

## Gender differences of heart rate variability in healthy volunteers

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### Abstract

**Objective:** To identify the basic values of heart rate variability in Pakistani population and to verify our hypothesis that there are gender differences in cardiovascular autonomic modulation.

**Methods:** The descriptive cross sectional study based on convenience probability sampling was conducted at Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD) Pakistan. The duration of the study was from December 2009 to July 2010.

It involved 24-hour holter monitoring of 45 healthy individuals using holter electrocardiography (ECG) recorder. Heart rate variability was analysed in time (SDNN, SDANN, SDNNi, rMSSD, pNN50) and frequency domains (power, VLF, LF, and HF).

**Results:** The time domain indices; SDNN (male=140±36ms vs. females=122±33ms;  $p=0.09$ ), SDANN (male=123±34ms vs. females=111±34ms;  $P=0.23$ ), SDNNi (male=64±19ms vs. females=52±14ms;  $P=0.03$ ), and pNN50 (male=14±10ms vs. females=12±7ms;  $P=0.43$ ) were decreased in female volunteers when compared with males. Comparison of frequency domain indices; Total power (male=4041±3150ms<sup>2</sup> vs. females=2750±1439ms<sup>2</sup>;  $P=0.07$ ), VLF (male=2912±2675ms<sup>2</sup> vs. females=1843±928ms<sup>2</sup>;  $P=0.06$ ), LF (male=788±397ms<sup>2</sup> vs. females=556±346ms<sup>2</sup>;  $P=0.04$ ) and HF (male=318±251ms<sup>2</sup> vs. females=312±277ms<sup>2</sup>;  $P=0.94$ ) amongst males and females showed attenuated heart rate variability in females. Of all the observed values, SDNNi and LF were found significantly ( $p<0.05$ ) decreased in women.

**Conclusion:** In healthy population, heart rate variability is low in women than men. It reflects sympathetic dominance in women in our population.

**Keywords:** Autonomic nervous system, Healthy volunteers, Ambulatory electrocardiography (JPMA 62: 422; 2012).

### Introduction

Heart rate variability (HRV) refers to the beat-to-beat variation in heart rate generated by the interplay of sympathetic and parasympathetic nerve activity at the sinus node of the heart. Variations in sinus node impulse formation are depicted by heart rate variability derived from RR intervals — time difference between R waves of two heartbeats. Atrioventricular nodal conduction also adds to the RR variability but it seems to be insignificant under clinical conditions.<sup>1</sup> The utilisation of this technique in describing physiological response of patients with diverse diseases has been studied extensively. Especially spectral analysis techniques can differentiate among the intrinsic sources of HRV because these rhythms take place at various frequencies.<sup>2</sup>

It had been reported that African Americans had a decreased low frequency (LF) and an increased high frequency (HF) than Caucasian Americans, while a recent research in young male subjects revealed that African Americans had decreased LF and HF power and an aggravated LF/HF ratio than non-African Americans.<sup>3,4</sup> Data of one report conducted on Caucasians suggest lower level of efferent sympathetic nerve activity in

women than men.<sup>5</sup> Some studies on white subjects reported significantly lower sympathetic nerve activity in young and middle-aged women.<sup>6,7</sup> Work done on the population of Belgium documented that HRV indices, denoting vagal activity, were not significantly different between men and women, whereas the spectral indices, LF power and LF/HF ratio were significantly higher in men.<sup>8</sup> Another study documented a decrease in all the time domain parameters in females as compared to the males.<sup>9</sup>

Racial differences had been observed in different studies among different populations based on the variations in their autonomy. There is only limited data among young children<sup>10</sup> and none had compared adult Asians and Caucasians. We planned a study to evaluate HRV in normal healthy Pakistani subjects to look for the effects of variations in autonomic nervous system. The gender variation in time and frequency domains of HRV was also studied.

### Subjects and Methods

The study involved 45 (27 males and 18 females) apparently and electrocardiographically healthy individuals

without any cardiovascular complaints. Their physical examination was unremarkable and resting ECG was normal. Subjects were between 29 and 80 years of age with a mean age of  $42 \pm 14$  years. Subjects with diabetes mellitus, cardiovascular, neurological or psychiatric diseases were excluded. Smoking behaviour, age, height and weight were recorded.

The study was conducted at Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD) Pakistan and was approved by the Medical Ethics Committee and Institutional Review Board of Army Medical College and the Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD), Pakistan. The duration of the study was from December 2009 to July 2010. Informed consent was obtained from all the 72 individuals who initially volunteered to participate in the study. Of them, 14 were excluded due to diabetes mellitus, 2 due to arrhythmias, 4 due to history of myocardial infarction and 2 due to depression. The 50 volunteers underwent holter monitoring, but 5 of them were excluded due to technical failure, excess artifacts or insufficient hours of monitoring. HRV was thus analysed in 45 healthy volunteers.

A 12-lead standard electrocardiography (Motara ELI 250 EKG Machine; Absolute Medical Equipment, New York) was performed on all the subjects. Roughly 10 cardiac cycles were recorded to evaluate heart rhythm.

For HRV analysis, 'DMS 300-3A Serials Holter Recorder' and 'DMS Serials Holter Software Premier 11' (Diagnostic monitoring software, Kingsbury, UK) were utilised. The whole data was edited using visual checks for the exclusion of artifacts.

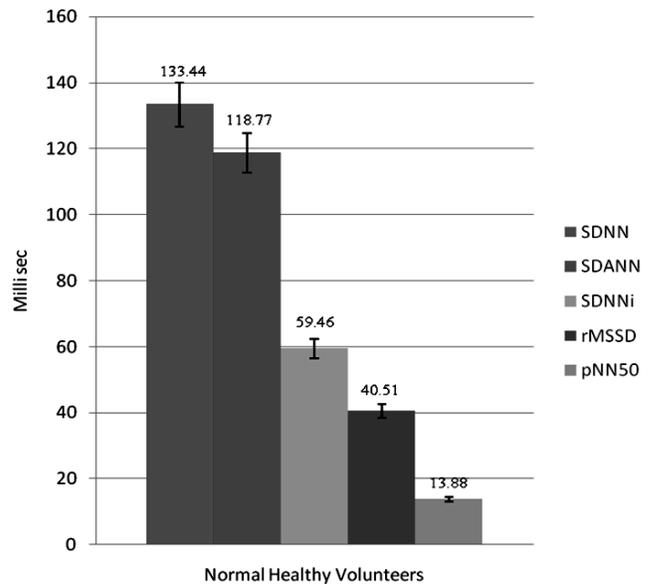
The beat-to-beat variation during normal sinus rhythm is expressed as heart rate variability (HRV). Variations in impulse formation are depicted by HRV derived from RR or NN (node-to-node) intervals on ECG. HRV was analysed in time and frequency domains according to the recommendations of the Task Force of the European Society of Cardiology (ESC) and the North American Society of Pacing and Electrophysiology (NASPE).<sup>10</sup> We considered time domain parameters; SDNN (standard deviation of R-R intervals), SDANN (standard deviation of average NN intervals), SDNNi (SDNN index; a measure of variability due to cycles shorter than 5 minutes), RMSSD (square root of the mean squared differences of successive NN intervals), and pNN50 (the number of interval differences of successive NN intervals greater than 50 ms (NN50)/total number of NN intervals). The frequency domain parameters were also analysed that included total power, VLF, LF, and HF. The basis of HRV lies in the fact that fluctuations in the heart rate reflect variations of sympathovagal activity.

Data was analysed by using computer software SPSS version 15. Variables were expressed as mean standard deviation. Student's t-test was applied for comparison between men and women in the study

population. P value < 0.05 was considered significant.

## Results

The values of time domain indices of normal healthy volunteers were recorded (Figure-1). SDNN in normal healthy volunteers was  $133 \pm 35$  ms. SDANN in normal healthy volunteers was  $118 \pm 34$  ms, while SDNNi was  $59 \pm 18$  ms. RMSSD was recorded as  $40 \pm 17$  ms and pNN50 was



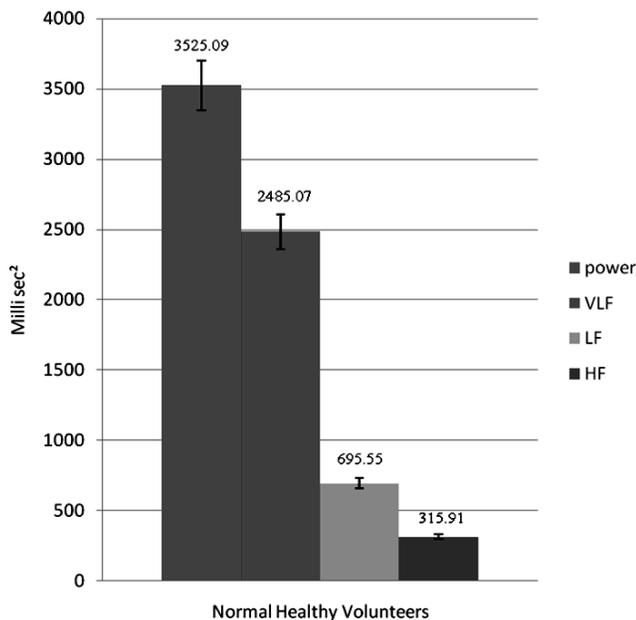
SDNN: Standard Deviation of RR Intervals. SDANN: Standard Deviation of Average NN Intervals. SDNNi: SDNN Index; a measure of variability due to cycles shorter than 5 minutes. rMSSD: Square root of the mean squared differences of successive NN intervals. pNN50: The number of interval differences of successive NN intervals greater than 50ms (NN50)/total number of NN intervals.

Figure-1: Time Domain Parameters in healthy volunteers.

Table: Comparison of time and frequency domain parameters between male and female healthy volunteers.

HRV Parameters	Group of individuals		P value
	Males (n=27)	Females (n=18)	
<b>Time Domain Parameters (ms)</b>			
SDNN	140±36	122±33	0.09
SDANN	123±34	111±34	0.23
SDNNi	64±19	52±14	0.03
rMSSD	40±14	40±22	0.9
pNN50	14±10	12±7	0.43
<b>Frequency Domain Parameters (ms<sup>2</sup>)</b>			
Total Power	4041±3150	2750±1493	0.07
VLF	2912±2675	1843±928	0.06
LF	788±397	556±346	0.04
HF	318±251	312±277	0.94

HRV: Heart rate variability. SDNN: Standard Deviation of RR Intervals. SDANN: Standard Deviation of Average NN Intervals. SDNNi: SDNN Index; a measure of variability due to cycles shorter than 5 minutes. rMSSD: Square root of the mean squared differences of successive NN intervals. pNN50: The number of interval differences of successive NN intervals greater than 50ms (NN50)/total number of NN intervals. VLF: Very low frequency. LF: Low frequency. HF: High frequency.



VLF: Very low frequency. LF: Low frequency. HF: High frequency.

Figure-2: Frequency Domain Parameters in healthy volunteers.

13 ± 9 ms in the volunteers.

The values of frequency domain indices were also recorded (Figure-2). Total power in the volunteers was found to be 3525 ± 2671 ms<sup>2</sup>. Likewise, the frequency band, including VLF, LF and HF exhibited mean values of 2485 ± 2201 ms<sup>2</sup>, 695 ± 391 ms<sup>2</sup> and 315 ± 259 ms<sup>2</sup> respectively.

When the HRV in males and females was compared, it was found that the relevant indices were decreased in females compared to the males with the exception of pNN50, in which difference between male and female subjects was found to be negligible. The difference in values of SDNNi (males= 64±19ms vs. females= 52±14ms; p = 0.03) was statistically significant (P<0.05) between male and female subjects (Table).

Similarly, the frequency domain indices like total power spectral component, VLF, LF and HF were found attenuated in females as compared to the male subjects, but the difference was not statistically significant. Only the difference in values of LF (males=788±397ms<sup>2</sup> vs. females= 556±346ms<sup>2</sup>; p = 0.04) was found statistically significant (P<0.05) between male and female subjects.

## Discussion

HRV is a representation of integrated response of the cardiovascular system to several different influences. Ethnic disparity in the correlations amid age and HRV parameters in African Americans and Caucasians had been documented

where young African Americans displayed a pattern of response that was analogous to older Caucasian Americans, indicating premature aging of their autonomic nervous system.<sup>2</sup> Racial differences with blacks having a lower sympathetic drive than age-matched whites was also documented.<sup>11</sup> Other studies also depicted the racial differences in autonomic status as measured by HRV indices.<sup>12,13</sup> HRV had been explored exclusively in Asian populations in Japanese children, but had not been compared with other races.<sup>14</sup> Our study aimed at documenting the values of time and frequency domain indices of HRV in the study population.

Quintana and colleagues documented HRV values in the normal population, but the sample size was very small (n=24).<sup>15</sup> Likewise, Ramaekers et al studied the HRV in normal healthy volunteers during the day and night separately and did not document the values during 24 hours.<sup>8</sup> Khan et al<sup>16</sup> conducted a study in healthy Pakistani individuals and showed the values of three time domain parameters (SDNN, SDANN and rMSSD), but the frequency domain parameters and gender differences were not described. The documented values of SDNN (139.48 ± 28.36 ms), SDANN (125.86 ± 21.35 ms) and rMSSD (27.05 ± 7.07 ms) in the previous study were greater than identified in our study (SDNN =133 ± 35 ms, SDANN=118± 34 ms, RMSSD = 40± 17 ms).

The time and frequency domain indices of our study population revealed decrease in SDNN, SDANN, total power, LF and increase in SDNNi, VLF, pNN50 and HF unlike the values documented in the study by Bigger et al<sup>17</sup> in which 274 normal subjects were studied. Increase in SDNNi, rMSSD, pNN50, HF and VLF indices was found statistically significant (P<0.05). Increased rMSSD, pNN50 and HF suggested the increased parasympathetic activity in our population and decreased risk of arrhythmogenesis.<sup>18</sup> It has been documented that HF power is correlated with pNN50 and rMSSD in the time domain.<sup>8</sup> Likewise, SDNNi and VLF affected by sympathovagal activity are increased, proposing increased parasympathetic activity. Total power was found significantly decreased (P<0.05) in our volunteers which indicates increased sympathetic nerve traffic, suggestive of stressful lifestyle. The value of total power was not correlated with SDNN; the global marker of HRV thus, is required to be further investigated. The variation in total power could be attributed to the difference in the mean age of their population<sup>17</sup> in comparison to our population.

Women are less prone to the risk of ischaemic heart disease and serious arrhythmias as compared to men.<sup>19</sup> Therefore, there might be gender-related differences in beat-to-beat heart rate dynamics in the healthy population. In addition, decreased HRV had been related with increased risk of mortality in community studies of male and female populations like in the Zutphen study from Holland by Dekker et al.<sup>20</sup> Data of one report suggested lower level of efferent sympathetic nerve activity in women than in men.<sup>5</sup> Some studies have reported

significantly lower sympathetic nerve activity in young and middle-aged women than men.<sup>6,7</sup> In other reports, either women were found to have lower sympathetic activity than men when examined at the same arterial blood pressure, or the average of sympathetic drive in women was not significantly different from that in men.<sup>21,22</sup> In one study on HRV in men and women, lower sympathetic activity in women than in men was observed.<sup>7</sup> Umetani et al studied the time domain parameters of 260 healthy subjects and documented that SDNN, SDANN and rMSSD declined in females as compared to the males.<sup>9</sup> Likewise, Hoogenhuyze et al. reported higher HRV (SDNN, SDNNi) in male subjects (age 24 to 54 years).<sup>23</sup> Bigger et al.<sup>17</sup> also found higher levels of VLF and LF power in male than in female subjects (age 40 to 69 years).

In our study, when HRV in male and female volunteers were compared it was found that HRV indices decreased in females as compared to the males. Of all the time domain parameters, only SDNNi was decreased significantly ( $P < 0.05$ ) in the females, and out of all the frequency domain parameters, LF was significantly ( $P < 0.05$ ) decreased in the females. Our data suggested sympathetic hyperactivity in females as compared to males. Therefore, women might be at increased risk of tachyarrhythmias that might lead to cardiovascular and all-cause mortality. Lower literacy level, stressors of life, fewer vacations, homemakers with symptoms of anxiety, loneliness during daytime, household work adversely affecting health, and fear of cardiovascular problems have been identified as the risk factors in females.<sup>24,25</sup> These may contribute to increased sympathetic activity and decreased HRV in females.

The effect of the nature and magnitude of physical activity and exercise capacity on HRV was not considered which is a limitation of our study. Larger studies may help to identify the influence of age, race, ethnic and environmental factors on HRV. A larger sample size may also increase the validity of the results.

## Conclusion

The study was an effort to identify normal values in both time and frequency domains among healthy volunteers. Heart rate variability was found to be low among women in our study population. It reflects sympathetic dominance in women than in the case of men.

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