



# Heart Rate Variability a Cardiac Indicator in Diabetic Autonomic Neuropathy: A Systematic Review

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## ABSTRACT

**Background:** Cardiac indicator Heart Rate variability (HRV) is a significant sensitive and early predictor, which could be used for early deduction of complications among Diabetes Mellitus patients. Many studies have reported the usefulness of HRV as diagnostic method, however, there is a gap in the literature in the utilization of HRV in the clinical practice in planning, providing, and evaluating quality care for patients with diabetic autonomic neuropathy.

**Purpose:** The purpose of this systematic review it was to review the cardiac indicators of diabetic autonomic neuropathy.

**Method:** A Systematic Review of published clinical research articles from PUBMED data source was performed and the review is organized under method and result section. The research articles were selected for the review with inclusion criteria including clinical research studies, addressing concepts of HRV, diabetes mellitus, and autonomic neuropathy.

**Conclusion:** The review concluded that existing literature support that the HRV is a sensitive cardiac indicator, which may help to predict the cardiac morbidity and mortality among diabetes mellitus patients. HRV may be used as a significant cardiac indicator to predict diabetic autonomic neuropathy. This finding may be useful in the early diagnosis and treatment of complications among patients with diabetes mellitus.

## INTRODUCTION

The autonomic neuropathy (DAN) is a major complication of diabetes. DAN has been shown to be closely related to glycemic control. DAN is a complication that contributes significantly to the morbidity and mortality related to the disease, and it is an indicative of an increased risk of cardiovascular events. The tests assessing the function of the autonomic nervous system include assessing the response of heart rate and blood pressure to maneuvers stimulating the autonomic nervous system, including deep breathing. Valsalva maneuver and standing, allowed detecting signs of DAN in adolescents; however, the sensitivity of such tests in revealing an early impairment of the autonomic nervous system proved low. Several

studies found heart rate variability (HRV) to be useful in assessing the dysfunction of the autonomic nervous system in diabetic children and adolescents, but only in few studies HRV parameters were evaluated in most of them(1).

Cardiac indicator Heart Rate variability (HRV) is a significant sensitive and early predictor, which could be used for early deduction of complications among Diabetes Mellitus (DM) patients. Many studies have reported the usefulness of HRV, however, there is a gap in the literature in the utilization of HRV in the clinical practice in planning, providing, and evaluating quality care for patients with DAN. The purpose of this systematic review is was to review the cardiac indicators of diabetic autonomic neuropathy.

## METHOD AND REVIEW

A Systematic Review of clinical research articles from PUBMED data source was performed. The research articles were selected for the review with inclusion criteria including clinical research studies, addressing concepts of HRV, DM, and autonomic neuropathy.

### Morbidity and mortality from cardiac complications from diabetic autonomic neuropathy

Cardiovascular problems are prevalent in Diabetic patients. Diabetes mellitus is associated with cardiovascular problems such as coronary heart disease (CHD), stroke, peripheral arterial disease, nephropathy, retinopathy, and possibly neuropathy and cardiomyopathy. DAN is a serious complication of Diabetes mellitus. Individuals with long-standing type 1 or 2 DM may develop autonomic dysfunction involving the cholinergic, noradrenergic, and peptidergic (peptides such as pancreatic polypeptide, substance P, etc.). DM-related autonomic neuropathy can involve multiple systems, including the cardiovascular, gastrointestinal, genitourinary, sudomotor, and metabolic systems. Cardiac autonomic neuropathies cause a resting tachycardia and orthostatic hypotension. Reports of sudden death have also been attributed to autonomic neuropathy. According to American Heart Association, adults with diabetes are two to four times more likely to have heart disease or a stroke than adults without diabetes. Risks of cardiac complications and related morbidity and mortality are increased six times among perioperative non cardiac surgical patients with diabetes mellitus (2). While left ventricular systolic and diastolic abnormalities are common among diabetic patients, autonomic neuropathy coexists with the condition of left ventricular filling abnormalities among patients with DM (3). Cardiac vascular changes occur as a result of cardiac autonomic neuropathy and microangiopathic changes resulting in angina and non-anginal complications from DM. Microvascular changes, cardiac hyper functions, cardiac autonomic neuropathy, micro-angiopathic complications are associated with diabetes mellitus and they may be used as a prognostic markers of complications (4, 5). Post-operative complications are common among patients with DM, particularly risk of post-operative myocardial infarction is more common in this patient population (6). Measurement of HRV may serve as an early assessment method to identify and prevent cardiac complications in patients with DM.

### Mortality related with cardiac diseases among DM

According to American Heart association, heart diseases and stroke are the No. 1 causes of death and disability among people with type 2 diabetes. Cardiovascular disease is a major complication of diabetes and the leading cause of early death among

people with diabetes. About 65 percent of people with diabetes die from heart disease and stroke according to National Diabetic Education Program. Post-operative complications and hospital mortality are higher among patients with DM. majority of the patients, who undergo cardiac surgery have poor blood sugar control post operatively, and they do not have a diagnosis of DM prior to surgery. All-causes post-operative mortality was higher among patients who underwent non- cardiac surgical procedures and who were treated with insulin. Post-operative mortality is significantly higher among DM patients from complications (7). Early diagnosis of complication is the key to prevent mortality. HRV may be used as a predictive risk factor for cardiovascular morbidity and mortality in Type I DM patients (8), and it may be used as an early diagnostic indicator for cardiac morbidity among diabetic patients.

### Significance of Heart rate variability in diagnosis of DAN

Cardiovascular autonomic neuropathy diagnosed by heart rate variability (HRV) is strongly associated with an increased risk of silent myocardial ischemia and mortality. Autonomic neuropathy is more common among Type I DM patients. In a prospective clinical study with 58 type 1 and 51 type 2 diabetic patients, the results indicated that symptoms accompanied the signs of autonomic neuropathy in Type 1 DM but not in Type 2 DM (9). Autonomic neuropathy resulting from diabetes mellitus causes alteration of parasympathetic and sympathetic functions, which causes heart rate variations. Assessment of diabetic neuropathy can be achieved by assessing heart rate variations. A case control study's results, which contained 95 cases and 38 controls, by Oikawa et al. (1986) reported that diabetic patients had lower heart rate during deep breathing. The study concluded that there were significant sympathetic and parasympathetic impairments among patients with diabetic neuropathy (10).

Assessment of Heart Rate Variations (HRV) is a useful method to diagnose diabetic neuropathy at the early stage. Braune (1995) recommended measurement of Heart Rate Variations (HRV) for deducting polyneuropathies among diabetic patients. The researcher reported that there were significant differences in HRV between health volunteers and diabetic patients with neuropathy (11). HRV analysis may be used to diagnose the autonomic neuropathy in the early stages of diabetic mellitus before the development of somatic neuropathy. Measurement of HRV using power spectrum analysis is a sensitive indicator in the assessment of autonomic neuropathy related to DM (12). Another study report indicated that the measurement of HRV is a useful tool to diagnose autonomic neuropathy and peripheral neuropathy among patients with DM (13).

A clinical case control study, using 27 cases of diabetic neuropathy and 20 controls assessed the HRV using power spectrum analysis, reported that there was a significant difference between controls and severe diabetics due to autonomic neuropathy. There was reduction of the low frequency component in the standing position and a significant reduction of the percentage increase compared with the lying position, was found to discriminate diabetics from controls (14). Heart rate monitoring is a vital noninvasive tool in the diagnosis of autonomic neuropathy at the early stage before occurrence of symptoms. A prospective clinical study involving 301 diabetic patients between ages of 20 to 49 reported that HRV on deep breathing is a sensitive indicator to diagnose autonomic neuropathy, when compared with heart changes on standing (15). A natural history clinical study results indicated that Heart rate variation (HRV) on deep breathing proved to be the more sensitive diagnostic index of autonomic neuropathy and was abnormal or borderline in 62 of 64 patients with established autonomic symptoms. Abnormal tests appeared to represent permanent autonomic damage and may be present for years without the development of autonomic symptoms. Serial observations of HRV on deep breathing over 3 to 5 years showed little change, although overall there was a small deterioration of autonomic function, with a decrease of HRV score of 1.0 per year (16). Cardiac indicator HRV was found associated with DAN. Studies on prevalence of diabetic autonomic neuropathy results indicated symptomatic autonomic neuropathy was more frequently associated with Type 1 DM when compared to Type 2. In other words asymptomatic autonomic neuropathy was more common among patients with Type 2 DM(17, 18). Another clinical study results indicated that most had a sudden increase in heart rate in response to standing some had a prolonged gradual increase in heart rate on standing. A prevalence of 15% was suggested by the study for diabetic autonomic neuropathy in this age group(19). In addition, clinical studies, which assessed the diabetic autonomic neuropathy by heart rate variations, indicated the differences in mean heart rate, Standard deviation and coefficient of HRV was more significant in patients with neuropathy however the pulse wave velocity indices did not show significant differences (20,21).

### HRV in Early Diagnosis

HRV may be useful in the early diagnosis of DAN among patients with DM. A clinical study on early diagnosis of diabetic autonomic neuropathy indicates that heart rate variability can detect early subclinical alterations of autonomic nervous system (1). A clinical study report indicated that HRV is a sensitive assessment method for DAN from the study using heart rate reserve and rating of perceived exertion to prescribe exercise intensity in

DAN. The results indicated that HRR was a better measure than RPE to prescribe exercise intensity in DAN(22).

Another clinical study on 186 Type 2 diabetes mellitus using QTc interval, heart rate variability and postural hypotension as indicators of Cardiac autonomic neuropathy reported that prolonged QTc interval, heart rate variability and postural hypotension in Type 2 diabetes mellitus patients with cardiac autonomic neuropathy.(23). Further, a clinical study on the effect of glycemic control on heart rate variability in Type 1 diabetic patients with cardiac autonomic neuropathy reported that early diagnosis of DAN has benefit of early treatment and reversible effect on DAN. The results indicated that in patients with early DAN with strict glycemic control there is a potential for reversibility.(24).

### DISCUSSION AND CONCLUSION

Early diagnosis and treatment is a hallmark of quality care. Early diagnosis of DAN may result in early treatment and which may promote reversible effect on the progression of the related cardiac morbidities. Identifying a significant, noninvasive, feasible cardiac indicator may help to prevent morbidity and mortality among patients with DAN. Many studies have reported that cardiac indicator HRV is a significant predictor of cardiac morbidities and DAN among patients with DM. It has higher utility value in the clinical practice, as it is a noninvasive assessment method and it is a feasible method, which could be easily used by health care professionals.

HRV has a diagnostic implication in preventive care as it is a sensitive indicator in prediction of DAN related cardiac morbidity. Regular HRV testing provides early detection and thus facilitates timely diagnostic and therapeutic interventions. It is a simple, non-invasive technique which in the average clinic, hospital, or diagnostic center with the use of available technology. Thus, HRV is an important diagnostic tool in Diabetic autonomic neuropathy. The review concluded that existing literature support that the HRV is a sensitive cardiac indicator, which predicts the cardiac morbidity and mortality among diabetes mellitus patients. HRV may be used as a significant cardiac indicator to predict DAN. This finding may be useful in the early diagnosis and treatment of DM-DAN patients.

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