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A preliminary study on the effect of age and heart rate on the short-term heart rate variability

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Abstract:
Reduced heart rate variability (HRV) is associated with poor prognosis in diseases and healthy population. HRV is also influenced by physiological factors like age, gender, ethnic origin as well as various diseases.This study aims to establish the normal value of heart rate variability of subjects of Imphal-East, Manipur and also to see if there is any effect of age and heart rate on the HRV. Study included 100 subjects (66 males and 34 females) which was grouped into 2 according to age: group A (19-<40 years) and group B (>40-60 year). HRV analysis was done using the Lab Chart Prov8.1.13 with HRV module version 2.0; AD Instruments, Australia). Time-domain (SDNN and RMSSD) and frequency-domain (LF, HF and LF/HF ratio) were estimated. Comparison of variables between the two groups and also between the males and females were done using independent t-test. Correlation of HRV with age and heart rate were made using Pearson correlation test. Comparison of HRV indices between the groups are found to be statistically significant in all the variables except the LF/HF ratio. The SDRR, RMSSD, LF, HF showed statistically significant negative correlation with age except LF/HF. The HF shows significantly negative correlation with heart rate while the LF/HF shows positive correlation with heart rate which was statistically significant.We found that there is a negative correlation between age and HRV. We also observed inverse correlation between HF and heart rate, and a positive correlation between LF/HF ratio and heart rate.

Key words: HRV, age, gender, heart rate

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I. Introduction :

Heart rate variability (HRV), as recorded by ECG, is the variability of intervals between QRS complexes generated by sinus node depolarisation in one continuous recording.[1] These beat-to-beat variations are the result of the opposing influences of parasympathetic and sympathetic divisions of autonomic nervous system. The activation of sympathetic nervous system causes an increase in the heart rate while that of the parasympathetic nervous system leads to an inhibition of the cardiac rhythm activity and therefore, a decrease in the heart rate.[1] The higher the heart rate variability, the faster and more flexible the organism can adapt to internal and external influences, by optimizing the interplay of the sympathetic and parasympathetic nervous system. So, it reflects the ability of an organism to change the frequency of the cardiac rhythm on a beat-to-beat basis.

Many studies have revealed that reduced HRV is a strong, independent, and consistent risk factor for cardiovascular morbidity and mortality in previous myocardial infraction.[2] Moreover, an association between reduced HRV and poor prognosis has also been shown for many other diseases, including diabetes mellitus, alcoholism, and dilatative cardiomyopathy.[3,4,5] Similarly, study in general population documented reduced HRV as a predictor of an adverse prognosis[6].

The study of HRV offers a non-invasive and quantitative method of investigating autonomic effects on the heart. There are different methods available for the analysis of HRV. However, the most widely-used methods are the time domain, frequency domain and Poincare plot. According to Task force[1], the following four are recommended for time–domain HRV assessment: Standard deviation of interbeat intervals of normal sinus beats (SDNN; estimate of overall HRV); standard deviation of average normal to normal interval (SDANN; estimate of long-term components of HRV), and root mean square of successive differences between normal heart beats (RMSSD; estimate of short-term components of HRV). The RMSSD method is preferred to percentage of adjacent NN intervals that differ from each other by more than 50 ms (pNN50) and number of adjacent NN intervals that differ from each other by more than 50 ms (NN50) because it has better statistical properties. For the frequency domain (short term recordings) the three main spectral components are very low frequency (VLF, ≤0.4 Hz), low frequency (LF, 0.04-0.15 Hz), high frequency (HF, 0.15- 0.4 Hz) and ratio of LF/HF. HRV is influenced by physiological factors like age, gender, ethnic origin as well as various diseases.

Several changes in autonomic activity occur with healthy aging in adult. It has been reported that there is decrease of HRV with increasing age[7] which may be due to the offset of hemodynamic impact of the increases in sympathetic nervous system tone by the decrease in adrenergic sensitivity with the age.[8]

Cardiac autonomic modulation has been found to be significantly influenced by sex. Previous study has observed lower HRV in healthy women as compared to healthy men while the vagal modulation was similar in both sexes.[9] However, other study reported HF power was higher in young women and in middle aged women than in age-matched men.[10]

In a meta-analysis based on a systematic reference survey involving 17 studies and a total of 11,162 test persons, Hill et al [11] established a significantly higher short-term resting HRV in Afro-American persons than in American persons of European origin. Similarly, Choiet al[7] reported there is a significant ethnic disparity in correlation between age and HRV indices in African Americans and Caucasian Americans.

This study aims to establish the normal value of heart rate variability of subjects of Imphal-East, Manipur and also to see if there is any effect of age and heart rate on the HRV.

II. Materials and Methods:

This is a cross-sectional study which consisted of 100 subjects (66males, 34 females), within the age group of 19 - 60 years. The subjects were students (medical and dental) and employees (medical and non-medical) of the Jawaharlal Nehru Institute of Medical Sciences, Imphal-East, India. They were grouped into two according to the age: group A (63 subjects) comprised of age from 19 to 39 years and Group B (37 subjects) comprised of age from 40 to 60 years. They were given detailed verbal explanations regarding the nature, purpose and requirements of the study. The subjects were also given time to consider participation and written consent was taken from the participants after clearance from the Ethical Committee of the Institute.

Evaluation of the medical condition of the patients was based on full medical histories and undertaking a general physical and neurologic examination. Exclusion criteria included the presence of diseases known to affect HRV (eg, cardiovascular, endocrinologic, neurologic and psychiatric disorders). No subject took medications regularly, the only exceptions being oral contraceptives and the occasional intake of nonsteroidal anti-inflammatory drugs (eg, acetylsalicylate or paracetamol).

All the subjects were asked to come to Autonomic Laboratory, Department of Physiology. Body mass index (BMI) was assessed using a standardised weighing machine and height scale according to the following formula: Body mass index (BMI) = weight in kilogram / (height in meters)^2 . Heart rate variability examinations were performed between 9:00 am and 12.00 noon. All participants were instructed to have a light meal only prior to the test. The subject was requested to lie down on the couch where electrodes for lead II ECG acquisition by Labchart Prov8.1.13(AD Instruments, Australia) were attached. The recording was performed in a controlled ambient temperature of 23 to 25°C. After an initial period of rest of 10 minutes, a 5-minute lead II ECG (sampling rate 1KHz) was recorded for later analysis. The subjects were asked to breathe regularly and calmly, and to avoid movement during data acquisition to prevent artefacts in the recording; they were also asked to stay awake.

ECG signal was stored by data acquisition software (Lab Chart Prov8.1.13 with HRV module version 2.0; (AD Instruments, Australia) using PowerLab 26T (AD Instruments, Australia). “R” waves were detected and artefact-free signals were stored for later analysis of time-domain and frequency-domain variables of HRV using Lomb Scargle Periodogram. Time domain variables of HRV consisted of SDRR (standard deviation of interbeat interval for all sinus beats) which denotes overall HRV and RMSSD (square root of the mean squares differences between adjacent RR intervals) which denotes vagal activity. Under frequency-domain, low frequency (LF: 0.04–0.15Hz) and high frequency (HF: 0.15–0.40Hz) power were calculated in absolute values of power (ms^2) ; LF/HF ratio was also calculated. The High frequency power reflects vagal activity, low frequency denotes combination of sympathetic and parasympathetic input while LF/HF ratio is an indicator of sympathovagal balance.

Statistical Analysis:

The data was analysed using Statistical Package for the Social Sciences (SPSS) version 20. Comparison of variables between the two groups and also between the males and females were done using independent t-test. Correlation of HRV indices with age and heart rate were made using Pearson correlation test. All the values were expressed as mean (±SD) and "p value" less than 0.05 was taken as significant.

III. Results:

Table 1 shows the mean values of age, height, weight and body mass index. The mean ages of group A and group B were 23.11 ± 3.83 year and 42.3 ± 3.43 year respectively. The average weight of group A was 63.01 ± 11.39 Kg and that group B was 67.96 ± 9.26 Kg which was statistically significant. BMI of group A was 24.95 ± 3.62 Kg/m^2 as compared to 27.51 ± 3.01 Kg/m^2 of group B which was statistically significant. The mean heart rates of group A and group B were 81.69 ± 7.75 beats per minute and 81.56 ± 7.34 beats per minute respectively which showed no significance.

Table 2 shows the normal values of heart rate variability of different age groups. The mean value of SDRR was 41.82 ± 14.33 ms^2 and RMSSD was 30.14 ± 12.11 ms^2 for time domain for group A. Again, the mean value of LF was 866.41 ± 662.70 ms^2, HF was 608.01 ± 603.56 ms^2 and LF/HF ratio was 1.68 ± 0.73 for Group A. Similarly, the mean value of SDRR was 33.85 ± 12.33 ms^2 and RMSSD was 21.65 ± 6.49 ms^2 for time domain for group B. Additionally, the mean value of LF was 241.61 ± 113.53 ms^2, HF was 149 .53 ± 84.18 ms^2 and LF/HF ratio was 1.77 ± 0.56 for Group B.

Comparison of HRV indices between the groups was found to be statistically significant in all the variables except the LF/HF ratio (table 2).

Table 3 shows the comparison of HRV indices between the males and females. The average values of SDRR, RMSSD, LF, HF and LF/HF ratio for males were 39.19 ± 14.21 ms^2, 27.20 ± 10.78 ms^2, 673.89 ± 652.37 ms^2, 475.25 ± 402. 27 ms^2 and 1.74 ± 0.71 respectively. Similarly, the average values of SDRR, RMSSD, LF, HF, LF/HF ratio for females were 40.67 ± 14.37 ms^2, 29.28 ± 13.23 ms^2, 738.98 ± 574.42 ms^2, 491.50 ± 326.13 ms^2 and 1.59 ± 0.61 respectively. All the HRV indices showed no significance statistically between males and females.

Table 4 shows correlation between the HRV indices and age and heart rate. The SDRR, RMSSD, LF, HF show statistically significant negative correlation with age except LF/HF. The HF shows significantly negative correlation with heart rate while the LF/HF shows positive correlation with heart rate which was statistically significant.

IV. Discussion:

In the present study, the value of SDRR, RMSSD, LF,HF and LF/HF ratio were 41.82 ± 14.33 ms^2, 30.14 ± 12.11 ms^2, 866.41 ± 662.70 ms^2, 608.01 ± 603.56 ms^2 and 1.68 ± 0.73 respectively for Group A. Similarly, the values of SDRR, RMSSD, LF, HF and LF/HF ratio were 33.85 ± 12.33 ms^2, 21.65 ± 6.49 ms^2, 241.61± 113.53 ms^2, 149 .53 ± 84.18 ms^2 and 1.77 ± 0.56 respectively for Group B. Moodithaya and Avadhany[12] conducted study on 267 healthy volunteers between age group of 6-55 years in Bangalore, South India and reported the comparison of HRV (frequency-domain) between different age groups. The HRV indices in frequency-domain for young adults of their study are lower than ours while that of the middle-aged are higher than us.

The comparison of HRV indices between the men and women is a controversial issue.Some studies found the differences while others documented no differences. Stein et al[13] revealed that the HRV was comparable in older men and women. Another study by Corrales et al[14] has concluded from their study that there was no significant difference between men and women in HRV indices which is similar with our study. However, previous study has reported that the average levels of HRV were lower for men than for women for participants with cardiometabolic condition in cross sectional analysis.[15] Park et al[16] observed men had higher total power, LF and LF/HF values than women while there were no significant differences in SDNN, RMSSD and HF between sexes. Agelink et al[17] also revealed that women upto 55 years of age have lower LF and LF/HF ratio compared to age-matched men. Another study documented no influence of gender in HRV indices in children and middle aged while changes were observed in young adult and middle-aged suggesting possible involvement of female sex hormone in regulating the autonomic balance.[12] Eventhough, the values of HRV are different between sexes, these differences diminish with age [18] which is believed to have greater impact on HRV.

Our study also found a negative correlation between the age and HRV indices except for LF/HF ratio. Park et al[16] have done study on 637 healthy Koreans (366 males and 271 females) and found that all the values of short term HRV were significantly decreased with age except LF/HF ratio which are similar with our findings. Another study by Abhishekh et al[19] found a negative correlation of SDNN, RMSSD and total power with age while LF/HF ratio showed a positive correlation which suggested sympathetic tone increases with age.

HRV measures decreased significantly with aging which may be the result of gradual decrease of overall fluctuation in cardiac autonomic input and by gradual reduction in parasympathetic modulation.[15] These parasympathetic changes may be due to decrease in muscarinic receptor activity[20] or disturbed cardiac acetylcholine release response to stimulation[21] with aging. Also adrenergic function decreases more linearly with age than parasympathetic function, which may be due to the decrease in sympathetic input[22] and /or reduced β-adrenoreceptor.[23]

Our study also revealed inverse correlation between HF and heart rate while the LF/HF ratio showed positive correlation with heart rate which was statistically significant. Agelink et al[17] reported a weak correlation of LF/HF with heart rate while there was a significant inverse correlation with heart rate and RMSSD. Bhati and Moiz[24] demonstrated a significant inverse correlation between HR and pNN50, RMSSD, and total power.

Our study demonstrated a significant inverse correlation between HF and heart rate which is indicator of a parasympathetic activity. The modulation of vagal tone helps maintain the dynamic autonomic regulation important for cardiovascular health. So, reduced vagal activity is implicated in increased morbidity.[6] LF/HF ratio reflects the absolute and relative changes between the sympathetic and parasympathetic components. The LF/HF ratio is used with the belief that there is a sympathovagal balance that modulates the sinus node activity (i.e., increased activity in one system is accompanied by decreased activity in the other system). So, the strong correlation between heart rate and HRV does have physiological significance.[25] Cardiac physiology aims to adapt quickly to any situation, implying flexibility and harmony between HRV and heart rate which deteriorate each time cardiac function is impaired.

Limitations:

Greater sample size would have been better in supporting the findings. The number of female subjects are much lesser than that of the males which might affect the result of comparison between males and females.

V. Conclusion:

We found a negative correlation between age and HRV. It reflects that with age there is a gradual decrease of overall fluctuation in cardiac autonomic input and reduction in parasympathetic modulation. The inverse correlation observed between HF and heart rate is an indicator of parasympathetic activity modulation which, maintains the dynamic autonomic regulation input for cardiovascular health.

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Table 1: The Mean (±Standard Deviation) Values of Demographic Data of different age groups.

Variable	Group A (n=63)	Group B (n=37)
Age (Years)	23.11 ± 3.83	42.3 ± 3.43
Ht (cm)	158. 52 ± 9.91	157.46 ± 8.60
Wt (Kg)	63.01 ± 11.39	67.96 ±9.26*
BMI (Kg/m2)	24.95 ± 3.62	27.51 ±3.01***
Heart rate (bpm)	81.69 ± 7.75	81.56 ± 7.34

n: number of subjects; P*< 0.05; p***<0.001; Ht: Height ;Wt: Weight; BMI: Body mass index; bpm: beats per minute

Table 2: Normal ranges of heart rate variability of different age groups

Variables	Group A	Group B	p
SDRR (ms^2)	41.82 ± 14.33	33.85 ± 12.33	.01*
RMSSD (ms^2)	30.14 ± 12.11	21.65 ± 6.49	.001***
LF(ms^2)	866.41 ± 662.70	241.61± 113.53	0.001***
HF(ms^2)	608.01 ± 603.56	149 .53 ± 84.18	0.001***
LF/HF ratio	1.68 ± 0.73	1.77 ± 0.56	0.553

P*<0.05; p***<0.001;SDRR: standard deviation of interbeat intervals for all sinus beats, RMSSD: square root of the mean squares differences between adjacent R R intervals; LF: low frequency ; HF: high frequency ; LF/HF ratio : ratio of low frequency and high frequency

Table 3: Comparison of HRV indices between the males and females

Variables	Male(mean±SD) (n = 66)	Female (mean ±SD) (n=34)	p-value
SDRR(ms^2)	39.19 ± 14.21	40.67 ± 14.37	0.64
RMSSD (ms^2)	27.20 ± 10.78	29.28 ± 13.23	0.42
LF (ms^2)	673.89 ± 652.37	738.98 ± 574.42	0.64
HF (ms^2)	475.25 ± 402. 27	491.50 ± 326.13	0.89
LF/HF ratio	1.74 ± 0.71	1.59 ± 0.61	0.33

n: number of subjects; SDRR: standard deviation of interbeat intervals for all sinus beats , RMSSD: square root of the mean squares differences between adjacent R R intervals; LF: low frequency ; HF: high frequency; LF/HF ratio: ratio of low frequency and high frequency

Table 4: Correlation between the HRV indices and age and heart rate

Variables	Age		Heart rate	
	correlation coefficient (r)	p-value	Correlation coefficient (r)	p-value
SDRR	-0.261	.009**	.007	0.94
RMSSD	-0.343	.001***	-0.147	0.14
LF	-0.48	.001***	-0.153	0.12
HF	-0.428	.001***	-0.30	0.002**
LF / HF	0.179	.07	0.316	0.001***

p**<0.01; p***<0.001; SDRR: standard deviation of interbeat intervals for all sinus beats , RMSSD: square root of the mean squared differences between adjacent R R intervals; LF: low frequency ; HF: high frequency; LF/HF ratio: ratio of low frequency and high frequency.