Cardiac autonomic neuropathy in type 2 diabetes mellitus using Bellavere’s score system

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ABSTRACT

Objective: Determine the frequency of cardiac autonomic neuropathy (CAN) in type 2 diabetics using Bellavere’s score system.

Subjects and Methods: The present cross-sectional study was conducted at the Department of Medicine, Isra University Hospital Hyderabad from March to November 2011. Sixty voluntary participants of type 2 diabetes mellitus (DM) were selected through non-probability purposive sampling. Cardiac autonomic nerve function was assessed using Bellavere’s score system. The data were analyzed on the Statistix version 10.0 (USA) using Student’s t-test, Chi-square test, one-way ANOVA, and Tukey-Cramer test ($P \leq 0.05$).

Results: Of 60 diabetics, CAN was observed in 29 (41.4%). Abnormal heart rate variability (HRV), valsalva ratio, 30-15th ratio, blood pressure (BP) response to standing, and handgrip was noted in 43 (61.4%), 27 (38.5%), 17 (24.2%), 5 (7.14%), and 18 (25.7%), respectively. The hemoglobin A1c was negative correlated with HRV, valsalva ratio, 30-15th ratio, and BP response to sustained handgrip; and positively correlated with BP response to standing, systolic BP, and diastolic BP. Duration of DM was not correlated with cardiac autonomic nerve function tests.

Conclusion: The CAN was observed in 29 (41.4%) using Bellavere’s score system. The CAN score may be used as feasible and reproducible bedside clinical test in diabetic patients.

Keywords: Bellavere’s score, Cardiac autonomic neuropathy, diabetes mellitus, Sindh

Introduction

The Pakistan ranks sixth position in the world regarding the burden of diabetes mellitus (DM). The chronic hyperglycemia of DM, in the long-term, causes damage of the target organs; eyes, nerves, kidney, heart, and blood vessels. The damage to nerve fibers both somatic and autonomic including cardiac autonomic nerve fibers is a feature of DM. Cardiac autonomic neuropathy (CAN) is a debilitating and life-threatening complications of DM. The CAN is an established indicator of cardiovascular mortality because of cardiac arrhythmias. There are three stages of the CAN; Early stage: Abnormality of heart rate with a deep breath alone. Intermediate stage: An abnormality of valsalva response. Severe stage: The presence of postural hypotension. Extensive clinical studies have been reported on CAN during the past two decades due to the availability of simple non-invasive tests of cardiac autonomic nerve function. The CAN can be tested as bedside technique using a battery of cardiovascular reflex tests; the heart rate variability (HRV) with deep breathing, valsalva ratio, 30-15th ratio, blood pressure (BP) response to active standing, and sustained handgrip. The original Ewing’s criteria are used in previous studies, however, present study uses Bellavere’s scoring for evaluation of cardiac autonomic nerve function. As Pakistan is passing through an epidemic of DM and many new cases are being diagnosed, there is dire need to study the cardiovascular autonomic nerve function. The present study intends to determine the frequency of CAN in type 2 DM in our tertiary care hospital using simple non-invasive tests of cardiovascular autonomic nerve function.

Subjects and Methods

The study was conducted at the Isra University Hospital Hyderabad from March to November 2012. Sixty voluntary participants of type 2 DM were selected through non-probability purposive sampling. A verbal consent was taken from the participants. Medical history of duration of DM, and symptoms of diabetic complications, ischemic heart disease, and brain stroke were recorded on a structured pro forma. Type 2 DM participants of ≥5 years were included and those complicated with ischemic heart disease, renal failure,
limb amputation, and brain stroke were excluded from the study. DM was defined as Random blood glucose level of ≥200 mg/dl or fasting blood glucose level of ≥126 mg/dl. The body mass index (BMI) was calculated from the weight and height by formula; BMI = Weight (kg)/Height (m²). Stadiometer was used to measure height and a calibrated beam balance for weight. Systemic BP was recorded with a mercury sphygmomanometer after the patient had taken 5 min rest. For each participant, the average of two readings was recorded in supine and standing position. Systemic hypertension was defined as; the “systolic BP ≥140 mmHg” or “diastolic BP ≥90 mmHg.” The blood samples were collected after asепsis was secured; using standard methods of blood sampling by trained paramedics.

The hemoglobin A1c (HbA1c) was used as an indicator of glycemic control, measured on automated clinical chemistry analyzer (Hitachi 902, Roche Diagnostics, the USA).

The cardiac autonomic nerve function was assessed using a battery of five cardiovascular autonomic reflex tests of Bellavere’s score system as shown in Table 1.8-10

The diagnosis of CAN is established; if two or more of the tests results are abnormal.13,14

The sum of the score obtained from each test determines the final classification of the patient’s degree of CAN. The total score ranges from 0 to 10. Classification of patients is done according to the total score. It is shown in Tables 1 and 2.

**Data analysis**

The data were analyzed by Statistix version 10.0 (USA). The continuous variables were analyzed using Student’s t-test, one-way ANOVA, and post-hoc Tukey-Cramer testing. The Pearson’s correlation was used to analyze association of continuous variables. The Chi-square test analyzed the categorical variables. A $P \leq 0.05$ was considered statistically significant.

**Results**

Seventy type 2 DM, selected according to inclusion and exclusion criteria at our tertiary care hospital. The type 2 DM participants were divided into groups designated as having HbA1c <7% or ≥7% as shown in Table 3. The mean age was noted as 46 ± 5.47 and 45 ± 8.8 years, respectively. Of 70 participants, 40 (57.1%) were male and 30 (42.8%) female. The male to female ratio is 1.3:1. A significant difference was noted for the gender, HbA1c, systolic, and diastolic BP between groups with HbA1c <7% or ≥7%. The demographic characteristics of study population are shown in Table 3. The HRV, valsalva ratio, 30-15th ratio, BP response to standing, and BP response to sustained handgrip are shown in Table 4. The CAN test abnormalities are described 0-5 as shown in Table 5. Of seventy diabetics, CAN was observed in 29 (41.4%) (Table 6). The frequency of cardiac autonomic nerve reflex tests is shown in Table 7. The association of HbA1c with

| Test | Score | Category |
|------|-------|----------|
| Normal | Borderline | Abnormal |
| Heart rate variability | >15 | 10-15 | <10 |
| Valsalva ratio | ≥1.21 | 1.11-1.20 | ≤1.10 |
| 30-15th ratio | ≥1.04 | 1.01-1.03 | ≤1.0 |
| BP response to standing (mmHg) | ≥10 | 11-29 | ≥30 |
| BP response to handgrip (mmHg) | ≥16 | 11-15 | ≤10 |

BP: Blood pressure

| Score | Categories |
|-------|------------|
| 0-1   | No autonomic neuropathy |
| 2-4   | Early autonomic neuropathy |
| 5-10  | Severe autonomic neuropathy |

**Table 3: Demographic characteristics of study population (n=70)**

| Demographic characteristics | Groups | Mean (±SD) | P value |
|-----------------------------|--------|------------|---------|
| Age (years) | HbA1c<7% | 46.39 (5.47) | 0.46 |
|               | HbA1c>7% | 45.02 (8.85) |
| Male | HbA1c<7% | 14 | 0.0001 |
|               | HbA1c>7% | 26 |
| Female | HbA1c<7% | 11 |
|               | HbA1c>7% | 19 |
| HbA1c% | HbA1c<7% | 9.16 (3.41) | 0.03 |
|               | HbA1c>7% | 10.67 (1.62) |
| Random blood sugar (mg/dl) | HbA1c<7% | 215 (81) | 0.01 |
|               | HbA1c>7% | 253 (98) |
| Fasting blood sugar (mg/dl) | HbA1c<7% | 135 (56) | 0.02 |
|               | HbA1c>7% | 148 (79) |
| Body mass index (kg/m²) | HbA1c<7% | 26.5 (3.21) | 0.28 |
|               | HbA1c>7% | 25.8 (2.18) |
| Systolic blood pressure (mmHg) | HbA1c<7% | 140.1 (21.70) | 0.003 |
|               | HbA1c>7% | 124.8 (17.01) |
| Diastolic blood pressure (mmHg) | HbA1c<7% | 79.2 (12.37) | 0.002 |
|               | HbA1c>7% | 70.1 (9.59) |
| Duration of DM | HbA1c<7% | 9.6 (3.67) | 0.17 |
|               | HbA1c>7% | 10.8 (3.88) |

HbA1c: Hemoglobin A1c, DM: Diabetes mellitus, SD: Standard deviation
HRV, valsalva ratio, 30-15<sup>th</sup> ratio, BP response to standing, BP response to sustained handgrip, systolic BP, and diastolic BP was analyzed using Pearson’s correlation as shown in Table 8.

### Discussion

One of the most overlooked complications of DM is the CAN. The prevalence of CAN is highly variable as reported in several studies. It varies from as low as 7.7% to as high as 90%. The present study included seventy type 2 DM participants to evaluate the CAN using Bellavere’s score. The present study reports a frequency of CAN of 41.4%, which is comparable to previous study. The high frequency of CAN of present study is most probably due to the bad glycemic control of our study participants because of lack of health facilities. The Nayak et al. studied fifty type 2 DM participants and reported a frequency of CAN of 40% (20% early CAN and 20% severe CAN). Another recent study from India reported frequency of CAN in 42% of long standing type 2 DM participants by cardiac autonomic nerve function testing. Yet another study has reported a frequency of CAN in 22% of diabetic participants. The frequency of CAN of aforementioned studies are comparable to present study. The Canani et al. reported CAN in 79.7% of type 2 DM participants suffering from peripheral arterial disease. The CAN of 79.7% is very high compared to our present and previous studies. A frequency of 70% has been reported from a recent study from Egypt.

The Keen et al. and Noronha et al. have reported a frequency of CAN in 32% AND 38.5% of the type 2 DM patients. In present study, we found a mean CAN score of 2.14, with males having CAN score of 2.28 and females 2.018. Similar observations have been reported by Nayak et al. mean of CAN score of 2.04 and Noronha et al. reported mean CAN score of 2.23. The present study reports a negative correlation of HRV, valsalva ratio, 30-15<sup>th</sup> ratio, BP response to sustained handgrip.
handgrip, systolic, and diastolic BP with statistically significant difference. The BP response to standing is found positively correlated with glycemic control. However, duration of DM was not correlated with cardiac autonomic reflex tests. The findings are comparable to Nayak et al.10 and Noronha et al.18 but contrary to reported by Toyry et al.20 The Mansour et al.4 reports a frequency of 42.6% of CAN in type 2 DM, the findings are comparable to present study. In present study, the early and severe CAN had a valsalva ratio of 1.15 ± 0.03 and 1.05 ± 0.02, respectively. As the severity of CAN increases, the HRV in response to valsalva maneuver decreases. The findings are similar to as reported previously.3,10 A study by Khandelwal et al.22 reported a poor correlation of the HbA1c with the CAN score, but this might have been because of bias introduced by researcher. Further studies are recommended as Pakistan is having diabetic epidemic and study will help cope with the long-term complications of DM related to cardiovascular system.

Conclusion
The CAN was observed in 29 (41.4%) using Bellavere’s score system which is simple non-invasive CAN score, may be useful in the early diagnosis and treatment of DM to prevent mortality. The CAN score may be used as feasible and reproducible bedside clinical test in diabetic patients.

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