg) using a weighing machine (Krups) while subjects wore light clothing and no shoes. Height (cms) was measured using a stadiometer with sliding head board while the subject stood with his bare feet together on the fixed foot board. The mid-upper arm circumference (MAC) in cms was measured at the midpoint of the left upper arm with a non-stretchable tape. BMI (kg/m^2) was calculated using Quetelet's index.

Inclusion criteria

The weight & height was marked on the CDC (Centre's for Disease Control) growth

charts which represent the revised version of 1977 NCHS (National Centre for Health Statistics) weight for age, height for age & BMI for age charts (5, 6). In children, malnutrition was defined by IAP Classification: a weight of more than 80% of expected for age is designated as normal. Grade I (mild) – 71-80% and Grade II (moderate) – 61-70% of expected for age were recruited in this study (7).

Exclusion criteria

1) Subjects with congenital anomalies,

2) Endocrinal disorders leading to short stature,

3) Liver disease,

4) Central nervous system damage,

5) Diabetes mellitus

6) Other autonomic disorders (8).

Experimental protocol

The subjects and their guardians were explained in brief about the experimental procedure. Experiments were done in a quiet room during which subjects lay supine, awake and breathing normally. For examination the subjects were advised to have their meal by 9:00 pm on the previous night, to remain free from any physical or mental stress, not to take sedatives or any drugs affecting central nervous system and to have a good sleep at night before the day of examination. The subjects were also asked to avoid tea or coffee at breakfast and to attend the Research Laboratory in the Department of Physiology of Subharti Medical College between 9:00 to 11:00 a.m on the day of examination.

Assessment of HRV

Lead II ECG recordings were done at (25 mm/s & voltage at 10 mm/mV) for 330 seconds to obtain HRV, using data acquisition system, RMS Polyrite AD. For recording of short term HRV, recommendation of Task Force on HRV was followed (9). The ECG signals were converted through a 14-bit A/D converter at a sampling frequency of 256 Hz to PC and were analyzed offline after visual checking of abnormal ECG. After acquiring the signal in lying posture, data was checked for any artifact or ectopic beats, and only those ECG signals were kept for further analysis that were free of any artifacts or ectopic beats. High and low filters were set at 99 and 0.1 Hz respectively. The screen sweep speed was kept at 30 mm/sec.

The data recorded was subjected to time domain and frequency domain analysis using the HRV analysis software (RMS Polyrite D version 2.4). It included time domain parameters: SDNN, RMSSD & pNN50. 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 number of instances in which two consecutive NN intervals differ by more than 50 msec. Frequency domain analysis was performed using non- parametric method of Fast Fourier Transformation. HRV software used a peak detection algorithm to find the 'R' wave, which was done at a resampling rate of '4 Hz'. A minimum of 256 data points was required to perform a

spectral analysis. To attain 256 data points a duration of 5 minutes of ECG recording was required. 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.

Statistical analysis

All values were expressed as Mean±SD. Differences between the study group and controls were examined using the unpaired Student's t- test. Chi-square test was used to evaluate differences in gender between the groups. Pearson's correlations were used to assess associations between continuous variables. A two tailed test (P<0.05) was considered statistically significant. The data were analyzed using the statistical package of Analytical Software SPSS (version 11.5).

RESULTS

General parameters

There was no significant difference in age and gender between the two groups. However, body weight, height, MAC and BMI were significantly lower (P<0.01) in malnourished children than in the control group (Table I). There were no statistical differences between the systolic blood pressure (SBP) & diastolic blood pressure (DBP) obtained from both groups. However, BHR was found to be statistically increased in the study group (P=0.027) (Table I).

HRV parameters

On HRV analysis, LFnu was found to be statistically increased (P=0.000) while HFnu was decreased (P=0.000) in the study group. Also, increase in LF-HF ratio in the malnourished group was statistically significant (P=0.001) compared to the controls. SDNN, RMSSD and pNN50 did not differ significantly between the groups (Table II).

Correlation values

Main Pearson's correlations found between HRV and general & anthropometric parameters are shown in Table III. There

TABLE I: Anthropometric and basal cardiovascular parameters in malnourished & control groups (n=35 in each group).

Parameters	*Malnourished group*	*Control group*	*P value*
Age (years)	6.06±2.04	7.00±2.19	0.067
Gender (Male/Female)	17/18	19/16	0.811†
Body weight (kg)	15.24±3.88	29.23±7.15	0.000*
Height (cm)	107.86±12.35	124.89±11.64	0.000*
MAC (cm)	14.68±1.65	19.16±2.74	0.000*
BMI (kg/m^2)	13.08±1.9	17.57±1.46	0.000*
BHR (per min)	87.54±5.61	84.63±5.19	0.027*
Systolic BP (mmHg)	97.43±8.36	98.69±9.08	0.549
Diastolic BP (mmHg)	64.00±6.45	64.86±6.11	0.572

Data presented are mean±SD; The analysis of data was done using unpaired student's t test; *P<0.05; †Chi-square test was used to evaluate differences in gender between the groups: $\div^2$ =0.057; BMI: Body Mass Index; BHR: Basal Heart Rate; BP: Blood Pressure and MAC: Mid arm circumference.

TABLE II: Time domain and frequency domain indices of spectral HRV analysis in study and control groups (n=35 in each group).

Parameters	*Malnourished*	*Control*	*P*
SDNN (ms)	118.98±23.04	125.34±31.54	0.845
RMSSD (ms)	59.41±27.27	52.80±35.38	0.394
pNN50 (%)	33.17±13.95	28.42±9.31	0.098
LF (nu)	46.61±14.69	33.63±13.52	0.000**
HF (nu)	53.47±14.78	66.32±13.51	0.000**
LF-HF ratio	0.99±0.51	0.61±0.41	0.001**

Values are expressed as mean±SD; **P<0.01; 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 number of instances in which two consecutive NN intervals differ by more than 50 msec; LF: low frequency component & HF: high frequency component (expressed as nu.: normalized unit) and LF-HF ratio: ratio between low frequency and high frequency components.

TABLE III: Main Pearson Correlations between LF, HF & LF-HF ratio and other variables in malnourished and control groups.

Variables	*LF*	*HF*	*LF-HF ratio*
	r	*r*	*r*
BMI	–0.199	0.091	–0.124
MAC	–0.336**	0.061	–0.164
BHR	0.055	–0.296*	0.310**
SBP	0.251*	–0.013	0.114
DBP	0.173	–0.079	0.092

BMI: Body mass index (kg/m^2); BHR: Basal heart rate (beats per min.); MAC: Mid arm circumference (cm); SBP: Systolic blood pressure (mmHg); DBP: Diastolic blood pressure (mm Hg); LF: Low frequency & HF: High frequency (expressed as power %); **P<0.01; *P<0.05.

was a strong negative correlation between MAC and LF (power%) (P<0.01). Also, a significantly strong positive correlation between BHR and LF-HF ratio (P<0.01) and negative correlation between BHR & HF (power%) (P<0.05) was observed. LF was positively correlated with SBP (P<0.05), while no significant correlation between SBP & DBP and LF-HF ratio was seen.

DISCUSSION

According to the IAP classification, out of the thirty five children in the study group, seventeen (48.57%) had mild (Grade I) and eighteen (51.42%) had moderate (grade II) malnutrition. Besides being a noninvasive study procedure, an important advantage of spectral analysis of HRV is that it utilizes spontaneous fluctuation in heart rate to estimate tonic autonomic nervous functions. However, it should be noted that a controlled condition is required for spontaneous ANS function recording. In the present study, HRV was recorded while the subjects were in supine, relaxing and resting in a quiet condition. Since the daily physical activity level is considered as one of the potential confounders in the measurement of autonomic nerve activity (10), the study groups were controlled for physical activity levels.

The present study extends the observation of earlier study by Bedi et al (1), who have reported that resting heart rate was significantly higher in the malnourished group (P=0.001), the other parasympathetic function tests had significantly lower mean values than in the control group, namely, standing-to-lying ratio (P=0.026), lying-to-standing ratio (P=0.021) and Valsalva ratio (P=0.037). Of the sympathetic function tests conducted, there were no differences between the two groups for handgrip test but galvanic skin resistance was significantly higher in the malnourished subjects (P=0.001). In the present study, BHR was statistically

increased in the study group (P=0.027). The HRV analysis revealed significantly increased LFnu (P=0.000), decreased HFnu (P=0.000) and increased LF-HF ratio (P=0.001) in the study group. These changes may indicate a shift of autonomic balance toward a sympathetic predominance and a reduced vagal tone. During the last two decades a decreased HRV has been recognized as a factor related to cardiovascular mortality. And increase in LF-HF ratio, the most sensitive indicator of sympathovagal balance, has been implicated in the pathophysiology of arrhythmogenesis and sudden cardiac death (9, 11, 12). Moreover, children may be more vulnerable to adverse cardiac events due to immaturity in autonomic control of heart. These changes in autonomic regulation with age are incompletely understood and seem to be affected by many factors like centrally generated brainstem rhythms, baroreceptor feedback influences, as well as both sympathetic and vagal input (13). In contrast, however, Fuenmayor AJ et al (14), reported no significant difference in the heart rate variability parameters between the two groups (age group-12.2±14.4 months) which may be explained as the present study involves a higher age group. It has been established that age is a significant determinant of HRV and there is a progressive modification of HRV with age which may reflect progressive evolution of ANS (15, 16).

In the present study, weight, height and BMI were correlated negatively with LF & LF-HF ratio and positively with HF but these correlations were not significant. We also noted that MAC was a significantly stronger negative correlate of LF than BMI. Disparate results come from the study by Piestrzeniewicz K et al (17) who revealed a negative correlation between waist circumference and parameters reflecting parasympathetic activity (SDNN, SDANN, RMSSD, HF) in the obese patients suffering with myocardial infarction. However, they concluded that waist circumference was a better correlate of HRV parameters than BMI. Several authors have observed that BMI affect HRV (18). However, other authors (19) have detected no association between HRV and BMI. The strong positive correlations of BHR with LF-HF ratio and negative correlations with HF observed in this study were consistent with the findings of previous reports that HRV correlates negatively with BHR (20). Also, LF was positively correlated with SBP which was in accordance with some previous studies (21, 22). We have not come across any papers concerning the relationship of HRV parameters and anthropometrical parameters in malnourished children.

As RMSSD, SDNN and pNN50 represent long term vagal modulation of cardiac function, these parameters did not change significantly in malnourished group, the recording of present study being that of short term HRV.

Conclusion

We concluded that impaired cardiac autonomic nerve function characterized by sympathetic over activity may occur in mild/moderate malnutrition in children. MAC was a better correlate of HRV than BMI. This study also enables us to compare, in future works, HRV in pediatric subjects with different grades of malnutrition. Limitations include small sample size, short term HRV

analysis and software version (Polyrite 2.4 does not have the provision for measuring total power). 24–hour assessment of HRV (Holter monitoring), echocardiography and complex evaluation of autonomic nervous system including baroreceptor reactivity as well as prospective study with follow up observation on a bigger sample size are warranted to further elucidate the impact and mechanism of adverse effects of malnutrition.

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