

## ASSESSMENT OF CARDIAC AUTONOMIC DYSFUNCTION AMONG PATIENTS WITH DIABETES MELLITUS AND ITS ASSOCIATED FACTORS

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### ABSTRACT

**Background:** Autonomic neuropathy was only generally recognized as part of the spectrum of nerve damage in diabetes. Autonomic neuropathy is the ‘needle in the haystack’ in the complete evaluation of a diabetic patient. Most clinicians tend to neglect these symptoms even though their patients present only with them. **Material & methods:** the present prospective study including 100 diabetic patients which were selected by simple random sampling. Strict confidentiality was maintained with patient identity and data and not revealed, at any point of time. **Results:** Majority 17% of patients had early cardiac autonomic dysfunction, followed by 7% patients had definite, 3% patients had atypical and severe cardiac autonomic dysfunction respectively. Mean age in cases with autonomic dysfunction was 46.25 (S.D.±6.24) and 38.42 (S.D.±7.38) with no autonomic dysfunction. Z value worked out to be 3.38 which is statistically significant (p<0.05). Mean duration of diabetes in cases with autonomic dysfunction was 6.83 (S.D.± 2.01) and 5.24 (S.D.± 2.48) with no autonomic dysfunction. Z value worked out to be 2.43 which is statistically significant (p<0.05). Mean BMI in cases with autonomic dysfunction was 27.61 (S.D.±2.53) and 24.16 (S.D.±2.90) with no autonomic dysfunction. Z value worked out to be 3.52 which is statistically highly significant (p<0.05). Among 52 cases with >7 HbA1c, 22 had autonomic dysfunction and 30 cases did not have autonomic dysfunction. Among 48 cases with ≤7 HbA1c, 8 had autonomic dysfunction and 40 did not have autonomic dysfunction, which is statistically significant (p<0.05). **Conclusion:** We concluded from this study that incidence of cardiac autonomic dysfunction among patients of Diabetes Mellitus was more prevalent in age group 40 to 50 years. Other associated factors were high body mass index, increased duration of diabetes and raised HbA1c value for occurrence of cardiac Autonomic dysfunction secondary to Diabetes Mellitus.

Keywords: Diabetes, Autonomic Dysfunction, HbA1c.



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### INTRODUCTION

The Diabetes is a long-term disease with variable clinical manifestations & progression. Chronic

hyperglycemia from whatever cause, leads to number of complications-- cardiovascular, renal,

neurological, ocular & others such as intercurrent infection(1). Diabetes is now seen as a heterogeneous group of diseases, characterized by a state of hyperglycaemia, resulting from a diversity of aetiologies, environmental & genetic, acting jointly (2). Autonomic neuropathy was only generally recognized as part of the spectrum of nerve damage in diabetes following the work of Jordan in 1936 and Rundles in 1945 (3). Autonomic neuropathy is the ‘needle in the haystack’ in the complete evaluation of a diabetic patient. Most clinicians tend to neglect these symptoms even though their patients present only with them. It is indeed a curse for a person to have diabetes but the superimposed impotence or postural syncope may actually worsen his morale on the whole (4). It is proclaimed that these bedside methods of assessments calculate the prevalence of autonomic neuropathy in diabetes in a range of 10-100%. Autonomic failure is often very disabling in diabetes (5). A thorough understanding of diabetic autonomic neuropathy on the various systems is a must. Moreover, failure to recognize the symptoms in a diabetic, as due to autonomic neuropathy, may lead to a lot of unnecessary investigations and sometimes, to wasteful treatments such as testosterone in sexual impotence and cinnarizine for postural giddiness (6).

Thus it is very evident to make an effort to study of autonomic manifestations in diabetes mellitus, and to use the bedside clinical tests to detect early diabetic dystonia, and the varied relations and effects autonomic failure has on other complications in diabetes(7). Hence, the present study was conducted to assess the cardiac autonomic dysfunction among patients with diabetes mellitus and its associated factors at our tertiary care center.

## MATERIALS AND METHODS

The present cross-sectional study was conducted at department of Cardiology and department of General Medicine of our tertiary care hospital. 100 Diabetic patients were selected for study by simple random sampling. Institutional Ethics Committee Clearance was obtained before start of study and written and informed consent for the procedure was obtained from all the patients. Strict confidentiality was maintained with patient identity and data and not revealed, at any point of time. The enrolled Diabetic patients were questioned about the presence of symptoms reported to be related to autonomic neuropathy, postural giddiness, disturbances of bladder sphincter, nocturnal polyuria, constipation,

diarrhoea, impotence and bouts of localized sweating.

Patients with congestive cardiac failure, renal failure, severe anemia, liver diseases, cardiac arrhythmias, pregnant females, age more than 60 years, electrolyte imbalance, central or peripheral neuropathies due to cause other than diabetes and exposure to lead, drugs (like isoniazid) and drugs affecting the autonomic function were excluded from the study. All the patients were subjected to a detailed clinical examination in accordance with proforma. The cases were subjected to five non-invasive autonomic functions tests to assess cardiovascular autonomic reflexes as recommended by Ewing-Clarke which are tests reflecting Parasympathetic functions (heart rate variation during deep breathing, heart rate response to Valsalva Maneuver, immediate heart rate response to standing) and tests reflecting Sympathetic functions (blood pressure response to standing, blood pressure response to sustained handgrip)(8). All the data was recorded on Microsoft excel spread sheet and data analysis was done at 10% alpha and 90% confidence interval using SPSS v22 software. Test of significance were applied on collected and organized data and p value less than 0.05 was considered as statistically significant association between study variables.

## RESULTS

In present study out of total 100 patients, majority 34% are in the age group 40 to 50 years, followed by 29% who are in the age group 30 to 40 years and 23% are in age group of 50 to 60 yrs. Only 14% are in the 20 to 30 yrs. Out of total enrolled patients 59% were male and 41% were females. The majority 17% of patients had early cardiac autonomic dysfunction, followed by 7% patients had definite, 3% patients had atypical and severe cardiac autonomic dysfunction respectively. 70% patients did not have cardiac autonomic dysfunction in study group. (Table 1)

**Table 1: Distribution of study participants according to incidence of cardiac autonomic dysfunction.**

Cardiac Autonomic dysfunction	No of cases
Early	17%
Atypical	3%
Definite	7%
Severe	3%
No	70%

Mean age in cases with autonomic dysfunction was 46.25 (S.D.  $\pm$  6.24) and 38.42 (S.D.  $\pm$  7.38) with no autonomic dysfunction. Z value worked out to be 3.38 which is statistically significant ( $p < 0.05$ ). Mean duration of diabetes in cases with autonomic dysfunction was 6.83 (S.D.  $\pm$  2.01) and 5.24 (S.D.  $\pm$  2.48) with no autonomic dysfunction.

Z value worked out to be 2.43 which is statistically significant ( $p < 0.05$ ). Mean BMI in cases with autonomic dysfunction was 27.61 (S.D.  $\pm$  2.53) and 24.16 (S.D.  $\pm$  2.90) with no autonomic dysfunction. Z value worked out to be 3.52 which is statistically highly significant ( $p < 0.05$ ). (Table 2)

**Table 2: Comparison of parameters with autonomic dysfunction in study group**

Parameter	Autonomic dysfunction				Z Value	P Value
	Yes		No			
	Mean	SD	Mean	SD		
Age (Yrs)	46.25	6.24	38.42	7.38	3.38	<0.05
Duration (Yrs)	6.83	2.01	5.24	2.48	2.43	<0.05
BMI	27.61	2.53	24.16	2.90	3.52	<0.05

Among 59 males, 18 had autonomic dysfunction and 41 cases did not have autonomic dysfunction. Among 41 females 12 had autonomic dysfunction and 29 did not have autonomic dysfunction ( $p > 0.05$ ). Among 28 cases with type I diabetes 4 cases had autonomic dysfunction and 24 did not have autonomic dysfunction.

Among 72 cases with type II diabetes 26 had autonomic dysfunction and 46 did not have autonomic dysfunction ( $p > 0.05$ ). Among 52 cases with  $>7$  HbA1c, 22 had autonomic dysfunction and 30 cases did not have autonomic dysfunction. Among 48 cases with  $\leq 7$  HbA1c, 8 had autonomic dysfunction and 40 did not have autonomic dysfunction, which is statistically significant ( $p < 0.05$ ).

Among 68 cases with good compliance 14 cases had autonomic dysfunction and 54 did not have autonomic dysfunction. Among 32 cases with poor compliance 16 had autonomic dysfunction and 16 did not have autonomic dysfunction ( $p < 0.05$ ). Among 38 cases with OHA, 16 had autonomic dysfunction and 22 cases did not have autonomic dysfunction. Among 62 cases with insulin 14 had autonomic dysfunction and 48 did not have autonomic dysfunction ( $p > 0.05$ ). (Table 3)

**Table 3: Association between parameters and autonomic dysfunction in study group**

Parameters		Autonomic dysfunction		P value
		Yes	No	
Sex	Male	18	41	$>0.05$
	Female	12	29	
Type of diabetes	I	4	24	$>0.05$
	II	26	46	
HbA1c	$>7$	22	30	<0.05
	$\leq 7$	8	40	
Currently on OHA/insulin	OHA	16	22	$>0.05$
	Insulin	14	48	
Compliance	Good	14	54	<0.05
	Poor	16	16	

## DISCUSSION

The present study was conducted to find out autonomic dysfunction in diabetic patients and its correlation with age, sex, duration, signs and symptoms and type of diabetes. In present study out of total 100 patients, majority 34% are in the age group 40 to 50 years, followed by 29% who are in the age group 30 to 40 years and 23% are in age group of 50 to 60 yrs. Only 14% are in the 20 to 30 yrs. Out of total enrolled patients 59% were male and 41% were females. The majority 17% of patients had early cardiac autonomic dysfunction, followed by 7% patients had definite, 3% patients had atypical

and severe cardiac autonomic dysfunction respectively. 70% patients did not have cardiac autonomic dysfunction in study group.

Age was significantly higher among cases with autonomic dysfunction as compared to cases without autonomic dysfunction in study group; Mean age in cases with autonomic dysfunction was 46.25 (S.D.  $\pm$  6.24) and 38.42 (S.D.  $\pm$ 7.38) with no autonomic dysfunction. Z value worked out to be 3.38 which is statistically significant ( $p < 0.05$ ). Similar finding was also observed in a study conducted by Seung-Hyun ko et al (2008) who investigated whether cardiovascular autonomic dysfunction was associated with glycaemic control status over time in patients with type 2 diabetes. Mean age of cases in study group suffered from diabetic autonomic neuropathy was 53.2 and among cases without autonomic neuropathy were 48.8. The mean difference was statistically highly significant(9).

Sex was not significantly associated with occurrence of autonomic dysfunction in study group. Similar finding was observed in a study conducted by Aggarwal S et al, who investigated incidence of autonomic neuropathy in diabetes and its correlation with age and sex of the patient, duration and type of diabetes and hyperglycaemia. Among 31 males, 22 had autonomic dysfunction and among 19 females 13 had the same. This difference was statistically not significant in the study (10). Type of diabetes was not significantly associated with occurrence of autonomic dysfunction in study group. Similar finding was observed in a study conducted by Aggarwal S et al who investigated incidence of autonomic neuropathy in diabetes and its correlation with age and sex of the patient, duration and type of diabetes and hyperglycaemia. Among 37 cases with Type II diabetes, 26 had autonomic dysfunction and among 13 cases with Type I diabetes 9 had the same. This difference was statistically not significant in the study(10).

Duration of diabetes was significantly higher among cases with autonomic dysfunction as compared to cases without autonomic dysfunction in study group; Mean duration of diabetes in cases with autonomic

dysfunction was 6.83 (S.D.  $\pm$ 2.01) and 5.24 (S.D.  $\pm$ 2.48) with no autonomic dysfunction. Z value worked out to be 2.43 which is statistically significant ( $p < 0.05$ ). Similar finding was observed in a study conducted by Prabhakar Rao et al intends to detect the prevalence of QTc prolongation in diabetic patients as well as its relationship with cardiac autonomic neuropathy. Duration of diabetes among 70% autonomic neuropathy cases was 5 to 10 years. Only 14% cases had duration of diabetes less than 5 yrs and 16% cases had duration of diabetes more than 10%(11).

Mean BMI in cases with autonomic dysfunction was 27.61 (S.D.  $\pm$ 2.53) and 24.16 (S.D.  $\pm$ 2.90) with no autonomic dysfunction. Z value worked out to be 3.52 which is statistically highly significant ( $p < 0.05$ ). Similar finding was also observed in the study conducted by Elisabeth Gulichsen et al who evaluated the prevalence of cardiac autonomic neuropathy diagnosed by reduced heart rate variability (HRV) in hospital-based population of patients with diabetes. BMI was 28.9 among the cases with autonomic dysfunction and 27.1 in normal cases; this difference was statistically significant in the study(12).

Among 48 cases with  $\leq 7$  HbA1c, 8 had autonomic dysfunction and 40 did not have autonomic dysfunction, which is statistically significant ( $p < 0.05$ ). Among 68 cases with good compliance 14 cases had autonomic dysfunction and 54 did not have autonomic dysfunction. Among 32 cases with poor compliance 16 had autonomic dysfunction and 16 did not have autonomic dysfunction ( $p < 0.05$ ). Among 38 cases with OHA, 16 had autonomic dysfunction and 22 cases did not have autonomic dysfunction. Among 62 cases with insulin 14 had autonomic dysfunction and 48 did not have autonomic dysfunction ( $p > 0.05$ ). Similar finding was also observed in the study conducted by Kempler P et al (2002) assessed the prevalence and risk factors for autonomic neuropathy in the EURODIAB IDDM Complications Study. The prevalence of autonomic neuropathy was 36% with no sex differences out of 3007 patients. Significant correlations were observed between autonomic neuropathy and age ( $P < 0.01$ ),

duration of diabetes ( $P < 0.0001$ ), HbA1c ( $P < 0.0001$ )(13).

## CONCLUSION

We concluded from the present study that incidence of cardiac autonomic dysfunction among patients of Diabetes Mellitus was more prevalent in age group 40 to 50 years. Other associated factors were high body mass index, increased duration of diabetes and raised HbA1c value for occurrence of cardiac Autonomic dysfunction secondary to Diabetes Mellitus.

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