



To Assess The Autonomic Nervous System Activity in Type 2 Diabetic Patients and The Relationship of Autonomic Neuropathy in Type 2 Diabetic Patients with the Duration of the Disease

¹Dr. Mamta Sharma, Senior Resident, Department of Physiology, Government Medical College, Kathua (J&K)

²Dr. Sheetal Kotwal, Senior Resident, Department of Physiology, Government Medical College, Jammu

³Dr. Nindiya Slathia, Medical Officer, Shri Mata Vaishno Devi Shrine Board, Katra (J&K)

⁴Dr. Mohit Sharma, Ex-Lecturer, Government Medical College, Jammu

Corresponding Author: Dr. Mamta Sharma, Senior Resident, Department of Physiology, Government Medical College, Kathua (J&K).

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Abstract

Background: Diabetic neuropathy, a common and serious complication of diabetes, encompasses a range of clinical syndromes affecting peripheral and autonomic nerves. Autonomic nervous system activity (AN) is associated with the duration of diabetes. This study aimed to assess the relationship between AN and diabetes duration.

Methods: The study involved 200 patients with type 2 diabetes attending the OPD and were divided into four groups based on their duration of illness: Group 1 (less than 2 years), Group 2 (2-5 years) Group 3 (6-10 years), and Group 4 (more than 10 years). The collected data was entered in the Microsoft excel sheet and the data was analyzed by using SPSS software version 16.0.

Results: Abnormal sweating was most prevalent in Group 2, while Intermittent Nocturnal Diarrhea was most common (38.8%) in Group 3. Postural hypotension was reported most in Group 3, followed by Group 1 and Group 2. Systolic blood pressure (SBP) and diastolic pressure (DBP) showed statistically significant differences between diabetes duration of 2 years and >10 years ($P=0.010$). In pre-test SBP and DBP, lying down SBP, Standing SPB, Handgrip Test SPB and DBP, significant differences were observed between diabetes length of 2-5 years, 6-10 years, and > 10 years.

Conclusions: The study concluded that the duration of the disease, rather than the patient's age, is an independent risk factor for autonomic dysfunction, as the age of diabetes onset can vary.

Keywords: Diabetic Neuropathy, Abnormal Sweating, Autonomic Dysfunction.

Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. The long-term complications of diabetes affect multiple organ systems, including the cardiovascular, renal, nervous, and visual systems ¹.

Diabetic neuropathy, a common and serious complication of diabetes, encompasses a range of clinical syndromes affecting peripheral and autonomic nerves. Autonomic neuropathy, a form of diabetic neuropathy, involves damage to the nerves that control involuntary bodily functions, such as heart rate, blood pressure, digestion, and bladder function ^{2,3}.

The prevalence of AN in individuals with diabetes varies depending on the diagnostic criteria and population studied. Still, it is estimated to affect up to 60% of patients with long-standing diabetes⁴. AN can manifest in a wide range of symptoms, including resting tachycardia, orthostatic hypotension, gastrointestinal dysfunction (gastroparesis, diarrhoea, constipation), genitourinary dysfunction (erectile dysfunction, bladder dysfunction), and sudomotor dysfunction (anhidrosis, gustatory sweating). The presence of AN in diabetic patients is associated with increased morbidity and mortality, particularly due to cardiovascular complications ⁵.

Several pathophysiological mechanisms contribute to the development of AN in diabetes. Hyperglycaemia plays a central role, leading to the accumulation of advanced glycation end products, oxidative stress, and activation of inflammatory pathways, which damage nerve fibers and impair nerve function ⁶. Vascular factors, such as

microvascular disease and endothelial dysfunction, also contribute to nerve ischemia and hypoxia, further exacerbating nerve damage ⁷.

A diagnosis relies on a combination of clinical assessment and specialized tests of autonomic function. Symptoms such as orthostatic hypotension, resting tachycardia, and gastrointestinal or genitourinary dysfunction may suggest the presence of AN ^{8,5}. However, many patients with AN are asymptomatic, particularly in the early stages of the disease. Therefore, objective tests are essential for confirming the diagnosis and assessing the severity of AN. These tests may include cardiovascular autonomic reflex tests (e.g., heart rate variability, Valsalva maneuver, deep breathing test), quantitative sudomotor axon reflex test, and gastrointestinal motility studies ⁹

The relationship between the duration of diabetes and the development of AN has been investigated in several studies and reported a positive correlation between diabetes duration and the prevalence and severity of AN ¹⁰.

This study aims to assess autonomic nervous system activity in type 2 diabetic patients and investigate the relationship between AN and the duration of diabetes.

Material and Methods

The study was year-long cross-sectional research conducted at the Postgraduate Department of Physiology, GMC, Jammu in collaboration with the Department of Endocrinology at Superspeciality Hospital, Jammu, after obtaining ethical clearance.

The inclusion criteria for this study are that participants must be diagnosed with type-2 diabetes mellitus and be over 18 years old. Both males and females are eligible to participate. Additionally, all subjects must be willing to take part in the study.

Individuals who will be excluded from the study include those with drug addiction, a history of drug sensitivity, or those who do not provide consent. Additionally, patients with acute illnesses or chronic diseases like leprosy, as well as those with type 2 diabetes who have severe comorbidities at the time of enrollment, will be excluded. Individuals with disabilities, patients with type 1 or gestational diabetes, and aphasic patients who cannot cooperate in examinations were also excluded from participation.

The study involves 200 patients with type 2 diabetes attending the OPD and were divided into four groups based on the duration of their illness: Group 1 (less than 2 years), Group 2 (2-5 years), Group 3 (6-10 years), and Group 4 (more than 10 years).

All participants provided informed consent, and relevant information such as name, age, gender, consanguinity, marital status, medical history, and drug history was collected using a structured form after eligibility was confirmed. To assess sympathetic nervous system activity, blood pressure, orthostatic testing, and the hand grip test were performed. Conversely, to evaluate parasympathetic nervous system activity, the standing-to-lying ratio, 30:15 ratio, Valsalva ratio, and tachycardia ratio were measured. Additionally, the body weight and height of each subject were recorded.

Statistical Analysis

All the collected data were entered in the Microsoft Excel sheet and the data were analysed by using SPSS software version 16.0. Quantitative variable was reported as mean (SD) and Qualitative variables were reported as proportions. Significance was tested by an appropriate test and P value < 0.05 was considered as significant.

Results

This study involved 200 patients with type 2 diabetes divided into four groups based on the duration of their illness: Group 1 (less than 2 years), Group 2 (2-5 years), Group 3 (6-10 years), and Group 4 (more than 10 years). The study population consisted predominantly of individuals in the 41-50 years (53.5%) and 51-60 years (33%) age groups, with a mean age of 50.87 ± 7.2141 years. The majority of participants were female (79.5%), and the most common weight range was 61-65 kg (27.0%), followed by 66-70 kg (15.5%) and 71-75 kg (12.0%).

The study participants had a range of heights, with the majority (39.5%) being between 151-155 cm tall. Additionally, 21.0% were between 151-155 cm, 15.0% were up to 150 cm, 13.0% were between 166-170 cm, and 9.0% were between 161-165 cm. Only 2.5% were taller than 170 cm. In terms of body build, 60.0% had an average build, 28.5% had a well-built frame, and 11.5% were obese.

Table 1: Duration of Diabetes

Duration of diabetes	Frequency	Percent
< 2 years	43	21.5
2-5 years	77	38.5
6-10 years	56	28.0
>10 years	24	12.0
Total	200	100.0

Table-1 depicts the duration of diabetes among study subjects. The majority of subjects (38.5%) had a diabetes duration of 2-5 years, followed by 28.0% with 6-10 years, 21.5% with less than 2 years, and 12.0% with

more than 10 years. The mean duration was 5.57 ± 3.92 years. Most subjects (92.5%) were on oral medications, while 4.5% used insulin, and 3.0% received no treatment.

Table 2: Family History of Diabetes Mellitus

	Frequency	Percent	Valid Percent	Cumulative Percent
Yes	111	55.5	55.5	55.5
Nil	89	44.5	44.5	100.0
Total	200	100.0	100.0	

Table 2 depicts the family history of DM among study subjects. 111 (55.5%) had family history of DM.

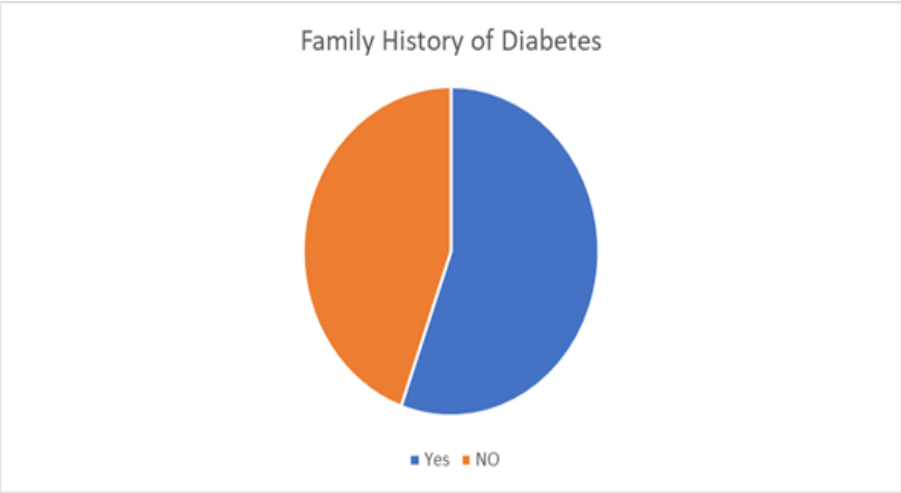


Figure 1: Family History of Diabetes Mellitus

Table 3: Distribution of autonomic symptoms of subjects according to duration of diabetes

		Diabetes Duration			
		< 2 years (Group-1)	2-5 years (Group-2)	6-10 years (Group-3)	>10 years (Group-4)
Abnormal Sweating	Count	23	36	23	10
	%	25.0%	39.1%	25.0%	10.9%
Intermittent Nocturnal Diarrhoea	Count	12	10	19	8
	%	24.5%	20.4%	38.8%	16.3%
Fullness after Meals	Count	17	20	20	10
	%	25.4%	29.9%	29.9%	14.9%
Postural Hypotension	Count	0	2	10	4
	%	.0%	12.5%	62.5%	25.0%
Abnormalities of Micturition	Count	10	15	17	12
	%	18.5%	27.8%	31.5%	22.2%

Table 3 depicts the distribution of autonomic symptoms of subjects according to the duration of diabetes mellitus. The table shows that as the duration of diabetes increased, the frequency of autonomic symptoms also rose. Abnormal sweating was most prevalent (39.1%) in Group 2, while Intermittent Nocturnal Diarrhoea was most common (38.8%) in Group 3. Fullness after meals was reported in 29.9% of cases in both Group 2 and Group 3. Postural Hypotension was seen in 62.5% of cases in Group 3, and Abnormalities of Micturition were reported in 31.5% of Group 3 and 27.8% of Group 2.

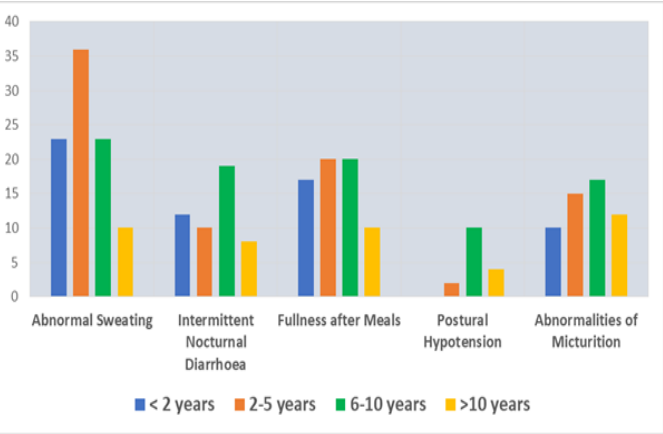


Figure 2: Autonomic symptoms of subjects according to duration of diabetes

In pre-test SBP, a statistically significant difference was observed between diabetes duration of 2-5 years and 6-10 years ($P=0.002$) and between 2-5 years and >10 years ($P=0.001$). In pre-test DBP, the statistically significant difference was observed between diabetes duration of <2 years and >10 years ($P=0.010$).

Table 4: Blood Sugar Profile on the basis of Diabetes duration

Dependent variable	Diabetes duration	Mean	Std. Deviation	P value
HbA1c	< 2 years	7.3605	.96588	<0.001*
	2-5 years	8.4429	1.59839	
	6-10 years	9.2339	2.29745	
	>10 years	9.3500	1.87918	
	Total	8.5405	1.88640	

In our study, in lying down SBP, the statistically significant difference was observed between diabetes duration of 2-5 years and 6-10 years ($P=0.040$) and between 2-5 years and >10 years ($P=0.005$). Other differences were not found to be statistically significant ($P>0.05$). In lying down DBP, the statistically significant difference was observed between diabetes duration of <2 years and >10 years ($P=0.015$). Other differences were not found to be statistically significant ($P>0.05$).

The study found statistically significant differences in various autonomic function tests based on the duration of diabetes. Specifically, In standing SBP and DBP, significant differences were observed between diabetes duration of <2 years and >10 years, as well as between 2-5 years and >10 years. In handgrip test SBP, significant differences were found between diabetes duration of <2 years and 6-10 years, and between 2-5 years and 6-10 years. In handgrip test DBP, a significant difference was observed between diabetes duration of <2 years and >10 years.

Further, Significant differences were also found in S/L ratio, 30:15 ratio, Valsalva ratio, and Tachycardia ratio when comparing different diabetes duration groups.

Fasting Blood Sugar	< 2 years	148.325	50.15819	0.670
	2-5 years	141.935	39.63662	
	6-10 years	145.285	42.39327	
	>10 years	154.500	61.04239	
	Total	145.755	45.54908	
PP Blood Sugar	< 2 years	190.790	59.37474	0.953
	2-5 years	187.480	49.49152	
	6-10 years	189.339	54.76704	
	>10 years	194.666	64.48638	
	Total	189.575	54.71998	

*Statistically significant (P<0.05, Analysis of Variance)

Table 4 shows the comparison of blood sugar profile among patients with different duration of diabetes mellitus. Analysis of blood sugar profile showed a statistically significant difference in HbA1c across different diabetes durations. Specifically, significant differences were observed between patients with <2 years and 2-5 years of diabetes, between those with >2 years and 6-10 years, and between <2 years and >10 years of diabetes.

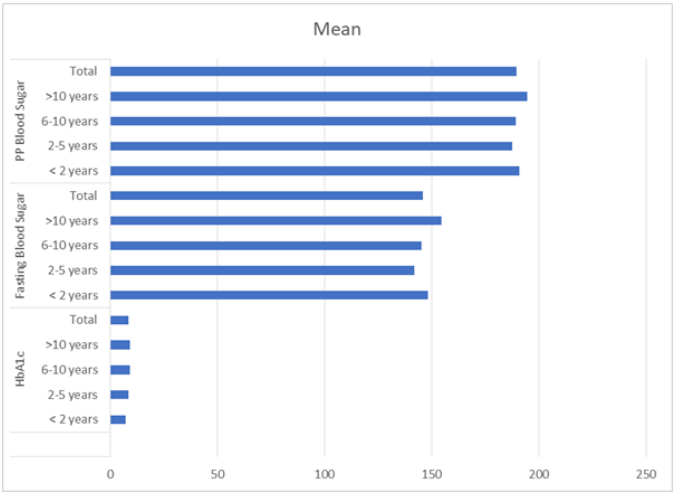


Figure 3: Blood Sugar Profile on the basis of Diabetes duration

Discussion

Diabetic neuropathy is a common complication of chronic diabetes, affecting around 50% of patients.

Elevated blood glucose levels can lead to nerve damage, causing various symptoms such as pain, numbness in the limbs, and systemic effects on the digestive system, urinary tract, blood vessels, and cardiovascular system ¹¹.

The tests used in this study assess both sympathetic and parasympathetic nervous system functions. Measures of sympathetic activity include blood pressure, orthostatic changes, and handgrip tests. Measures of parasympathetic activity include standing-to-lying ratio, 30:15 ratio, Valsalva ratio, and tachycardia ratio.

The study participants were primarily middle-aged, with the majority (107 subjects) in the 41-50 year age group, followed by 66 subjects in the 51-60 year age group. There were also 17 participants over 60 years old, 8 in the 31-40 year age group, and 2 under 30 years old. The mean age of the study population was 50.87 ± 7.2141 years, and there were 159 female and 41 male participants. The findings are consistent with the study conducted by Jonnalagadda K et al ¹².

The study found that the majority of participants (77 subjects) had been diabetic for 2-5 years, followed by 6-10 years (56 subjects), less than 2 years (43 subjects), and over 10 years (24 subjects). The mean duration of diabetes was 5.57±3.92 years. The findings are in

accordance with the study conducted by Cha SA et al, and ANLN Murthy et al^{13,14}.

In the study, the majority of participants (92.5%) were on oral medications for diabetes, while 4.5% were on insulin and 3.0% were not receiving any treatment. Most of the patients (93.0%) had not reported any recent or past illness, while 4.0% reported hypertension, and smaller percentages reported rheumatoid arthritis (1%), heart disease (1%), and hypothyroidism (1%). The findings are comparable with the study conducted by Motataianu A et al¹⁵.

The study found that the majority of participants had a family history of diabetes mellitus, and a significant proportion also had a family history of hypertension and ischemic heart disease. The findings are correlated with the study conducted by Kim YH et al, reported that 77.9% patients had family history of cardiovascular disease¹⁶.

The study found that abnormal autonomic symptoms were more prevalent in groups with longer diabetes duration. Abnormal sweating was most common in Group 2 (2-5 years), followed by Group 3 (6-10 years) and Group 1 (<2 years). Nocturnal diarrhea was reported most in Group 3, then Group 1 and Group 2. Fullness after meals was reported in Groups 2 and 3, followed by Group 1. Postural hypotension was most prevalent in Group 3, followed by Group 4 (>10 years) and Group 2. Abnormal micturition was reported most in Group 3, followed by Group 2 and Group 4. The results are consistent with the study conducted by Pan Qi et al,¹⁷.

In pre-test SBP and DBP, lying down SBP and DBP, Standing SBP and DBP, Handgrip Test SPB and DBP, a statistically significant difference was observed between diabetes duration of 2-5 years, 6-10 years and >10 years.

The results are comparable with the study conducted by Ewing et al and Akbar Md et al^{18, 19}

The present study found statistically significant differences in several autonomic function tests, including the S/L ratio, 30:15 ratio, Valsalva ratio, and Tachycardia ratio. Specifically, the multiple comparisons showed significant differences in these measures between patients with diabetes duration of less than 2 years and 2-5 years, as well as between those with 2-5 years and over 10 years of diabetes. The outcome of the present study is consistent to the study conducted by Gluck et al and N Khamisi et al.^{20, 21}

Our study found statistically significant differences in HbA1c levels across different diabetes durations. Specifically, significant differences were observed between those with diabetes for less than 2 years and 2-5 years, between those with more than 2 years and 6-10 years, and between those with less than 2 years and over 10 years of diabetes. In similar studies conducted by Dafaalla MD et al and Deshmukh DP et al determined a statistically significant association between with the development of diabetic cardiovascular autonomic neuropathy^{22,23}.

Conclusion

This study found a clear link between the duration of diabetes and the presence of autonomic dysfunction. Sustained hyperglycemia, as indicated by blood sugar levels, was associated with the development of complications like autonomic neuropathy. The study concluded that the duration of the disease, rather than the patient's age, is an independent risk factor for autonomic dysfunction, as the age of diabetes onset can vary.

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