International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR)

ISSN: 2347-6567

IJAMSCR |Volume 3 | Issue 4 | Oct – Dec - 2015
www.ijamscr.com

Research article *Medical research*

Evaluation of cardiac autonomic neuropathy in diabetes mellitus using electrocardiographic changes and ANSiscope device

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ABSTRACT

AIM

Evaluation of cardiac autonomic neuropathy in diabetes mellitus. Patient using electro cardio graphic changes of heart rate variability and correlate the ECG changes with beat to beat variation using ANSiscope device.

MATERIALS

STUDY POPULATION

50 diabetic patients attending Diabetology Outpatient Department, of RMMCH, Chidambaram. These subjects were selected after scrutinizing them for exclusion criteria. 50 patients attending General Medical Outpatient Department at RMMCH, Chidambaram. These subjects were age matched controls.

METHODOLOGY

After selecting the patients on basis of the criteria history will be elicited and clinical examination done as per proforma. The necessary investigations [fasting blood sugar, post prandial blood sugar, ECG, ANIscope] will be done and statistically analyzed.

CONCLUSION

The resting heart rate (86.16±7.6) was significantly (P<0.05) higher than that of non diabetic controls (76.64±9.18). There was a leftward deviation of QRS axis among diabetics (31.6°) as compared to controls (54°). QTc interval was prolonged (400.62 ± 32.18 msec) in diabetic study population which was significant (P0.0000). Cardiac dysautonomia was demonstrated in the study population using the following parameters. Abnormal E:I ratio (<1.1) (50%). Postural fall in systolic blood pressure (>10mmHg) (42%) Ratio of 10^{th} RR interval to 5^{th} RR interval was abnormal in (60%). Dyansys ANSi scope score was abnormal in 80% of the study group.

KEY WORDS: Diabetes mellitus, cardiac autonomic neuropathy

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that of several distinct types of DM are caused by a complex interaction of genetics and environmental factors. Depending on the etiology

of the DM, factors contributing to hyperglycemia include glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. The diabetes control and complications trial showed that intensive control of the blood sugar over a 7 year study interval reduced the progression of diabetic retinopathy, nephropathy and neuropathy[13]. At the San Antonio Consensus Conference in 1988, it was agreed that diabetic neuropathy (DN) 'is a descriptive term meaning a demonstrable disorder, either clinically evident or subclinical, that occurs in the setting of diabetes mellitus without other causes for peripheral neuropathy'.[1] A later international consensus meeting on the outpatient diagnosis and management of DN defined DN as 'the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes'.[2] This same definition was adopted by the American Diabetes Association in 2OO5.[3] DN is the most common complication of diabetes. In the United States, DN is the leading cause of diabetes related hospital admissions and non-traumatic amputations and is associated with a poor quality of life.[4,5] The American Diabetes Association estimates that DN costs $22 billion per year. It is estimated that approximately 50% of patients have DN, although estimates vary from 10 to 100%. Depending on the diagnostic criteria used.[6] Probably the most frequently cited prospective observational study of DN was completed in an outpatient clinic by Pirart.[7] He examined 4400 patients 10% of whom had neuropathy at the time of diagnosis. After 25 years of diabetes, half (50%) of the patients had neuropathy.[7] A similar prevalence was reported in the Rochester Diabetic Neuropathy Study, in which 59% of type 2 and 66% of type 1 diabetic patients had DN.[8] Another large cross-sectional study of 6487 type 1 and type 2 diabetic patients in the United Kingdom found the prevalence of DN to be 29%.[9] Among type 1 diabetic patients older than 30 years of age followed in the Pittsburgh Epidemiology of Diabetes Study, 58% had DN.[10,11] Prior to entering the Diabetes Control and Complication Trial (DCCT), 39% of 278 otherwise healthy type 1 diabetic patients met the clinical criteria for DN. The EURODIAB IDDM Complications Study found that the prevalence of DN, across 3250 randomly selected type 1 diabetic patients from 16 European countries, was 28% with no significant geographical differences.[12] DN appears to be less common in children, with a prevalence of 2% or less.[6] The reported differences in prevalence of DN arise partially from differences in age, but primarily from the differences in the criteria used for the diagnosis of DN. In most of these large, prospective studies, the prevalence of DN increased with duration of disease.

AIM

- Evaluation of cardiac autonomic neuropathy in diabetes mellitus. Patient using electro cardio graphic changes of heart rate variability.
- To correlate the ECG changes with beat to beat variation using ANSiscope device.

METHODOLOGY

MATERIALS

STUDY POPULATION

Fifty diabetic patients attending Diabetology Outpatient Department, of RMMCH, Chidambaram. These subjects were selected after scrutinizing them for exclusion criteria.

CONTROL POPULATIONS

Fifty patients attending General Medical Outpatient Department at RMMCH, Chidambaram. These subjects were age matched controls.

PLACE OF STUDY

Diabetology Outpatients Department RMMCH Chidambaram.

PERIOD OF STUDY

November 2013 - April 2015.

INCLUSION CRITERIA

Male patients attending the diabetic outpatient Department of RMMCH.

EXCLUSION CRITERIA

1. Age – Greater than 65 years.
2. Known case of coronary artery disease with electrocardiogram changes like ST segment elevation ≥ 2mm in the chest leads or ≥1mm in limb leads in the corresponding leads.
3. Known case of valvular or congenital heart

disease by echocardiogram.

4. Known case of systemic hypertension. [140/90mm hg], either systolic or diastolic if higher than the value.
5. Known case of parkinsonism, [by clinical features; resting tremors, cog-wheel rigidity bradykinesia, mask like facies] any two of the above.

METHOD

After selecting the patients on basis of the criteria history will be elicited and clinical examination done as per proforma. The necessary investigations [fasting blood sugar, post prandial blood sugar, ECG, ANIscope] will be done and statistically analyzed. ECG will be recorded at a speed of 50mm/second, with patient in deep respiration i.e:(breath held in expiration for ten seconds, inspiration for ten seconds). The E:I Ratio is measured by the longest RR interval during expiration to the shortest RR interval during inspiration. Heart rate response to variation in posture standing from supine posture, patient is made to stand from and then ECG is recorded. The ratio of 10^{th} RR interval to the 05^{th} RR interval is calculated. Blood pressure is recorded initially in supine posture and then patient is made to stand and blood pressure is again recorded after 2 minutes but within 5 minutes.

ANSISCOPE DEVICE

Heart rate variability can also be measured by spectral analysis in the time domain by continous recording of RR intervals for 5 minutes. The Dyansys ANSiscope is a device which does the spectral analysis in the time domain and is approved by the FDA for the analysis of heart rate variability.

RESULTS

The following ECG parameters were abnormal in Diabetic study group as compared to control population.

- The resting heart rate (86.16±7.6) was significantly (P<0.05) higher than that of non diabetic controls (76.64±9.18).
- The RR interval was narrow in diabetic (701.6 ± 72.9 msec) as compared to control subjects (794 ± 92.25 msec) which was statistically significant.
- The PR interval in diabetics (163 ± 32.84 msec) was prolonged as compared to control (136 ± 19.794) and was statistically significant (P= 0.0003).
- There was a leftward deviation of QRS axis among diabetics (31.6°) as compared to controls (54°).
- QTc interval was prolonged (400.62 ± 32.18 msec) in diabetic study population which was significant (P0.0000).
- Interventricular conduction blocks were prevalent in diabetics (6%).
- Cardiac dysautonomia was demonstrated in the study population using the following parameters.
- Abnormal E:I ratio (<1.1) (50%).
- Prolonged QTc interval (>460 msec) (6%)
- Postural fall in systolic blood pressure (>10mmHg) (42%)
- Ratio of 10^{th} RR interval to 5^{th} RR interval was abnormal in (60%).
- Dyansys CAN score
- Early CAN (15%)
- Late CAN (15%)
- Advanced CAN (10%)

This study shows the high prevalence of cardiac dysautonomia in type 2 diabetics. Most of these patients remain asymptomatic. Some of the patients with CAN had diabetes for only as few as 5 years proving the DCCT result that the disease process begins early and it may remain asymptomatic until later stages. It can be recommended that a baseline determination of cardiac autonomic function be performed upon. Diagnosis in type 2 diabetes followed by a yearly repeat test.

Table – 1 Autonomic Dysfunction Score

Groups	Autonomic dysfunction score				Total
	0	**1**	**2**	**3**	
Study group	19	4	9	18	50
Control group	48	2	0	0	50
Total	67	6	9	18	100

Chi-Square Tests

	Value	df	P value
Pearson Chi-Square	40.219	3	0.000

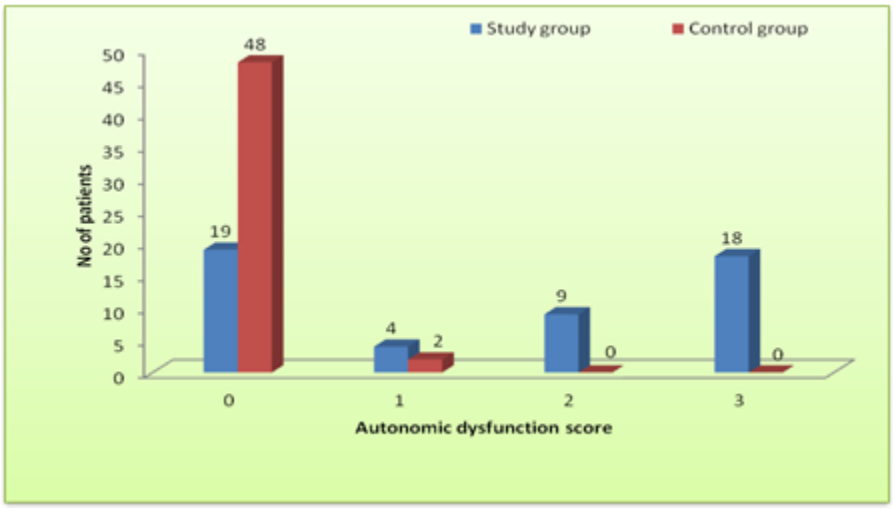


TABLE – 2 Dyansys ANSiscope grade

Group	Dyansys ANSiscope grade				Total
	0 (<11%)	1 (11.1-23%)	2 (23.1-51%)	3 (>51%)	
Study group	10	15	15	10	50
Control group	47	2	1	0	50
Total	57	17	16	10	100

Chi-Square Tests

	Value	df	P value
Pearson Chi-Square	56.209	3	0.000

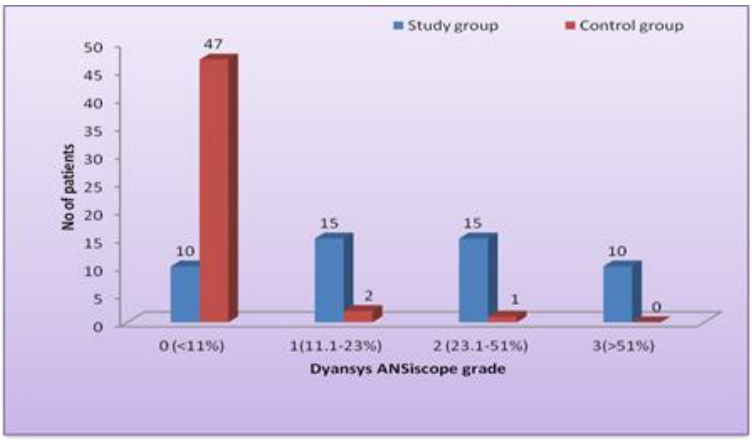
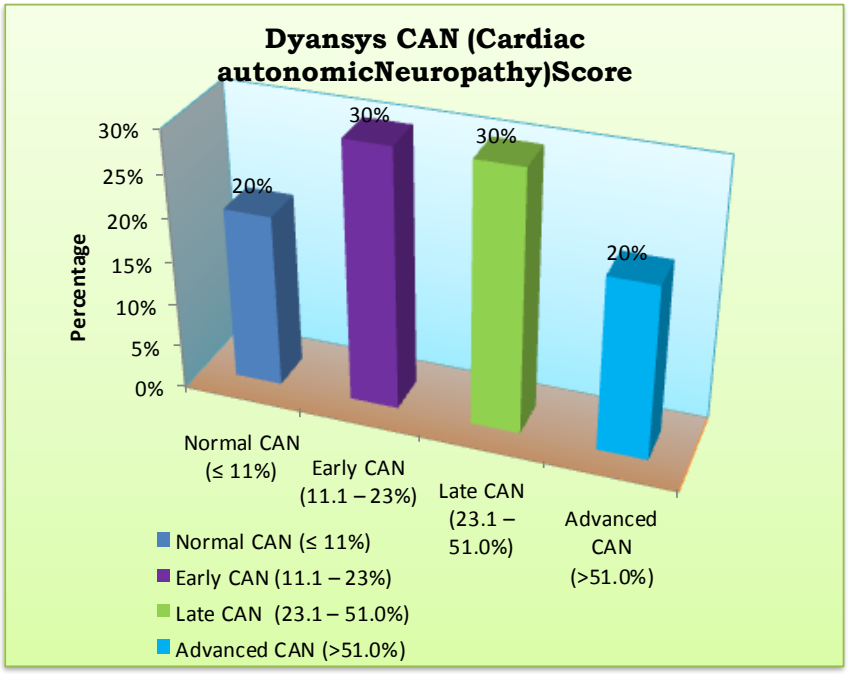


Table – 3 Dyansys Can (Cardiac Autonomic Neuropathy) Score Study Population

CAN Score	Number	Percent %
Normal CAN (≤ 11%)	10	20%
Early CAN (11.1 – 23%)	15	30%
Late CAN (23.1 – 51.0%)	15	30%
Advanced CAN (>51.0%)	10	20%



DISCUSSION

The diabetic population had a mean resting heart rate that was (86.16 bpm) higher than that of the control population (76.64 bpm). This difference was statistically significant implying higher resting heart rate in diabetic population. This is probably due to cardiac autonomic dysfunction, more specifically parasympathetic damage. Ewing et al. found that the parasympathetic nerves are the earliest to be involved followed by sympathetic nerves in autonomic neuropathy. The clinical utility of the knowledge that the resting heart rate is often higher in diabetics due to parasympathetic damage is that such patients need to be studied in great detail for cardiac autonomic neuropathy, since they are prone to develop sudden and unexpected cardiac arrest more so during procedures like anaesthesia. Mangoni AA, Mircoti L. showed that resting tachycardia decreases the distensibility of the vascular wall, and increases the risk of atherosclerosis, all favouring coronary artery disease. That the resting heart rate is higher in diabetics when compared to non-diabetics is reaffirmed by the fact that R-R interval is lower in study group (701 .6msec) than that of the non-diabetic group (794msec). Freeman R, Saul P et al. in their spectral analysis of heart rate in DAN; Arch, Neurol; 1991 established that R-R interval analysis served as a means for early assessment of CAN. The PR interval was significantly prolonged in diabetics suggesting a delayed conduction across atrioventricular node paving way for conduction abnormalities. This evidence of first degree heart block could be the cause for syncope. It has been established in studies that some cases of PR

prolongation associated with CAN can predispose to atrial fibrillation. The leftward axis (31.6°) is also indicative of bundle branch blocks. There is an increased incidence of intra ventricular conduction blocks in diabetics (6%). Conduction blocks at various levels and in varying degrees makes patients with CAN prone to symptoms of heart block and sudden cardiac death as was shown by Erickson et al. in his Primary Prevention study which asserted the fourfold risk of higher atrio ventricular block in patients with RBBB. A prolonged corrected QT interval, as evidenced in this study, where the QTc in study population is 400.62 msec as against 361.10 msec of the control population, indicates an imbalance between right and left sympathetic innervations. JM Cronin, MM Kadrifrek, EJ Bastyr University of Michigan; Diabetes Care; Vol.13, showed that as a group, diabetic patients with greater than or equal to 2 abnormalities of cardiac autonomic function had a longer QTc interval than those with no evidence of cardiac autonomic neuropathy. Diabetic patients with a regional sympathetic imbalance and QTc interval prolongation may be at greater risk for arrhythmias predisposing them to sudden cardiac death. Eric A. Witset, Pentittii M. Rautaharju, Sheila A. Veinmami. Diabetes Care; 28:20415 - 20417 in a population based study examined the risk of primary cardiac arrest associated with QTc prolongation and concluded that diabetic patients in the upper quartile of QT index distribution had a three fold risk of primary cardiac arrest. Kahn et al. demonstrated that prolongation of the QTc interval increased the risk of intractable ventricular arrhythmias and sudden death. Silent ischemia is significantly more frequent in diabetic patients with than in those without autonomic neuropathy. A reduced appreciation of ischemic pain can impair early recognition of myocardial ischemia or infarction and delay appropriate therapy making it necessary to screen diabetic patients for ischemia and CAN frequently. Heart rate variability to deep breathing was abnormal in 50% of study subjects. Decreased HRV is considered the earliest indication of CAN and is often the most frequent finding in symptomatic CAN. The demonstration of loss of HRV during deep breathing indicates the presence of vagal denervation of the heart and is also associated with increased rate of progression of coronary atherosclerosis. Decreased vagal activity limits exercise tolerance making these individuals prone to syncope and predisposed to sudden cardiac death. 42% of the diabetic study group showed orthostatic hypotension, which is usually due to damage to efferent sympathetic vasomotor fibers, particularly in splanchnic vasculature. Diminished cardiac acceleration and cardiac output, particularly in association with exercise may also be important in the presentation of this disorder. Some of these patients presented with light headedness and pre syncopal symptoms, while some were asymptomatic. Apart from the pain of peripheral neuropathy, symptoms of orthostatic hypotension is the most troublesome to treat in diabetic patients. CAN can occur as early as one year after diagnosis of type 2 DM. In this study 54% of population had diabetes for 5 years and the age at diagnosis was between 40-50 years of age for most indicating late diagnosis and hence higher prevalence of CAN.

CONCLUSION

62% of the study population had autonomic dysfunction of varying levels according to the score assessed using electro cardio graphic changes and blood pressure. Whereas 80% of the same study population had autonomic dysfunction of varying levels according to the dyansys ANSiscope device. Henceforth periodical assessment of diabetes mellitus patient for complications like cardiac autonomic neuropathy on a yearly basis is advised to have reduced incidence of sudden cardiac death and arrhythmias which are known to occur more in diabetics compared to normal population.

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How to cite this article: Arun Kumaran P, Rama Krishna Rao M, Evaluation of cardiac autonomic neuropathy in diabetes mellitus using electrocardiographic changes and ANSiscope device. Int J of Allied Med Sci and Clin Res 2015;3(4):419-425.
Source of Support: Nil. **Conflict of Interest:** None declared.