

## Effects Of Generalized Anxiety Disorder On Heart Rate Variability

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**Abstract:** Background: Heart rate variability (HRV) is an easy, non-invasive, accurate and reliable tool in assessing autonomic function. Aim: Aim of this study was to determine whether the patients with generalised anxiety disorder have lower heart rate variability compared to healthy controls or not. Objective: To determine and compare heart rate variability in generalized anxiety disorder patients and in age and sex matched healthy controls. Method: Study had been done in 2 groups: 1st group comprises adult patients of generalized anxiety disorder (n=50) & the 2nd group of healthy controls (n=50). It was carried out on instrument windows based Heart rate variability analysis system Variowin-HR at Govt. Medical College, Bhavnagar. Heart-rate variability was studied using the standard protocol and was statistically analyzed. Result: Significantly reduced variability of the heart rate was observed in both the time domain parameters like SDNN (Standard deviation of all NN interval), RMSSD (The square root of the mean of the sum of the squares of differences between adjacent NN intervals), SDSD (Standard deviation of differences between adjacent NN intervals), NN50count (Number of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording), pNN50 (NN50 count divided by the total number of all NN intervals) as well as frequency domain parameters like LF( low frequency), HF (high frequency), LF/HF ratio in the disorder group as compared to the control group which are statistically significant (p<0.05). Conclusion: According to this study, generalized anxiety disorder (GAD) is associated with significantly lower Heart Rate Variability (HRV).

**Key Words:** Generalized Anxiety Disorder, Heart Rate Variability, Time Domain parameters, Frequency Domain parameters.

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**Introduction:** Generalised anxiety disorder (GAD) is characterized by excessive, uncontrollable and often irrational worry about everyday things that is disproportionate to the actual source of worry and rigid, inflexible response patterns. Anxiety disorders in the youth are receiving increasing attention. Such attention is understandable considering that an estimated 10 - 20% of the youngsters suffer from anxiety and anxiety-related symptoms. Anxiety disorders comprise the most prevalent set of psychiatric disorders in children and adolescents<sup>1, 2, 3</sup>. Diminished variability in HR may be common to clinical anxiety and the related psychopathologies. Non-invasive assessment of the intrinsic sources of HR variability is an area of great interest in psychophysiology<sup>4,5</sup>.

Heart rate variability (HRV) is the physiological phenomenon of variation in the time interval between heartbeats. It is measured by the variation in the beat-to-beat (R-R) interval. It is a noninvasive electrocardiographic marker

reflecting the activity of the sympathetic and vagal components of the autonomic nervous system (ANS) on the sinus node of the heart and has become the conventionally accepted term to describe variations of both instantaneous heart rate and RR intervals. Thus degree of variability in heart rate provides information about functioning of the autonomic nervous control on the heart rate and heart's ability to respond.

Disorders of affect such as anxiety disorders have been viewed as distorted emotional states in which an individual is not able to respond in an appropriate, flexible way to environmental demands<sup>6</sup>. Activation of the sympathetic nervous system enables the organism to organize an alarm reaction to respond appropriately to a stressful situation, also known as a "fight-or-flight" reaction. However, when the sympathetic nervous system dominates for prolonged periods of time, the energy demands on the body become excessive and eventually cannot be met, contributing to

wear-and-tear of bodily systems. Dysregulation of the ANS is thus associated with a number of physical and psychological symptoms and diseases, and is associated with increased risk of all-cause mortality<sup>7</sup>. As HRV is one of the non invasive tests for ANS function, dysregulation of ANS can be easily accessed by HRV and can prevent further complications occurring due to this. Reduced heart rate variability (HRV) is a prognostic factor for cardiac mortality<sup>8</sup>. The current study Aim at assessing the HR variability among subjects with generalised anxiety disorder as compared to healthy controls.

**Material and Method:** This study was carried out at Dept.of Physiology and Dept.of Psychiatry, Govt. medical college and Sir T Hospital, Bhavnagar, Gujarat, India. The study groups were comprised of Group-A (case) 50 patients of Generalised Anxiety Disorder came in psychiatry OPD and diagnosed clinically as having GAD by psychiatrist and severity of GAD was assessed by BECK ANXIETY INVENTORY and Group-B (control) 50 normal age and sex matched healthy subjects with no present or past history of any anxiety disorders (Table-1) of Bhavnagar district. After they were informed about the procedures and objectives of the study a written consent was taken as per standard protocol from all participants. All participants were advised to avoid eating and drinking (tea, coffee and alcohol) at least six hour prior to test as these may affect the results. Patients with Cardiovascular disorders (hypertension, h/o myocardial infarction, cardiac arrhythmia, having pacemaker) and other diseases like diabetes mellitus, renal failure, liver failure, cancer, AIDS and tuberculosis etc. terminal illnesses were excluded from the study.

**Procedure:** After giving information about the procedure, all participants were allowed to relax for ten minutes in a separate quiet testing room before starting the test. Case record form containing personal information of subjects, clinical history- diagnosis and vitals were filled up. Subjects were asked to lying down in a supine position and remain quiet, without speaking or making any movements for 5

minutes. ECG electrodes for HRV measurement were placed at both infraclavicular and both lumber regions of the subjects. The changes in the heart rate were measured with an instantaneous heart rate variability analyses software system – Variowin -HR interfaced with computer.

HRV were measured by continuous lead II ECG recording for 5 minutes (Short term HRV) based on R-R interval. Both time domain (SDNN, RMSSD, SDDSD, NN50Count, pNN50%) and frequency domain (LF, HF, LF/HF ratio) parameters of HRV analyses were measured and taken into calculation in the study.

**Other Physiological Measurements:** In this study, other physiological parameters like height, weight, BMI, temperature, heart rate, blood pressure and respiratory rate were measured and documented in the case record form.

**statistical Analysis:** All data were represented as a Mean  $\pm$  SD and statistical analysis was done by using unpaired t-test. We were using graphpad instat statistical software for data analysis.

**Result:** A Total of 100 subjects were recruited in the study of which 50 were in the generalised anxiety disorders group and 50 were in the healthy controls group. Table-1 shows that participants with GAD (group-A) did not significantly differ from healthy controls (group-B) with regard to age, sex, height and weight.

Heart rate variability exhibited significant differences for both time domain and frequency domain parameters between the generalised anxiety disorder group (A) and healthy control group (B). Time domain and frequency domain measures of heart rate variability are depicted in table-2 and table-3 respectively. In Time domain, GAD group(A) had reduced all parameters like SDNN(ms), RMSSD (ms), SDDSD, NN50 Count, pNN50(%) compared to the control group (B) and all values were statistically extremely significant ( $p < .05$ ) except the SDDSD.

**Table 1: Physiological Characteristics (Mean ±SD) of Disorder group and Control group.**

Physiological Parameters	(A)Disorder Group(50) (Mean ± Sd)	(B)Control Group(50) (Mean ± Sd)	P Value
Age(yrs)	33.28 ± 10.126	37.64 ± 12.317	0.0561
Weight(kg)	56.10 ± 10.533	60.16 ± 10.479	0.0562
Height(cms)	162.94 ± 8.819	161.18 ± 10.484	0.3659
BMI	21.17 ± 3.890	23.22 ± 4.143	0.01249
Sex			
Male-----→	19(38%)	21(42%)	
Female----→	31(62%)	29(58%)	

SD=Standard Deviation, p value < 0.05 indicates significance.

**Table 2: Comparison between Time domain parameters (mean ± SD) of both groups and P values of each parameters.**

Time Domain Parameters	(A)Disorder Group(50) (Mean ± Sd)	(B)Control Group(50) (Mean ± Sd)	P Value
SDNN (ms)	34.39 ± 15.85	45.78 ± 9.96	<0.0001
RMSSD (ms)	27.19 ± 17.70	36.18 ± 11.69	0.0035
SDSD (ms)	33.84 ± 58.97	35.42 ± 11.91	0.8529
NN50 Count	30.1 ± 41.42	51.3 ± 31.60	0.0049
pNN50 (%)	8.36 ± 11.61	13.22 ± 8.95	0.0211

SD=Standard Deviation, P value < 0.05 indicates significance.

HF: Power in the high frequency (HF) band (~0.15–0.4 Hz in adults) has been associated with respiratory sinus arrhythmia and it is considered to reflect vagal modulation of the heart.

LF: power in the low frequency (LF) band (~0.05–0.15 Hz) probably reflects a complex interplay between sympathetic and vagal influences.

In frequency domain measures, the disorder group patients had significantly lower values of

LF and HF compared to the control group (p<.05). These findings signify decreases in both sympathetic and parasympathetic activities in patients with generalised anxiety disorder. The value of LF/HF ratio is significantly higher in group-A than group-B, which indicates dominance of sympathetic activity.

**Table 3: Comparison between frequency domain parameters (mean ± SD) of both groups and P values of each parameters.**

Frequency Domain Parameters	(A)Disorder Group (50) (Mean ± Sd)	(B)Control Group(50) (Mean ± Sd)	P Value
LF (ms2/HZ)	612.57 ± 652.47	1080.72 ± 645.50	0.0005
HF (ms2/HZ)	484.53 ± 497.20	889.57 ± 600.29	0.0004
LF/HF Ratio	1.81 ± 1.23	1.39 ± 0.78	0.0460

SD=Standard Deviation., P value < 0.05 indicates significance.

**Discussion:** The current study is aimed at finding the differences in heart rate variability (HRV) among the patients with generalised anxiety disorder (GAD) as compared to healthy controls. We have included an age and sex matched control group.

Literature reveals that anxiety disorders in the youth are receiving increasing attention. It is also prevalent in childrens and adolescents<sup>1, 2, 3</sup>. Anxiety is often accompanied by somatic manifestations that suggest morbid changes in the autonomic nervous system (ANS) activity, such as rapid heart rate (HR), shortness of breath and sweating. The autonomic characteristics of depression and panic disorder have been studied extensively. However, relatively few studies have examined the autonomic characteristics of generalised anxiety disorder<sup>9</sup>.

In the current study, heart rate variability (HRV), a measure of both sympathetic and parasympathetic activity exhibited significant differences between the generalised anxiety disorder group (A) and healthy control group (B)

for both the time and frequency domain parameters of HRV. The time domain parameters shows significantly reduced heart rate variability in generalised anxiety disorder group. These findings shows a pattern of decreased parasympathetic activity in the GAD group. This was similar to a previous study done on adults aged 23-40 years<sup>10</sup> which was postulated that anxiety was related to a reduced vagal control (parasympathetic activity) of the heart. Licht et al.<sup>11</sup> reported a lower HR variability among adults with anxiety disorders.

The present study findings of frequency domain parameters shows that decreases in sympathetic and parasympathetic activity in the disorder group, thus representing diminished physiological variability at rest<sup>12</sup>. The parameter that increased its value significantly, and that are related to sympathetic activity is LF/HF. The value of LF/HF ratio is significantly higher in group-A than group B, which indicates dominance of sympathetic activity (sympathetic modulation of heart rhythm) over parasympathetic control. The actual results are in line with those obtained for phobic anxiety<sup>13</sup> and according to level of anxiety<sup>14</sup>. This is in conform with the studies that reported a decrease in vagal activity with anxiety disorders<sup>15,16</sup>.

It is important to note that HRV measures fluctuations in autonomic inputs to the heart rather than the mean level of autonomic inputs. Thus, both autonomic withdrawal and saturatingly- high level of sympathetic input lead to diminished Heart rate variability (HRV)<sup>17</sup>.

Heart rate variability (HRV) measurement is useful in investigating the pathophysiology of various psychiatric disorders<sup>18</sup>. Several behavioural and psychological states such as acute and chronic smoking, acute and chronic alcohol ingestion, sedentary lifestyle, depression, panic disorders and aging have all been associated with a loss of heart rate variability and complexity<sup>19, 20, 21, 22</sup>.

The presence of a high vagal tone seems to be a marker of physiological and psychological

flexibility. So, decreased vagal tone as in generalised anxiety disorder group in our study may cause loss of flexibility in physiological systems in general, and in the cardiovascular system in particular which has recently been linked with a number of diseases and dysfunctions. Certain conditions such as sudden cardiac death, ventricular fibrillation, hypertension, diabetes mellitus and coronary atherosclerosis have been associated with reduced HR variability<sup>23, 24</sup>.

Hence, reduced heart rate variability in our study indicates that psychological states like generalised anxiety disorder can impact dramatically on dynamic autonomic control of heart. This is an issue that requires interdisciplinary approaches across multiple levels of analysis, ranging from the psychological to the biological.

**Conclusion:** This study indicates that generalised anxiety disorder (GAD) is associated with reduced HRV and vagal tone. Reduced heart rate variability (HRV) in GAD is a prognostic factor for cardiac mortality and associated with autonomic dysfunction that seems likely to play a pathogenetic role in the long term.

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