INTRODUCTION

Diabetes mellitus is a chronic metabolic non-communicable disorder that burdens the healthcare system in India.[1-2] Our country has the distinction of having the largest diabetics in the world, second to China.[3] Epidemiological evidence suggests that, without effective prevention and control programs, the burden of diabetes is likely to increase globally. WHO defined Diabetes mellitus as "A metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both".[4] Several distinct types of diabetes mellitus are caused by a complex interaction of genetics and environmental factors. Effects of diabetes mellitus are long–term tissue damage, dysfunction and failure of various organs, including cardiovascular, renal, nervous system, eyes and skin.[5] Diabetic neuropathy occurs in ~50% of individuals with long-standing type 1 and type 2 diabetes mellitus. It may manifest as polyneuropathy, mononeuropathy, or autonomic neuropathy. Autonomic dysfunction affects cardiovascular, gastrointestinal, genitourinary, sudomotor, and metabolic systems. Autonomic neuropathy results in anhidrosis and altered superficial blood flow in the foot, which promotes drying of the skin and fissure formation.[6] Diabetic foot ulcers are a common cause of amputation in people with diabetes. Sudomotor dysfunction can be tested with sympathetic skin reflex (SSR), and peripheral autonomic neuropathy can be diagnosed early. This study is aimed to determine the utility of sympathetic skin reflex response in type 2 diabetes mellitus subjects and to compare and analyze the latency time and amplitude of sympathetic skin reflex of diabetics with that of controls.

MATERIALS AND METHODS

This study was conducted at Tirunelvelvi Medical College Hospital, and the Institutional ethical committee approved the study. Informed written consent was obtained from all the study subjects, and...
the procedure was explained to subjects before testing. Thirty healthy subjects as the control and thirty type-2 diabetes mellitus subjects were in the study group.

**Inclusion Criteria**
Age groups between 30 to 70 years of both genders were included.

**Exclusion Criteria**
Subjects with other co-morbidities, alcoholics, and subjects on medications that can produce autonomic neuropathy were excluded. Demographic details were obtained, and a history of the duration of diabetes, treatment particulars, other diseases, other medications history and history of consumption of alcohol were enquired. Sudomotor skin response was tested in the Department of Neurology, Tirunelveli Medical College Hospital.

The test was performed with the subject in a prone position, relaxed condition, in a semi-darkened quiet room with an ambient temperature between 22°C to 24°C. Body temperature was checked and found normal during the test. Surface silver disc electrodes were used. After thoroughly cleaning the area, the active electrode was placed with electrode jelly over the right palm and sole. The reference electrode was placed over the dorsal aspect of the right palm and right sole. A ground electrode was placed around the right arm. A single electrical stimulus was given for 0.1 msec duration with 10 mA intensity to contra lateral median and lateral posterior tibial nerve. The absence of SSR from at least one extremity after electrical stimulation followed by deep inspiration was considered absent. Latency time in seconds and amplitude of wave in mV were noted. Results were tabulated in MS office excel sheets. Statistical analysis was done by applying an independent sample t-test. SPSS software version 16 was used. Latency time in seconds and amplitude in mV were analyzed and compared between control and study groups.

**RESULTS**
Among 30 diabetic subjects, Sympathetic skin reflex was not observed in 6 study subjects and elicited in 24 study subjects. SSR was elicited in all the subjects in the control group.

<p>| Table 1: Mean age, latency time and amplitude |</p>
<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Control</td>
<td>55.57</td>
<td>6.88</td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>55.27</td>
<td>7.65</td>
</tr>
<tr>
<td>Upper limb latency time</td>
<td>Control</td>
<td>1.94</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>2.86</td>
<td>1.30</td>
</tr>
<tr>
<td>Upper limb amplitude</td>
<td>Control</td>
<td>4.49</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>3.26</td>
<td>2.01</td>
</tr>
<tr>
<td>Lower limb latency time</td>
<td>Control</td>
<td>2.26</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>3.76</td>
<td>1.52</td>
</tr>
<tr>
<td>Lower limb amplitude</td>
<td>Control</td>
<td>2.72</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>1.17</td>
<td>0.77</td>
</tr>
</tbody>
</table>

Both control and study groups were age-matched, and no significant difference between groups. The mean age in the control group was 55.57±6.88 years, and in the study group was 55.27±7.65 years. Sixteen males and 14 females in the control group and 12 males and 18 females in the study group participated. Latency time comparison of the upper limb showed a mean of 1.94 sec in the control group and 2.86 sec in the study group, which was statistically significant (p=0.002). The lower limb latency time mean was 2.26 seconds in the controls and 3.76 seconds in the study group, which was statistically significant (p<0.0001). It was observed that latency time in people with diabetes was prolonged. Short latency time was noted in the upper limb than in the lower limb both in the control and study groups.

The mean amplitude in the upper limb of the control group was 4.49 mV, and of the study group was 3.26 mV, which was statistically significant (p=0.006). The mean amplitude in the lower limb was 2.72 mV in the control group and 1.17 mV in the study group, which is statistically significant (p<0.0001) [Table 1].

**DISCUSSION**
Diabetes mellitus can be considered a Global health emergency. Type 2 diabetes mellitus is the commonest form of diabetes worldwide, attributing 90% of cases globally. Type 2 DM has become our country's major public health problem. From epidemiological studies, it is evident that without effective prevention and control programmes, the burden of diabetes is likely to increase worldwide. Because diabetes affects the workforce, it harms individual and national productivity in developed and underdeveloped countries. It is necessary to diagnose early and manage the observed risks to reduce the economic burden of this disease. The morbidity and mortality of diabetes mellitus is mainly due to its complications. Complications of diabetes mellitus can be vascular and non-vascular. Neuropathy is one of the microvascular complications of diabetes mellitus. Neuropathy includes polyneuropathy, mononeuropathy and autonomic neuropathy. Sudomotor dysfunction is one component of autonomic neuropathy. Sudomotor nerve dysfunction can be tested by sympathetic skin response.
The sympathetic skin response (SSR) is a change in skin potential following arousal stimulation, described first by Tarchanoff (1890). SSR is a polysynaptic reflex that is activated by a variety of afferent inputs.\textsuperscript{[10,11]} The final efferent pathway involves pre- and postganglionic sympathetic sudomotor fibres and, ultimately, activation of sweat glands by the sympathetic outflow. The reflex is coordinated in the posterior hypothalamus, upper brain-stem reticular formation, and spinal cord.\textsuperscript{[12]} A standard method of obtaining SSR is to place a recording electrode on the palmar and plantar surfaces because these recording sites yield higher amplitudes.

SSR waveforms can be triphasic, diphasic, or monophasic with an initial negative or positive peak.\textsuperscript{[11]} Maximal peak-to-peak amplitudes and mean latencies are measured. SSR measures the change of epidermal resistance due to sweat gland activity. The somatic afferent limb depends on the stimulus type (electrical shock, loud noise, visual threat, deep breathing); with electrical stimulation, the afferent limb occurs via large myelinated fibres. The efferent limb is a sympathetic pathway originating in the posterior hypothalamus, descending through the spinal cord to the intermediolateral cell column and paravertebral ganglia and then to the sweat gland via small unmyelinated fibres.\textsuperscript{[12]}

SSR is generated in deep layers of the skin by reflex activation of sweat glands via cholinergic sudomotor sympathetic efferent fibres.\textsuperscript{[12]} Although the central organization of the SSR is not completely understood, it is likely to be influenced by input from the basal ganglia, the premotor cortex, the temporal and frontal cortex, the hypothalamus, the limbic system and reticular formation. The efferent portion of the reflex arc involves fibres that originate from the hypothalamus and descend uncrossed along the lateral column of the spinal cord to form a small bundle between the pyramidal tract and the anterolateral tract. This tract terminates on sympathetic preganglionic neurons in the intermediolateral cell column. Sympathetic nerve fibres for the upper extremity leave the spinal cord at D5-7 segments, that for the lower extremity at D10 - L2.\textsuperscript{[12]}

Diabetes-related complications affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease. Diabetes mellitus-induced microvascular complications include autonomic neuropathy.\textsuperscript{[6]} Autonomic neuropathy involving the sudomotor nerve supplying eccrine sweat glands affects sweat gland secretion. SSR is a change in potential recorded on the skin's surface and represents sudomotor activity generated by reflex activation of the sweat gland with cholinergic mediation.\textsuperscript{[13]}

In our study, SSR was recorded from the right upper and right lower limbs of 30 control and 30 study subjects. SSR was observed in all 30 healthy subjects but only in 24 study subjects. Six study subjects showed no response and were considered absent SSR.

D. Clausa and R. Schondorf reported SSR evoked by peripheral nerve stimulation is absent in at least 50% of patients with obvious diabetic neuropathy.\textsuperscript{[12]} In our study, 20% of people with diabetes showed no response. The latency time and amplitude of the waves were measured in controls and type 2 diabetes mellitus subjects and compared. The mean latency time in the upper limb in controls was 1.94 seconds, and in the study was 2.86 seconds, with a p-value of 0.002. The latency time was prolonged in study subjects in the upper limb which was statistically significant. Latency time in the lower limb in controls was 2.26 seconds, and in the study was 3.76 seconds, with a p-value of <0.0001. It was observed that the latency time in the lower limb in study subjects was significantly prolonged when compared with healthy controls. These observations were consistent with the study by Levy DM et al.\textsuperscript{[13]} It was observed that upper limb latency was shorter than lower limb latency in both the controls and study subjects, consistent with Elie et al. study.\textsuperscript{[14]}

The mean amplitude from the upper limb in healthy subjects was 4.49 mV, and in study subjects was 3.26 mV with a p-value of 0.006. The amplitude from the upper limb in study subjects was less than controls. Mean amplitude of 2.72 mV and 1.17 mV was observed in the lower limb of the controls and study group, respectively, with a p-value of <0.0001. The amplitude from the lower limb of the study group was significantly less than the control group. D. Clausa and R. Schondorf reported decreased amplitude in diabetic subjects in their report.\textsuperscript{[12]} Our study observed that the amplitude was significantly higher in the upper limb than the lower limb both in the control and study groups, consistent with Braune HJ's study.\textsuperscript{[15]}

It was observed from this study that SSR latency was prolonged in diabetic subjects than in the control group, both in the upper limb and lower limb. Amplitude was less in diabetic individuals than in the healthy control group. Many earlier studies had reported that SSR was frequently used to diagnose than unmyelinated fibres dysfunction in diabetic neuropathy.\textsuperscript{[16-18]} SSR and quantitative sudomotor axon reflex test (QSART) may be useful for the assessment of autonomic neuropathy in diabetic patients with cardiac arrhythmia where direct measurement of heart rate variability cannot be carried out (Spitzer et al. 1997).\textsuperscript{[19]} The combined use of these different tests of sudomotor function may enhance the ability to uncover early distal sympathetic failure in diabetic neuropathy.

**CONCLUSION**

Sympathetic skin response is a simple, non-invasive useful procedure for assessing the sudomotor dysfunction earlier in type 2 diabetes mellitus individuals. "Prevention is better than cure" holds good in the prevention of diabetes-induced...
complications also. The early diagnosis of hyperglycemia, adequate glycemic control and simple tests to pick up the complications early will improve the quality of life and reduce the morbidity and mortality due to diabetes mellitus.

REFERENCES