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A Study On Assessment Of Autonomic Nervous System Function In Patients With Type 2 Diabetes Mellitus

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ABSTRACT

The autonomic nervous system (ANS) innervates the entire neuraxis and influences the functions of all organs. This study was undertaken for evaluating the autonomic dysfunction in diabetic patients using clinical autonomic tests and neuro- electrophysiology. A prospective study was carried out in 66 patients with type II diabetes mellitus in a tertiary care hospital for one year. Systemic examination, necessary investigations, nerve conduction study and clinical testing for the autonomic nervous system were done. The results were noted and analyzed. 65.2% were females, whereas 34.8% were males. Mean duration of diabetes was found to be 9.06 years (SD 4.121). 80.3% population was known to have type 2 diabetes for 5-10 years duration, 13.6% had diabetes for 10-15 years, and only 3.5% had diabetes for more than 15 years. Mean FBS was found to be 196.12(mg/dl) ±77.180 SD and mean PPBS was 303.26(mg/dl) ± 115.385 SD. Mean HbA1c levels were 10.95 ± 2.36 SD. 33.3% showed early parasympathetic involvement for cardiac autonomic neuropathy, 9% had definite parasympathetic involvement, and only 6% had both parasympathetic and sympathetic involvement. 62.12% showed abnormal responses in nerve conduction study, of which 48.78% had autonomic dysfunction. The main factor responsible for the development and progression of autonomic dysfunction is poor glycaemic status. If contributing factors can be detected, early identification of cardiac autonomic neuropathy (CAN) and appropriate management would halt its progression. Aggressive glycaemic monitoring and treatment shall bring down the progression and prolong the time interval in showing abnormal responses in autonomic function testing.

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INTRODUCTION

The autonomic nervous system (ANS) innervates the entire neuraxis and influences all organ systems. The autonomic nervous system regulates blood pressure, heart rate, sleep, bowel and bladder functions. The activity of the ANS is regulated by central neurons responsive to diverse afferent input. After the central integration of afferent information, the autonomic outflow is adjusted to permit the functioning of the major organ system per the need of the organism. The cerebral cortex, in

connection with the autonomic centres in the brain stem, coordinates autonomic outflow with higher mental function (Nijhawan *et al.*, 1993).

Its importance is recognized when ANS function is compromised, resulting in dysautonomia. Autonomic nervous system dysfunction is one of the significant complications and is generally associated with poor prognosis. A prolonged period of poor control of glycaemic status shall only increase the risk of developing advanced diabetic neuropathy, and studies had shown that this vital factor had contributed in the progression of autonomic dysfunction (Vinik and Erbas, 2001). Researchers, through various studies, had shown that the presence of autonomic neuropathy precedes the diagnosis of diabetes or may be the initial presentation.

Diabetic autonomic neuropathy (DAN) can either have a clinical or subclinical presentation. It is manifested by the abnormal function of one or more systems (e.g., cardiovascular, gastrointestinal [GI], genitourinary, sudomotor or ocular). Most of the systems are dually innervated, receiving fibres from the parasympathetic and sympathetic divisions of the ANS. DAN typically presents by affecting all parts of the ANS. Vagus nerve accounts for 75% of all parasympathetic activities. DAN affects first, the longer nerves (Aggarwal *et al.*, 2011). Clinical manifestations of autonomic neuropathy usually do occur many years after the onset of diabetes. More importantly, DAN can coexist with peripheral neuropathies and other diabetic-related complications. But it can also be an isolated presentation, preceding the appearance of other complications.

The present study was undertaken for evaluating the autonomic dysfunction in diabetic patients using clinical autonomic tests and neuro- electrophysiology (Ramachandran *et al.*, 2001). Our studies indicate that the correlation between various conventional tests of cardiac parasympathetic activity is low, the reason may be either due to methodological issues and in part to the fact that these tests have different afferent pathways while evoking.

MATERIALS AND METHODS

This prospective study was conducted by the department of general medicine and neurology in 66 patients with type II diabetes mellitus from April 2017 to April 2018 in a tertiary care hospital after getting approval from the institutional ethics committee and informed consent from the study population. Patients with type II diabetes mellitus of more than five years duration, age group between 25 years and 80 years were included in this study. Patients with Type I diabetes mellitus, alcoholic, chronic diseases like congestive cardiac failure, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, pregnancy, patients with underlying heart and rhythm disorders, thyroid disorders, Hansen disease, patients who underwent amputation, on drugs known to affect the autonomic nervous system including chemotherapeutic agents were excluded. Demographic details and investigation like urine analysis, fasting and postprandial glucose levels, HbA1C, renal function tests and electrocardiogram were done in addition to systemic examination and clinical testing for the autonomic nervous system (heart rate variability, expiration inspiration ratio, Valsalva, sustained handgrip). The data was collected and analyzed. All the statistical analysis were performed using Statistical Package for Social Science (SPSS, version 22) for Microsoft windows.

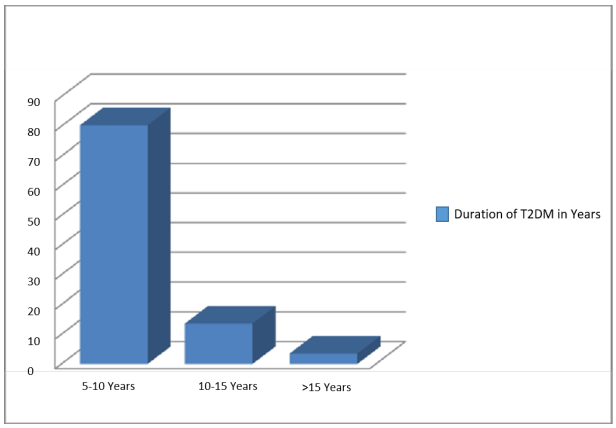

Figure 1: Duration of Type II DM in Years in the Study Group

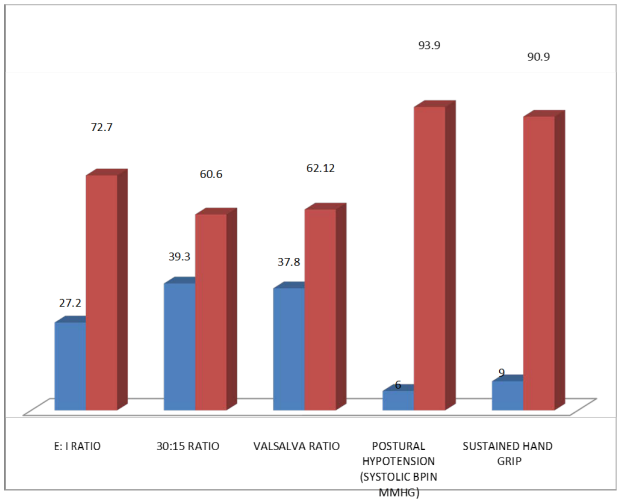

Figure 2: CAN test in the study population

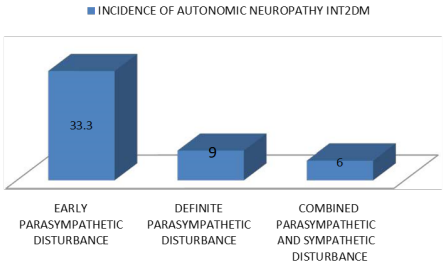

Figure 3: Clinical cardiac autonomic nervous testing in the study population

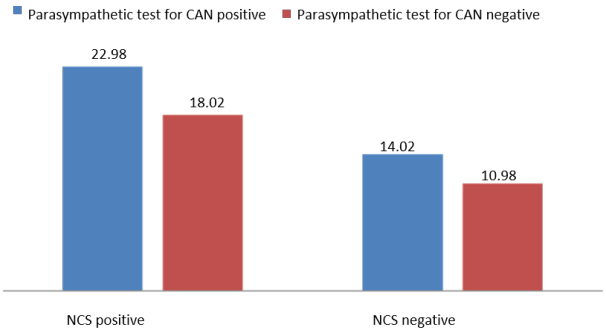

Figure 4: NCS in association with Parasympathetic test for CAN

RESULTS AND DISCUSSION

In our study, out of 66 patients 34.8% (n=23) were males and 65.2% (n=43) were females. Mean age in the study population was 55.36 years with a standard deviation of 11.36. 80.3% had type 2 diabetes for 5-10 years duration, 13.6% had diabetes for 10-15 years, and only 3.5% had diabetes for more than 15 years (Figure 1). The mean duration of diabetes was found to be 9.06 years, with a standard deviation of 4.121. The mean fasting blood sugar levels were 196.12(mg/dl) ± 77.180 SD, the mean postprandial blood sugar levels were 303.26(mg/dl) ± 115.385 SD and the mean HbA1c levels were 10.95 ± 2.36 SD. The mean systolic blood pressure was 123.79 (mmHg) ± 11.99 SD and the mean diastolic blood pressure were 79.24 (mmHg) ± 7.5 SD.

All the patients in our study underwent clinical examination for parasympathetic and sympathetic test for cardiac autonomic neuropathy. A simple and non-invasive method to assess the autonomic dysfunction is the measurement of resting Heart Rate Variability (HRV) (Chidambaram *et al.*, 2017).

27.72% of patients were found to have positive results for expiration to inspiration ratio (Figure 2). The 30:15 ratio (heart rate response to standing) was found to be abnormal in 39.39%. The findings were compared with the findings reported by Birajdar SV et al. and John L et al. (Birajdar *et al.*, 2017; John *et al.*, 1986).

Ewing et al. reported the incidence of abnormal 30:15 ratio to be 60%. (Ewing *et al.*, 1978). 37.87% were found to be abnormal results for Valsalva ratio.

In the present study, postural hypotension was observed in 4 patients (6.06%) which is comparable with previous studies (Birajdar *et al.*, 2017; Gupta and Pandit, 1992). 9.09% had positive results for the sustained handgrip.

In our study, autonomic neuropathy was noticed in 48.4% of patients. Only parasympathetic involvement was 33.3% of patients, while combined parasympathetic and sympathetic was observed in only 6.06% patients; no patient was noted with isolated sympathetic involvement (Figure 3). Various studies have noted a wide range of CAN. Ewing et al. reported parasympathetic dysfunction in 55.73% patients, and sympathetic dysfunction was seen in 26.33% of patients (Ewing *et al.*, 1978).

Birajdar SV et al. noted parasympathetic involvement in 48% patients and combined sympathetic and parasympathetic involvement in 10% of patients (Birajdar *et al.*, 2017). Gupta and Pandit reported an incidence of 66.3 % (Gupta and Pandit, 1992). Thus this study confirms that parasympathetic neuropathy is much more common than sympathetic neuropathy. With this concluding that every patient diagnosed to have type 2 diabetes should undergo these simple bedside clinical test for autonomic nervous system involvement.

The occurrence of peripheral neuropathy in association with autonomic neuropathy is frequent. Of these 66 diabetic patients in the present study, 41 diabetic patients were positive for peripheral neuropathy, of which 48.7% had autonomic neuropathy and the association observed was statistically significant (Figure 4). Ewing at el found that changes in the peripheral nervous system parallel abnormalities occurring in the autonomic nervous system (Ewing *et al.*, 1978).

Our study showed that early parasympathetic involvement is the most important factor in diagnosing DAN since 33.3% patients showed early parasympathetic involvement hence it becomes an important clue to investigate the patient for cardiovascular abnormalities further thereby reducing the mortality.

Recent studies confirmed the efficacy of intensive insulin therapy in slowing the progression of both diabetic peripheral neuropathy and CAN (Fisher and Tahrani, 2017). The results of the above study suggested there is a need for aggressive glycemic control in the patients with autonomic neuropathy. The best results on the prevention of autonomic dys-

function in patients with type 2 diabetes seem to be derived from multi-factorial treatment and lifestyle modification.

CONCLUSIONS

Our study showed that clinical testing for diabetic autonomic neuropathy plays a major role in detecting autonomic neuropathy at the earliest. All the patients with type 2 diabetes should be examined for parasympathetic and sympathetic test for autonomic nervous testing at the time of diagnosis to detect subclinical autonomic neuropathy at the earliest. Parasympathetic involvement is earlier as compared to sympathetic involvement, and orthostatic hypotension is a very late feature.Poor glycemic status is an important contributing factor in the development and progression of autonomic dysfunction. If contributing factors can be identified, early identification of cardiac autonomic neuropathy (CAN) and appropriate management would halt its progression. Aggressive glycaemic monitoring and treatment shall bring down the progression and prolong the time interval in showing abnormal responses in autonomic function testing. Clinical suspicion and early testing must be done to detect autonomic neuropathy and intensive approach in the management of diabetes shall decrease the mortality due to diabetic associated complications.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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