Changes In Heart Rate Variability In Depressed Patient

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Abstracts: Background: Major depressive disorder is most common mood disorder and is one of the most burdensome and disabling disease in the world. Abnormalities in the hypothalamic-pituitary adrenal (HPA) axis in depressed patients play a substantial role in autonomic dysregulation, as patient with depression have elevated levels of cortisol. The present study was conducted with a motive to compare and evaluate the effects of depression on cardiovascular autonomic functioning compared with healthy controls. Methodology: In this study 72 subjects were selected out of that 36 were depressed and 36 were control. All depressed patient were taken from outpatient department of Psychiatry. All subjects were between the age group of 18-60 years. Control group were students and employees of Surat Municipal Corporation (SMC) having no current or past psychiatric illness. HRV test was done in a well-lighted and ventilated room of Physiology Department. 5 minute ECG recording with 16 channel digital polywrite were taken at resting state. ECG was analysed on Kubios HRV analysis software version 1.1, for calculation of frequency domain parameter. Results: On analysis it was revealed that depressed patients showed altered values of HF component of HRV (23.33 $\pm$34.454) than control group (118.31 $\pm$ 201.186), which is significantly lower ($p < 0.05$) indicating lower parasympathetic activity. Conclusion**:** The findings from this study are consistent with the hypothesis that cardiac autonomic dysfunction is experienced by individuals with depression, especially decreased parasympathetic nerve. [Chaudhary R. NJIRM 2015; 6(2):61-65]

Key Words: Autonomic nervous system, Autonomic Function, Major Depressive Disorder.

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Introduction: Major depressive disorder (MDD) and cardiovascular disease (CVD) are leading burdens of disease worldwide, and there is increasing recognition that the two are related. Depression is associated with elevated rates of cardiovascular morbidity and mortality. This elevation seems to be due to a significantly increased risk of coronary artery disease and myocardial infarction leading to sudden cardiac death[1] .Recent data suggest that the increased rates of cardiovascular disease in patients with depression may be the result of one or more still-unrecognized underlying physiological factors that predispose a patient to both depression and cardiovascular disease[1] . Many theories exist about the relationship(s) between depression and coronary heart disease (CHD), ranging from neurobiological theories of stress (encompassing neuronal, hormonal, and immunologic responses) to sociological theories[2] . Several prospective studies have found an association between depression and the subsequent development of CHD[3] . The relative risk of fatal, as well as nonfatal, CHD ranged from 1.5 to 3.36 in those suffering from depression[1-4] . A recent study found that depression increased an individual's chance of experiencing myocardial infarction (MI) 4-fold[3] .In addition, recent findings suggest that depression is an independent risk factor for progression of heart disease[1-4] . Not much is known about how depression might contribute to this increased risk, although factors such as increased platelet aggregation and poor adherence to cardiac treatment regimens have been suggested[2-4].However, altered cardiac autonomic tone remains one of the most plausible explanations[5] . Increased sympathetic or decreased parasympathetic nervous system activity predisposes patients with CHD to ventricular tachycardia, ventricular fibrillation, and sudden cardiac death[2-5] . Since altered autonomic tone may account for the effect of depression on cardiac mortality, heart rate variability (HRV) analysis has been used widely as a method of assessing the cardiac autonomic modulation[6] . Low HRV reflects excessive sympathetic or inadequate parasympathetic tone and is a strong, independent predictor of post-MI mortality[7] .HRV is synonymous with "beat-to-beat variability" and is a measure of cardiac autonomic innervation by the brain. It is proposed that a reduction in parasympathetic tone allows unopposed stimulation by sympathetic nerves, which may result in arrhythmias and death. This chronic sympathetic stimulation (or loss of

vagal stimulation) is also noted in patients with major depression[6,7]

HRV can be assessed in two ways, either as a Time Domain Analysis or in the frequency domain as a Power Spectral Density (PSD) analysis. In either method, the time intervals between each successive normal QRS complex are first determined. Each of the methods has advantages and disadvantages. Time domain measures are the simplest to calculate but do not provide a means to quantify autonomic balance. On the other hand, the main advantages of power spectral density(PSD) analysis over the time domain measures is that it supplies information on how the power is distributed (the variance) as a function of frequency, thereby providing a means to quantify autonomic balance at any given time.

Our study aims to investigate the hypothesized link between HRV and major depression in a Indian depressed outpatient sample.

Material and Methods: After the permission of IRB, fresh untreated, clinically diagnosed for MDD (Major Depressive Disorder) according to DSM IV criteria having no any other disease attending OPD of Psychiatry Department of SMIMER Hospital, Surat were selected as cases . Severity of depression was assessed by Hamilton rating scale(HAMD) . After the clinical screening of the patient they were brought to the Physiology Department for further evaluation of autonomic function test. Control group were students and employees of Surat Municipal Corporation (SMC) having no psychiatric illness.

Written informed consent was taken from the subjects and controls prior to the tests and the procedure was explained to them. Detailed history was taken and complete physical examination was carried out.

5 minute ECG recording on 16 channel digital polywrite were taken at resting state. ECG was analysed using Kubios HRV analysis software version 1.1 for calculation of frequency domain parameter.

Statistical analysis was conducted using SPSS-statistics -20. The data were analysed by using unpaired T- test .

Results: Depressed patients showed altered values of HF component of HRV (23.33 $\pm$3.445) than control group (118.21 $\pm$ 20.118), which is significantly lower ($p< 0.05$) indicating lower parasympathetic activity. The values of LF component of HRV in depressed group (166.17 $\pm$ 22.028) was compared with that of control group (316.25 $\pm$ 40.461) which was significantly lower in depressed group ($p< 0.05$). The values of LF/HF in depressed group was (7.72 $\pm$ 5.02) compared with that of control group (6.11 $\pm$ 5.88) which was insignificantly higher in depressed group.

Table1: Resting Autonomic variables in study and control group.

Variables	Control group (n=36)	Depressed group (n=36)	P value
Heart rate (beats/mins)	77.53 + 8.677	86.25 + 9.708	.0001
SBP (mmHG)	119.28 + 11.057	122.56 + 10.216	.196
DBP (mmHG)	78.06 + 10.406	84.78 + 9.418	.005

Table2: Frequency domain variables of two groups.

Parameter (HRV)	Control	Depressed
LF (ms2)	316.25 $\pm$ 40.461	116.17 $\pm$ 22.028
HF (ms2)	118.21 $\pm$ 20.118	23.33 $\pm$ 3.445
LF/HF	6.11 $\pm$ 5.888	7.72 $\pm$ 5.023

Discussion: Relations between depression and autonomic function are potentially important clinically, because depression is an independent risk factor for cardiovascular disease and for cardiac morbidity and mortality[8,9,10]. Moreover, decreased heart rate variability and vagal control of the heart are negative predictors of outcome[11-13], which raises the possibility that the autonomic

correlates of depression (decreased vagal and increased sympathetic control) may mediate in part the relation between depression and cardiovascular disease. The current picture is somewhat more complex than this, heart rate variability remains a important predictor of cardiac risk[14] and HF(high frequency) component of heart rate variability is also a predictor of outcome in major depressive disorders[15].

Neurohumoral activation may play a particularly important role in the connection between depression and outcomes in heart failure). Levels of circulating catecholamine's (e.g. epinephrine and nor epinephrine) are elevated in patients with heart faliure, especially in those with decompansatedheart faliure, and higher levels of norepinephrine have been linked to greater mortality in this illness[16,17]. Furthermore, increases in plasma as well as CSF levels of nor epinephrine have been observed in patient with MDD to the extent of being capable of causing increased mortality in heart faliure[18]. Abnormalities in the hypothalamic-pituitary adrenal (HPA) axis may also play a substantial role , as cortisol,(and aldosterone) are independently linked with mortality in heart faliure, and patient with depression have elevated levels of cortisol[19]. Such increased level of cortisol and other HPA- related abnormalities in depression may impact medical outcomes in cardiac illness, as these abnormalities are associated with the development and progression of condition like dyslipidemia, truncal obesity, and insulin resistance and linked to cardiac morbidity and mortality.

Beyond elevated levels of circulating catecholamine's and cortisol, other abnormalities in the autonomic nervous system may also contribute to the relationship between depression and cardiac disease. Since the heart is innervated by both sympathetic and parasympathetic nervous systems, the interplay between these two opposing forces helps the heart make changes in response to stressors.

Depressed patient (with or without cardiac disease) exhibit a pattern of increased sympathetic and decreased parasympathetic activity; this is manifested by decreased baroreflex sensitivity and decreased heart rate variability (HRV), suggestive of imbalance between sympathetic and parasympathetic nervous systems.
This study demonstrated that, when compared with a healthy control group, patients of clinical depression exhibited altered cardiac nervous function, evidenced by lower high frequency domain index.

The findings of this study are consistent with the hypothesis that cardiac autonomic dysfunction is experienced by individuals with depression, especially decreased parasympathetic nerve activity (as evidenced by decreased values of the HF component of frequency domain index). This is supported by other studies of patients with depression that have applied other assessment techniques. For example, Bi et.al[20] found that patients with depression experienced autonomic nervous dysfunction using sympathetic skin response measures. There may be a number of explanations for this finding. A mood disorder may trigger a series of adverse cardiovascular factors that evoke pathophysiological changes,[21]. These study[22-24] have demonstrated a significant relationship between depression and cardiovascular risk factors that are known to lead to adverse outcomes. Battacharyya et al[25]. hypothesized that the relationship between depression and cardiovascular risk may be explained by enhanced parasympathetic control. We suggest that the decreased observed in our study (using frequency domain analysis) is indicative of reduced parasympathetic nerve activities and the imbalance of sympathetic and parasympathetic innervation, which may reflect dysregulation of sympathetic and parasympathetic coordination in depression.

HF may represent both vagus nerve activity and respiratory activity. However,Berger[26] found that while vagus activity was reduced in their group of depressed patients, there was no relationship between parasympathetic nervous activity and the frequency and rhythm of respiration. As there is a direct effect on HRV[27] , where HRV is smaller if parasympathetic activity is lower and vice versa, we propose that parasympathetic nervous activity predominantly influences cardioregulatory function. Pathophysiological links between

depression and cardiovascular system dysfunction include reduced HRV, changed sympathetic nerve activity, arrhythmia, and altered ventricular electrophysiological properties[28].

Conclusion: Our findings suggest that depression is accompanied by dysfunction of the cardiac autonomic nervous system. Individuals with depression appear to be susceptible to premature cardiovascular disease.

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