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Association of Sympathetic Skin Response with Severity of Diabetic Polyneuropathy

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Abstract

Background: *Diabetes mellitus has emerged as one of the major challenges to human health in the twenty-first century. Diabetic autonomic neuropathy is the least recognized and understood complication of diabetes, but it has a significant negative impact on survival and quality of life.* ***Objective:*** *The objective of this study is to identify the association of sympathetic skin response with severe diabetic polyneuropathy.* ***Materials and Methods:*** *This case-control study was carried out in the Department of Neurology, BSMMU, Dhaka, from May 2022 to September 2023. A total of 64 subjects were enrolled as the study population after satisfying inclusion and exclusion criteria. Among them, 32 were grouped as cases and the rest 32 were control. Toronto Clinical Scoring System (CSS) was used to detect the severity of diabetic polyneuropathy. The SSR was recorded on most standard equipment like NIHON KOHDEN Neuropack MEB-9400 S1 Series EMG/NCV/EP Measuring System in the Department of Neurology, BSMMU.* ***Results:*** *The study included 32 diabetic polyneuropathy patients as cases and 32 age-sex-matched controls. In 7 patients, it showed absent response in both upper and lower limbs. Among the control group, SSR response was present in all populations. There was a significant association between SSR and the severity of DPN.* ***Conclusion:*** *In this study, we found an increased prevalence of delayed and absent SSR in the moderate and severe DPN groups.*

Keywords: *Sympathetic Skin Response, SSR, Diabetic Polyneuropathy, DPN.*

Introduction:

Diabetes mellitus is a serious chronic condition where the level of blood glucose is increased because the body cannot produce enough insulin or cannot effectively use the insulin[1]. In Bangladesh, there were 13.1 million adults living with diabetes, and projected to almost double (22.3 million) by 2045. Over 6.7 million people aged 20–79 died from diabetes-related causes in 2021[2]. One of the most common complications of diabetes mellitus is peripheral neuropathy[3]. For the development of diabetic neuropathy metabolic disturbances and blood vessel damage play an important role[4]. Peripheral neuropathy in diabetes mellitus is usually manifested by symmetrical multiple sensory-motor neuropathy[5].

Diabetic autonomic neuropathy (DAN), either clinical or subclinical, is more difficult to diagnose or probably undiagnosed[6]. Major clinical manifestations of diabetic autonomic neuropathy include hypoglycemia unawareness, resting tachycardia, orthostatic hypotension,

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gastroparesis, constipation, diarrhea, fecal incontinence, erectile dysfunction, neurogenic bladder, and sudomotor dysfunction with either increased or decreased sweating[7]. By conventional nerve conduction studies, small fiber neuropathy is easily missed to identify and other methods to be used to quantify peripheral small nerve fibres dysfunction[8].

Among the tests, sympathetic skin response (SSR) is useful to assess the function of sympathetic postganglionic fibers[9]. Sympathetic skin response (SSR)is a momentary change of the electrical potential of the skin generated by the sweat gland. It originates by activation of reflex arc with different kinds of internal or externally applied arousal stimuli[10]. SSR testing is technically a much simpler, easy, and convenient method[11]. It can detect the severity of DAN[12].

The present study was undertaken to evaluate the clinical value of SSR in identifying the severity of diabetic polyneuropathy.

Materials and Methods:

After ethical clearance from the Institutional Review Board (IRB), 64 subjects were selected according to inclusion & exclusion criteria between June 2022 to September 2023 in the department of Neurology, BSMMU, Shahbag, Dhaka. Before data collection, the details of the study were explained to each patient and informed written consent from the respondents or attendants was obtained. A semi-structured questionnaire was developed in English. The data was collected through face-to-face interviews with the patients. The physical examination was done properly. Medical records, demographic profiles, and clinical and laboratory records of the patients were recorded in the data collection sheet. All the data was checked and edited after collection.

Toronto Clinical Scoring System (CSS) was used to detect the severity of diabetic polyneuropathy.

SSR assessment was done by using *NIHON KOHDEN Neuropack MEB-9400 S1 Series EMG/ NCV/EP Measuring System* in the department of neurology, BSMMU, Shahbag, Dhaka. Analysis was conducted on SPSS 27.0 for Windows software. Continuous parameters were expressed as mean±SD and categorical parameters as percentages. Comparisons between groups (continuous parameters) were done by unpaired *t-test* and ANOVA test. Categorical parameters were compared by the Chi-Square test and Fisher's exact test. A p-value of <0.05 was considered significant.

Results:

The mean age among cases was 53.41±7.62 years and among controls was 50.41±5.09 years. The difference in age distribution between cases and controls was not significant (p=0.069).(Table-I)

Table-I

Distribution of participants by age (case and control) (n=64)

Age (years)	Case (n=32)	Control (n=32)	P value
<30	0(0.0%)	0(0.0%)	
30-50	7(21.9%)	13(40.6%)	
50-60	25(78.1%)	19(59.4%)	0.069^{ns}
Total	32(100.0%)	32(100.0%)	
Mean±SD	53.41±7.62	50.41±5.09	

Data were expressed as frequency, percentage, and p-value obtained by Unpaired t-test.

*Significant, ns= not significant

The bar diagram shows that out of the 32 cases, 25 (78.1%) were male and 7 (21.9%) were female. Among the 32 control participants, 21 (65.6%) were male and 11 (34.4%) were female. The difference

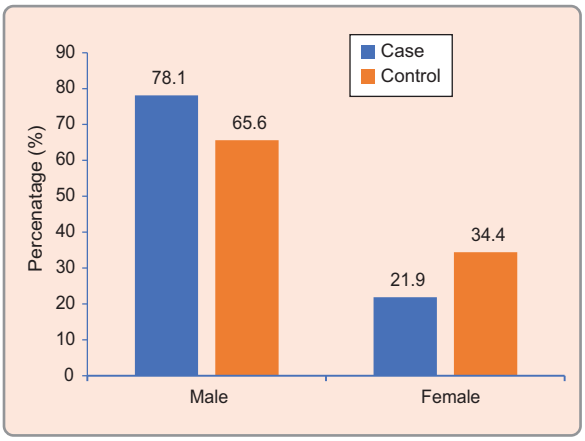

Fig-1: *Distribution of participants by gender (n=64)*

in gender distribution between cases and controls was not significant (p=0.266).

Table II shows that the most common presenting complaint was tingling, reported by all cases (100%), followed by numbness (96.9%) of cases. Weakness was observed in 15.65% of cases, while ataxia and foot pain were less frequent, reported by 9.4% and 6.3% of cases, respectively.

Among the autonomic symptoms, light-headedness was the most common affecting 53.1% of cases, difficulty obtaining an erection was reported by 52% of men. Notably, no cases were reported of dry mouth or dry eyes. Skin temperature abnormalities were observed in 6.3% of cases, while feet pale or blue were noted in 3.1% of cases. Sweating abnormalities in the foot were reported by 31.3% of cases, while sweating abnormalities in the hand were observed in 18.8% of cases. Gastrointestinal symptoms, including nausea, vomiting, or bloating, were documented in 25.0% of cases, while persistent diarrhea (>3 loose bowel movements per day) and persistent constipation (<1 bowel movement every other day) were less common, affecting 3.1% and 15.6% of cases, respectively. Leaking of urine was noted in 6.3% of cases.

The Bar diagram shows the distribution of DPN cases by severity (n=32). Among the cases, 15.6% were classified as having Mild Neuropathy, 25.0% had Moderate Neuropathy, and the majority, accounting for 59.4% of cases, had Severe Neuropathy. The mean severity score for the cases

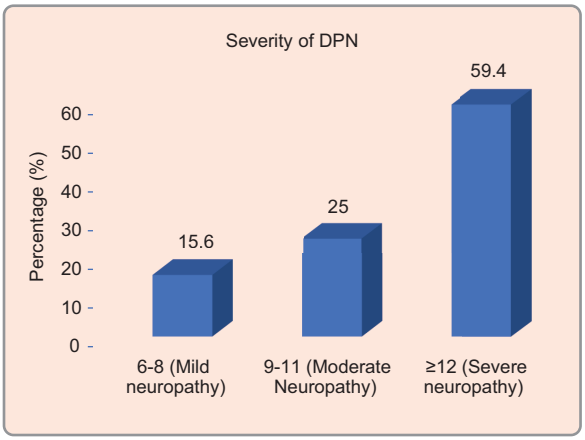

Fig-2: *The distribution of diabetic polyneuropathy (DPN) cases by severity (n=32).*

Table-II

Distribution of the cases by presenting complaints (n=32)

	Presenting complaints	Frequency	Percentage (%)
Somatic	Numbness	31	96.9
	Tingling	32	100.0
	Weakness	5	15.65
	Ataxia	3	9.4
	Foot Pain	2	6.3
Autonomic	Lightheadedness	17	53.1
	Dry mouth or dry eyes	0	0.0
	Skin temperature abnormalities	2	6.3
	Feet pale or blue	1	3.1
	Sweating abnormality in foot	10	31.3
	Sweating abnormality in Hand	6	18.8
	Nausea, vomiting, or bloating after a small meal	8	25.0
	Persistent diarrhea (>3 loose bowel movements/day)	1	3.1
	Persistent constipation (<1 bowel movement every other day)	5	15.6
	Leaking of urine	2	6.3
	Difficulty obtaining an erection (men)	13	52

Data were expressed as frequency and percentage

Table-III

Association of SSR with severity of DPN (n=32)

Severity of DPN	Number of cases	SSR in upper limb			p-value
		Normal No. (%)	Delayed No. (%)	Absent No. (%)	
6-8 (Mild)	5	5(100%)	0(0.0%)	0(0.0%)	0.007*
9-11(Moderate)	8	7(87.5%)	1(12.5%)	0(0.0%)	
e”12 (Severe)	19	5(26.32%)	7(36.84%)	7(36.84%)	
Total	32	17(53.125%)	8(25%)	7(21.875%)	
		SSR in lower limb			
6-8 (Mild)	5	1(20%)	2(40%)	2(40%)	0.025*
9-11(Moderate)	8	3(37.5%)	1(12.5%)	4(50%)	
e”12 (Severe)	19	2(10.52%)	0(0.0%)	17(89.48%)	
Total	32	6(18.75%)	3(9.38%)	23(71.87%)	

Data were expressed as frequency and percentage.
Chi-square test was done, *= significant

was 11.66±3.10, with a range of severity scores from 6 to 17.

The table-III shows a significant association between DPN severity and SSR abnormalities (p=0.007), with all cases in the mild group having normal SSR and the severe DPN group having the highest rate of abnormalities (36.84% absent SSR). The findings suggest that SSR abnormalities increase with the severity of DPN in the upper limb. This table also shows a statistically significant association between SSR in the lower limb and severity of DPN (p=0.025) in which mild DPN group, 20% had normal SSR in the upper limb, while 40% exhibited delayed and 40% absent SSR. Within the moderate DPN category, 37.5% displayed normal SSR, 12.5% had delayed SSR, and 50% had absent SSR. The severe DPN group showed a different pattern, with 10%.52% having normal SSR, and 89.48% having absent SSR while none of the patients exhibited delayed SSR.

Discussion:

The present study’s demographics were not limited by sex or religion and found that the mean age of cases was 53.41±7.62 years, compared to previous studies which reported 46.9± years for cases (Al-Moallem et al.,2008)[13] and 58.1±7.3 years (Gerawarapong,2015)[14]. The study had a higher proportion of male cases (78.1%) than female cases (21.9%), which is consistent with literature reporting a higher incidence of DPN in males than in females[4].

About presenting complaints in this study, the most common presenting complaint was tingling, reported by all cases (100%), followed by numbness (96.9%) of cases. Weakness was observed in 15.65% of cases, while ataxia and foot pain were less frequent, reported in 9.4% and 6.3% of cases, respectively.

The present study aimed to investigate the prevalence and types of autonomic symptoms among individuals with diabetes mellitus. The present study revealed that autonomic involvement was present in 71.88% of cases, which was comparable to the findings reported in the previous Soliven et al. study[15]. Among the autonomic symptoms, light-headedness and difficulty obtaining an erection in men were the most reported symptoms. Other less frequent complaints included skin temperature abnormalities, feet pale or blue, sweating abnormalities, nausea, vomiting, bloating, persistent diarrhea, persistent constipation, and leaking of urine. Interestingly, none of the cases reported having a dry mouth or dry eyes. These findings suggest that diabetes mellitus can have a significant impact on the autonomic nervous system, leading to various symptoms related to different organ systems.

The Toronto Clinical Scoring System was used to categorize the severity of DPN, which includes no neuropathy, mild neuropathy, moderate neuropathy, and severe neuropathy. The present study showed that the majority (59.4%) of cases had severe neuropathy, while 25.0% had moderate neuropathy, and only 15.6% had mild neuropathy. This is in contrast with the previous study conducted by Davies et al. (2006)[16] which reported a higher proportion of cases with mild neuropathy (60.12%), followed by moderate neuropathy (22.7%), and severe neuropathy (17.18%). This difference may be due to minor symptoms ignored by the people of our community.

The results of this study suggest that there may be a significant association between SSR and the severity of DPN in both upper and lower limbs. These findings were consistent with the study conducted by Bahnasy et al.,2018[17]. However, the present study offers unique insight into the specific patterns of SSR impairment relative to DPN severity, such as the increasing prevalence of delayed and absent SSR in the moderate and severe DPN groups.

Conclusion:

The present study observed the involvement of the autonomic nervous system by sympathetic skin response (SSR) and found a significant association between sympathetic skin response (SSR) and the severity of DPN. Sympathetic skin response (SSR) was absent predominantly in the lower limb.

Conflict of interests: None

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