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Peripheral nerve excitability among males in type-2 diabetes mellitus with and without diabetic neuropathy: A cross-sectional study

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ABSTRACT

Background and Aim: Diabetic neuropathy increases with the duration of diabetes and also poor glycemic control fasten the disability associated with neuropathy. This leads to a change in the nerve excitation and action potential propagation. Rheobase and Chronaxie values from SD curve give the excitability of the nerve. This study aims to find the peripheral nerve excitability by using Rheobase and Chronaxie values based on the neuropathy status of T2DM subjects. *Materials and Methods:* This was a cross-sectional study conducted on 213 subjects including 141 T2DM subjects and 72 non-diabetic subjects. T2DM subjects were classified into two groups based on the duration of diabetes (< 10 years & >10 years). All subjects nerve excitability from proximal and distal muscle groups by using Rheobase and Chronaxie value obtained from SD curve. *Results:* This study shows that 33.8% of T2DM with < 10 years and 68.60% of T2DM with > 10 years having neuropathy. In all the groups both Rheobase and Chronaxie, values show statistically significant differences ($p<0.001$) in all the muscle groups. The Rheobase and Chronaxie values were higher in T2DM with > 10 years followed by T2DM with < 10 year and Non diabetic group. *Conclusion:* Our study states that Rheobase and Chronaxie values are higher in T2DM with > 10 years and also failed to prove a statistically significant difference between neuropathic and non-neuropathic TDM in nerve excitabilities based on the duration of diabetes.

Keywords: Type-2 Diabetes Mellitus, Nerve Excitability, Rheobase, Chronaxie, SD Curve, Neuropathy, Peripheral Nerves

1. INTRODUCTION

Peripheral neuropathy associated with type 2 diabetes mellitus (T2DM) develops as sensory symptoms (pin & needle sensation) followed by motor disturbances (muscle strength reduction). Research proved that as the duration of T2DM increases & poor glycemic control increases the incidence of

diabetic neuropathy up to 50% and direct to extensive complications (Feldman et al., 2020). Research suggests that ischemia-associated microangiopathy causes neuropathy in diabetes, reconciled through energy-reliant Na+/K+ pump on the membranes of the axon (Krishnan et al., 2005). Any defacement in Na+/K+ pump despite the cause, alter the nerve depolarization because of the accumulation of intra-axonal Na+ (Kieman et al., 2000). The characteristic attribute of diabetic polyneuropathy is the combination of axonal and demyelinating damage from mechanical demyelination & channel or pump dysfunctions (Nodera & Kaji, 2006).

The changes in membrane potentials of excitable tissues (muscles & nerves) can be identified by finding the Rheobase and Chronaxie value from a strength-duration (SD) curve, which is a reliable and quick technique used by the physiotherapist in the clinical setting. SD curve corresponds to the intensity of a threshold stimulus to its duration. Rheobase is the measurement of excitability of membrane potential. A membrane can be stimulated by a change in the strength (intensity) and duration of the applied stimulus. Both these variables are inversely correlated. When the strength of the stimulus increases, the time required to elicit membrane potential reduces and vice versa to sustain an invariable effect (David et al., 2010).

Chronaxie is the tissue excitability factor that allows preference of optimal pulse duration to stimulate an excitable tissue. It is dependent on the density of sodium voltage-gated channels in the cell (Chronik et al., 2009). Scientifically, Rheobase is equal to half the current required to stimulate a tissue for the duration of Chronaxie. Chronaxie is a strength-duration time constant that corresponds to the time duration required to produce a response while the nerve is excited at twice the strength of Rheobase. There is a dearth of knowledge about the Rheobase and Chronaxie value in T2DM subjects with and without neuropathy. So the current study aims to find out the peripheral nerve excitability in T2DM subjects by using Rheobase and Chronaxie.

2. METHODOLOGY

The present cross-sectional study was conducted at the Department of Orthopedics, Srinivas Institute of Medical Sciences, Mangaluru, Karnataka, India for eight months (November 2021 to June 2022). After obtaining informed consent for participating in the study all T2DM subjects and controls were recruited. Ethical approval was given by the Institutional Ethics Committee of Srinivas University, Mangaluru, Karnataka, India (Ref: SUEC 2020/004 dated 02/01/2020), and the trial was registered with Clinical Trials Registry-India, CTRI No: CTRI/2021/07/035031 [Registered on: 22/07/2021].

Based on the study conducted by Sujata & Ramna, 2021 assuming 95% confidence interval, 80% power, and prevalence of diabetes among men (p = 2.63%), the sample size estimated for the study is 61.6, which is approximately 62 in each group. Sample size was estimated using formulae, $n = [(Z_{1-\alpha/2})^2 \times p \times (1-p)]/ I^2$, here $Z_{1-\alpha/2} = 1.96$, and absolute precision I = 4%. There are three groups in this study; Group A is the non-diabetic group, Group B is T2DM with < 10 year duration and Group C is T2DM with ≥ 10 Year duration.

Inclusion criteria: Male subjects with T2DM aged less than 75 years with a diabetic history greater than five years and non-diabetic subjects as controls.

Exclusion criteria: Females (hormonal influence), chronic cardio-respiratory disorders, neuroendocrine disorders, chronic musculoskeletal disorders, severe symptomatic vascular disorders, any previous history of nerve injuries in upper limb and lower limb, chronic dermatological conditions.

All the subjects were evaluated by an endocrinologist to confirm and classify their diabetic stages. Height was measured in meters by using a stadiometer, weight was measured by a weighing scale, and HbA1c levels of all the diabetic individuals were taken using standard laboratory methods. The peripheral nerve excitability of the upper limb and lower limb was estimated by Rheobase and Chronaxie test after plotting the strength-duration (S D) curve. S D curve (Figure 1) is the graphical representation between the pulse duration and intensity (mV or MA) required producing a minimum palpable and observable contraction (Chemali & Tsao, 2005). It is one of the routines and conventional electrodiagnostic tests of electrical activity in peripheral nerve lesions done by the physiotherapist in clinics. Rheobase and Chronaxie are obtained only after drawing a SD curve. A pulse of 300 ms duration was used to record Rheobase and is measured in mA (the device used was a constant current stimulator). It was measured using the cathode on the motor point of each nerve to be tested and the anode as an inactive electrode as mentioned in table 1. Chronaxie is measured in ms as it is the minimum duration required to produce muscle contraction when the current intensity is double the Rheobase.

Table 1 Anode placement for particular peripheral nerves.

Motor point	Nerve tested	Inactive electrode placement
Biceps Brachi (BB)	Musculocutaneous Nerve (C5, C6, C7)	Spinous process of C7
Triceps Brachi (TB)	Radial Nerve (C5, C6, C7, C8, T1)	Spinous process of C7

Quadriceps (Qceps)	Femoral Nerve (L2, L3, L4)	Femoral Triangle
Hamstring (Hams)	Sciatic Nerve (L4, L5, S1, S2, S3)	Spinous Process of S2
Gluteus Maximus (GMax)	Inferior Gluteal Nerve (L5,S1, S2)	Spinous Process of S2
Tibialis Anterior (TA)	Common Peroneal Nerve (L4, L5, S1, S2)	Neck of Fibula
Gastrocnemius (GNMS)	Tibial Nerve (L4, L5, S1, S2, S3)	Popliteal Fossa

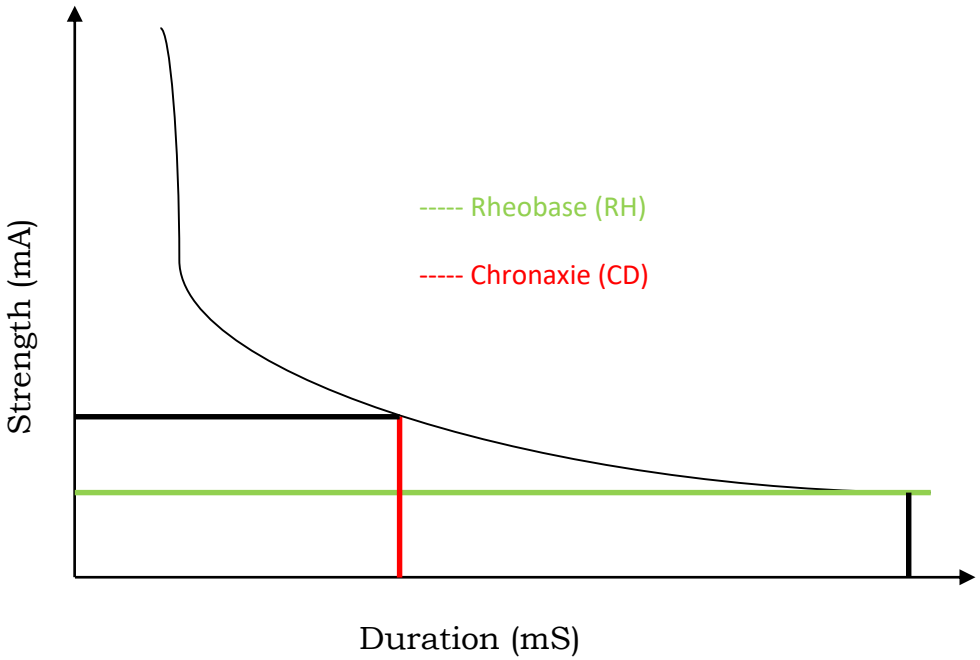

Figure 1 Strength duration curve for a particular muscle showing the Rheobase and Chronaxie.

Statistical analysis

Data were analyzed by using SPSS 21.0 (IBM Corp., Armonk, NY, USA). Kolmogorov Smirnov test was used to assess the normality of the distribution and found data is not following the normal distribution curve ($P < 0.05$). The descriptive data were summarized in Frequency, Median, and Range. Kruskal-Wallis test was used to compare the significant changes in all three groups (Non-diabetic, T2DM < 10 years, T2DM > 10 years). Mann Whitney U tests were used in the comparison of Rheobase and Chronaxie in neuropathy and non-neuropathy diabetic subjects based on the duration of T2DM. The significant level of this study was 5% ($p \leq 0.05$).

3. RESULTS

For the statistical analysis, 72 non-diabetics, 71 T2DM with < 10 years, and 70 T2DM with ≥ 10 years were included. The clinical data of the study subjects are displayed in Tables 2, 3 & 4 and Figure 2.

Table 2 Demographic data of the study subjects

Group	Age (Years)	Weight (Kg)	Height (cm)	BMI (Kg/M²)	HbA1c (%)
	Median (Range)				
Non-Diabetic (N=72)	55.5 (24)	70.5 (45)	165 (30)	25.09 (12.51)	5.75 (2.80)
T2DM < 10 Yrs (N=71)	54.0 (16)	65.0 (42)	160 (25)	25.63 (13.67)	8.90 (4.60)
T2DM > 10 Yrs (N=70)	58.5 (17)	75.0 (29)	174 (28)	24.84 (11.27)	8.90 (7.70)

Table 3 Categorical Classification of BMI of the sample

BMI	Non-Diabetic Group (N=72)	T2DM with < 10 years (N=71)	T2DM with > 10 years (N=70)
	Percentage (%)		
18.5 – 24.9 (Normal)	47.2%	36.6%	57.1%
25 – 29.9 (Over Weight)	44.4%	59.2%	28.6%
> 30 (Obese)	8.3%	4.2%	14.3%

Table 4 HbA1c Level in all three groups

HbA1c (%)	Group A: Non-Diabetic Group (N=72)	Group B: T2DM with < 10 years (N=71)	Group C: T2DM with > 10 years (N=70)
	Percentage (%)		
< 5.7% (Normal/Good DM Control)	38.9%	0%	0%
5.7 – 6.4% (Prediabetic or Moderate DM Control)	61.1%	0%	0%
> 6.5% (Diabetes/Poor DM Control)	0%	100%	100%

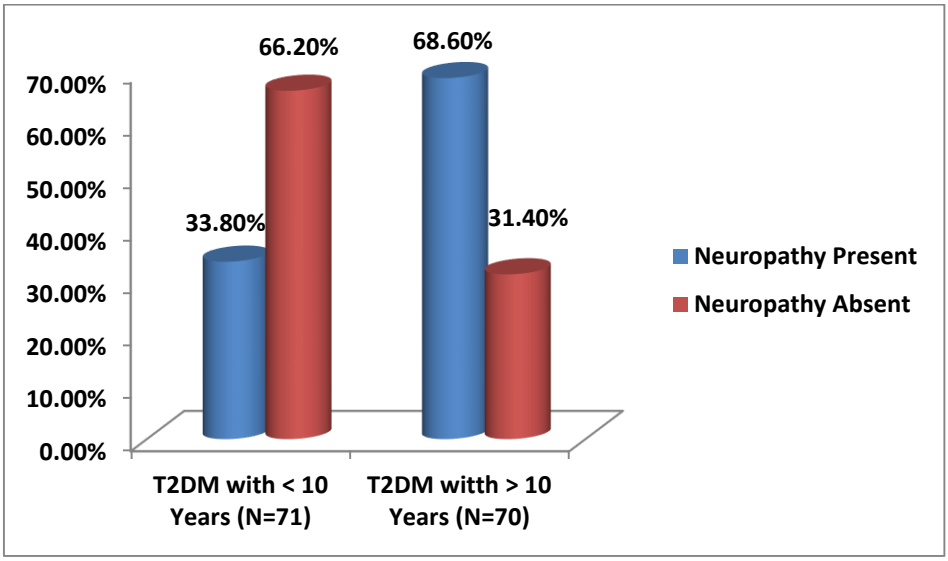

Figure 1 Neuropathy Status among the diabetes subjects based on duration.

Rheobase and Chronaxie values between the groups

In all the groups both Rheobase and Chronaxie values show statistically significant differences ($p<0.001$) in all the muscle groups. The Rheobase and Chronaxie values were higher in T2DM with > 10 years followed by T2DM with < 10 years and the Non-diabetic group. This shows as the diabetic duration increases the Rheobase and Chronaxie values also increase in the distal and proximal group of muscles (Table 5 & 6).

Table 5 Rheobase value between the groups

Rheobase Value		Non-Diabetic Group		T2DM with < 10 years		T2DM with > 10 years		Sig.*
Muscles	Side	Median (mA)	Range	Median (mA)	Range	Median (mA)	Range	
Biceps Brachi	Right	2.5	(1.7-3.3)	7.1	(6.8-7.5)	9.1	(8.8-9.5)	p<0.001
	Left	3.3	(2.9-3.4)	7.2	(6.8-7.5)	9.2	(8.8-9.5)	p<0.001
Triceps Brachi	Right	2.5	(2-3.1)	7.5	(7-7.8)	9.5	(9-9.8)	p<0.001

	Left	2.5	(1.9-3.4)	7.4	(7.1-7.9)	9.4	(9.1-9.9)	p<0.001
Quadriceps	Right	3.9	(3.7-4.5)	15.0	(13.2-15.8)	17.1	(15.2-17.8)	p<0.001
	Left	3.9	(3.7-8.2)	14.8	(13.2-15.8)	16.7	(15.2-17.8)	p<0.001
Hamstrings	Right	5.7	(5.4-5.9)	11.8	(11.4-12.5)	13.9	(13.4-14.5)	p<0.001
	Left	5.6	(5.1-5.7)	12.3	(11.2-12.8)	14.3	(13.2-14.8)	p<0.001
Tibialis Anterior	Right	3.9	(3.7-4.1)	7.5	(6.8-7.9)	9.5	(8.8-9.9)	p<0.001
	Left	3.8	(3.6-4)	7.6	(7.1-7.9)	9.6	(9.1-9.9)	p<0.001
Gastrocnemius	Right	3.3	(2.9-3.4)	7.5	(7.1-7.8)	9.6	(9.1-9.8)	p<0.001
	Left	2.5	(2-3.1)	7.3	(7.1-7.9)	9.3	(9.1-9.9)	p<0.001
Gluteus Maximus	Right	6.4	(5.5-6.9)	15.9	(15.1-17.8)	17.9	(17.1-19.8)	p<0.001
	Left	6.3	(5.8-6.8)	16.5	(15.2-17.8)	18.5	(17.2-19.8)	p<0.001
*Test performed was Kruskal-Wallis (one-way non-parametric test)								

Table 6 Chronaxie value between the groups

Chronaxie Value		Non-Diabetic Group		T2DM with ≤ 10 years		T2DM with ≥ 10 years		Sig.*
Muscles	Side	Median (mA)	Range	Median (mA)	Range	Median (mA)	Range	
Biceps Brachi	Right	0.300	(0.26-1)	1.200	(1.1-1.7)	2.150	(1.7-2.5)	p<0.001
	Left	0.300	(0.24-0.93)	1.400	(1.2-1.8)	2.100	(1.7-2.5)	p<0.001
Triceps Brachi	Right	0.825	(0.44-1)	1.500	(1.2-1.8)	2.600	(2.1-2.9)	p<0.001
	Left	0.855	(0.58-1)	1.600	(1.2-1.8)	2.500	(2.1-2.9)	p<0.001
Quadriceps	Right	0.825	(0.44-1)	2.300	(2-2.5)	2.900	(2.7-3.2)	p<0.001
	Left	0.785	(0.58-1)	2.200	(2.1-2.5)	2.900	(2.7-3.2)	p<0.001
Hamstrings	Right	0.635	(0.34-0.93)	2.500	(2.1-22.8)	3.100	(2.8-3.3)	p<0.001
	Left	0.720	(0.24-0.96)	2.400	(2.2-2.8)	3.050	(2.8-3.3)	p<0.001
Tibialis Anterior	Right	0.825	(0.44-1)	1.600	(1.2-1.9)	2.700	(2.4-2.9)	p<0.001
	Left	0.300	(0.24-0.93)	1.700	(1.2-1.9)	2.650	(2.5-2.9)	p<0.001
Gastrocnemius	Right	0.300	(0.26-1)	1.700	(1.4-1.9)	2.900	(2.6-3.2)	p<0.001
	Left	0.855	(0.58-1)	1.700	(1.4-1.9)	3.000	(2.7-3.2)	p<0.001
Gluteus Maximus	Right	0.960	(0.93-1)	2.600	(2.4-2.9)	3.800	(3.4-4.2)	p<0.001
	Left	0.960	(0.93-1)	2.700	(2.4-2.9)	3.850	(3.6-4.2)	p<0.001
*Test performed was Kruskal-Wallis (one-way non-parametric test)								

Rheobase & Chronaxie value based on neuropathy status

This study shows that 33.8% of T2DM with < 10 years and 68.60% of T2DM with > 10 years have neuropathy. The Mann-Whitney U test shows there is no significant difference (p>0.05) in Rheobase and Chronaxie values with neuropathy status in groups B and C (Table 7 & 8).

Table 7 Rheobase value based on the neuropathy status

Neuropathy Status		T2DM with ≤ 10 years				T2DM with ≥ 10 years			
		Present	Absent	U Value	P Value#	Present	Absent	U Value	P Value#
Muscles	Side	Median (Range) in mA	Median (Range) in mA			Median (Range) in mA	Median (Range) in mA		
Biceps Brachi	Right	7.1 (6.8-7.5)	7.1 (6.8-7.5)	529.0	.666*	9.1 (8.8-9.5)	9.2 (8.8-9.5)	531.0	.794*
	Left	7.2 (6.8-7.4)	7.2 (6.8-7.5)	540.5	.772*	9.2 (8.8-9.5)	9.15 (8.8-9.5)	508.0	.583*

Triceps Brachi	Right	7.5 (7-7.8)	7.5 (7-7.8)	521.0	.591*	9.5 (9-9.8)	9.5 (9-9.8)	503.0	.537*
	Left	7.4 (7.1-7.9)	7.4 (7.1-7.9)	543.5	.801*	9.4 (9.1-9.9)	9.45 (9.1-9.9)	545.5	.936*
Quadriceps	Right	15 (13.2-15.4)	15.2 (13.2-15.8)	499.0	.426*	17.0 (15.2-17.8)	17.5 (15.2-17.8)	491.0	.451*
	Left	14.4 (13.2-15.4)	14.8 (13.2-15.8)	464.5	.224*	16.7 (15.2-17.8)	16.8 (15.7-17.8)	492.5	.463*
Hamstrings	Right	11.9 (11.4-12.5)	11.8 (11.4-12.5)	545.5	.820*	13.9 (13.4-14.5)	13.8 (13.4-14.5)	510.5	.606*
	Left	12.2 (11.2-12.8)	12.3 (11.2-12.8)	519.0	.581*	14.2 (13.2-14.8)	14.3 (13.2-14.8)	518.5	.678*
Tibialis Anterior	Right	7.5 (6.6-7.3)	7.5 (6.8-7.9)	539.5	.763*	9.5 (8.8-9.9)	9.7 (8.9-9.8)	483.5	.395*
	Left	7.3 (7.1-7.9)	7.6 (7.1-7.9)	444.5	.142*	9.3 (9.1-9.9)	9.6 (9.2-9.9)	426.0	.118*
Gastrocnemius	Right	7.6 (7.1-7.8)	7.5 (7.1-7.9)	511.0	.511*	9.6 (9.1-9.8)	9.5 (9.1-9.8)	490.5	.441*
	Left	7.3 (7.1-7.9)	7.3 (7.1-7.3))	474.0	.261*	9.3 (9.1-9.9)	9.3 (9.1-9.9)	536.0	.840*
Gluteus Maximus	Right	15.9 (15.2-17.8)	15.8 (15.1-17.8)	502.0	.448*	17.9 (17.1-19.8)	17.7 (17.1-18.9)	420.5	.103*
	Left	16.5 (15.2-17.8)	16.5 (15.2-17.8)	484.5	.330*	18.5 (17.2-19.8)	18.5 (17.2-19.8)	520.5	.696*

[#]Test performed was Mann Whitney U Test
* Non-significant (P>0.05)

Table 8 Chronaxie value based on the neuropathy status

Neuropathy Status		T2DM with < 10 years				T2DM with ≥ 10 years			
		Present	Absent	U Value	P Value[#]	Present	Absent	U Value	P Value[#]
Muscles	Side	Median (Range) in ms	Median (Range) in ms			Median (Range) in ms	Median (Range) in ms		
Biceps Brachi	Right	1.3 (1.1-1.7)	1.2 (1.1-1.7)	528.5	.657*	2.2 (1.7-2.5)	2.1 (1.7-2.4)	398.0	0.056*
	Left	1.4 (1.2-1.8)	1.3 (1.2-1.8)	457.0	.183*	2.1 (1.7-2.5)	2.1 (1.7-2.5)	500.5	0.521*
Triceps Brachi	Right	1.5 (1.2-1.8)	1.5 (1.2-1.8)	548.0	.844*	2.6 (2.1-2.9)	2.6 (2.2-2.9)	458.0	0.240*
	Left	1.6 (1.2-1.9)	1.6 (1.2-1.9)	562.0	.985*	2.5 (2.1-2.9)	2.6 (2.1-2.8)	521.0	.701*
Quadriceps	Right	2.3 (2-2.5)	2.2 (2-2.5)	420.5	.073*	2.9 (2.7-3.2)	2.9 (2.7-3.2)	508.0	.570*
	Left	2.4 (2.1-2.5)	2.2 (2.1-2.5)	406.0	.050*	2.9 (2.7-3.2)	2.9 (2.8-3.2)	543.5	.913*
Hamstrings	Right	2.5 (2.1-2.8)	2.6 (2.1-2.8)	559.0	.950*	3.1 (2.8-3.3)	3 (2.8-3.3)	448.0	.194*
	Left	2.4 (2.2-2.8)	2.4 (2.2-2.8)	541.5	.774*	3.1 (2.8-3.3)	3 (2.9-3.3)	538.0	.858*
Tibialis Anterior	Right	1.8 (1.2-1.9)	1.6 (1.2-1.9)	445.5	.143*	2.7 (2.4-2.9)	2.7 (2.4-2.9)	445.5	.181*
	Left	1.8 (1.5-1.9)	1.7 (1.2-1.9)	492.0	.372*	2.7 (2.5-2.9)	2.6 (2.6-2.9)	398.0	.056*
Gastrocnemius	Right	1.8 (1.4-1.9)	1.7 (1.4-1.9)	548.0	.183*	2.9 (2.6-3.2)	2.9 (2.6-3.2)	411.0	.074*

	Left	1.8 (1.4-1.9)	1.7 (1.4-1.9)	562.0	.844*	3.0 (2.7-3.2)	3 (2.7-3.2)	428.0	.120*
Gluteus Maximus	Right	2.7 (2.4-2.9)	2.6 (2.4-2.9)	436.0	.112*	3.8 (3.4-4.2)	3.8 (3.5-4.2)	551.0	.990*
	Left	2.7 (2.4-2.9)	2.7 (2.4-2.9)	544.0	.804*	3.9 (3.6-4.2)	3.8 (3.6-4.2)	518.0	.665*
#Test performed was Mann Whitney U Test * Non-significant (P>0.05)									

Rheobase and Chronaxie value within the groups

Since the Rheobase and Chronaxie values show highly significant between the group using the Kruskal-Wallis test (one-way non-parametric) pairwise comparison were done to check the changes in all outcomes, which shows a higher value in group C, followed by group B and group A. This clinically states that Rheobase and Chronaxie values are higher in T2DM with > 10 years (Figure 3, 4, 5 & 6).

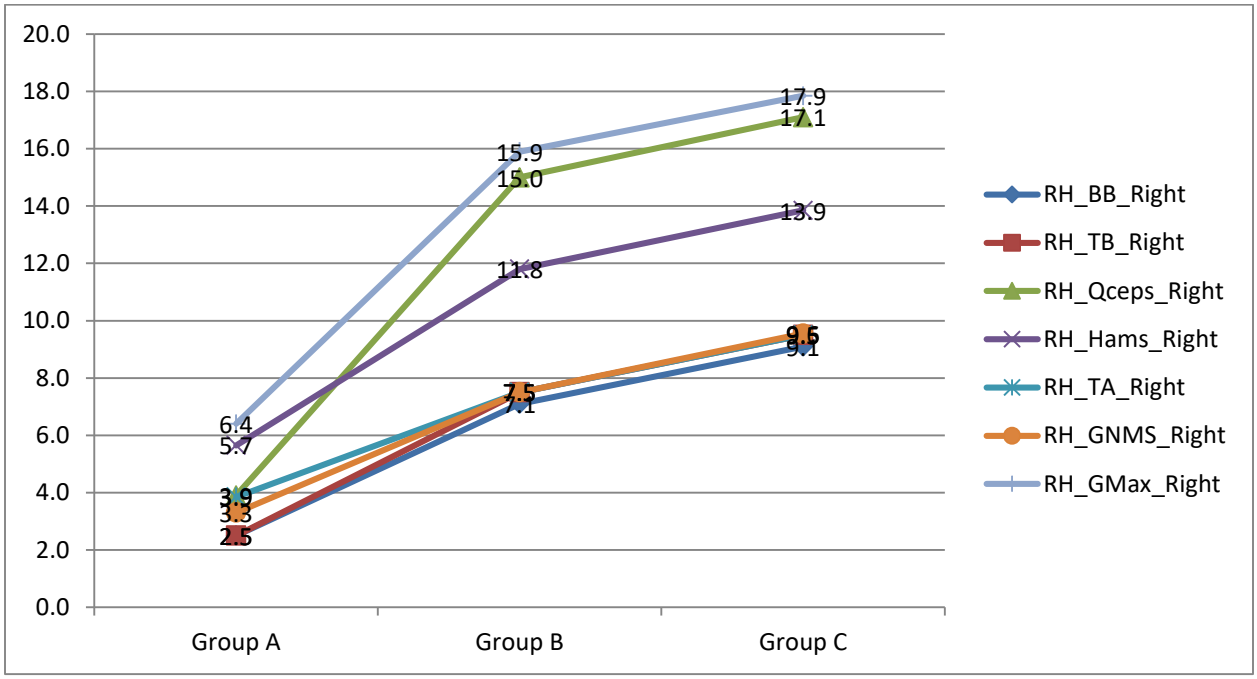

Figure 2 Rheobase in right side muscles in each group.

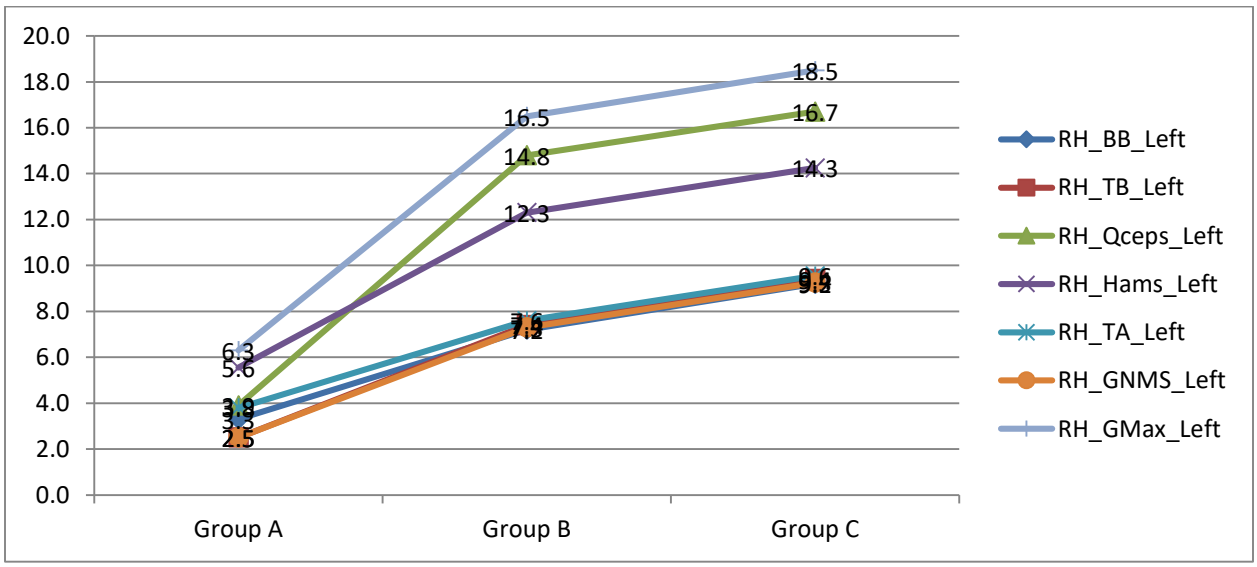

Figure 3 Rheobase in left side muscles in each group.

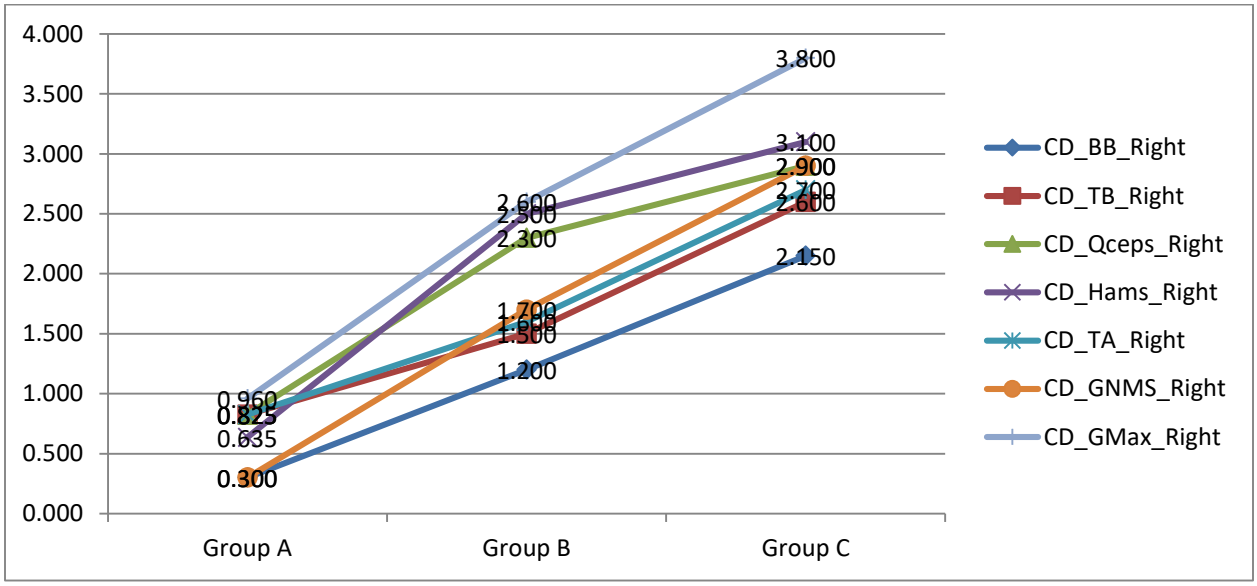

Figure 4 Chronaxie in right side muscles in each group.

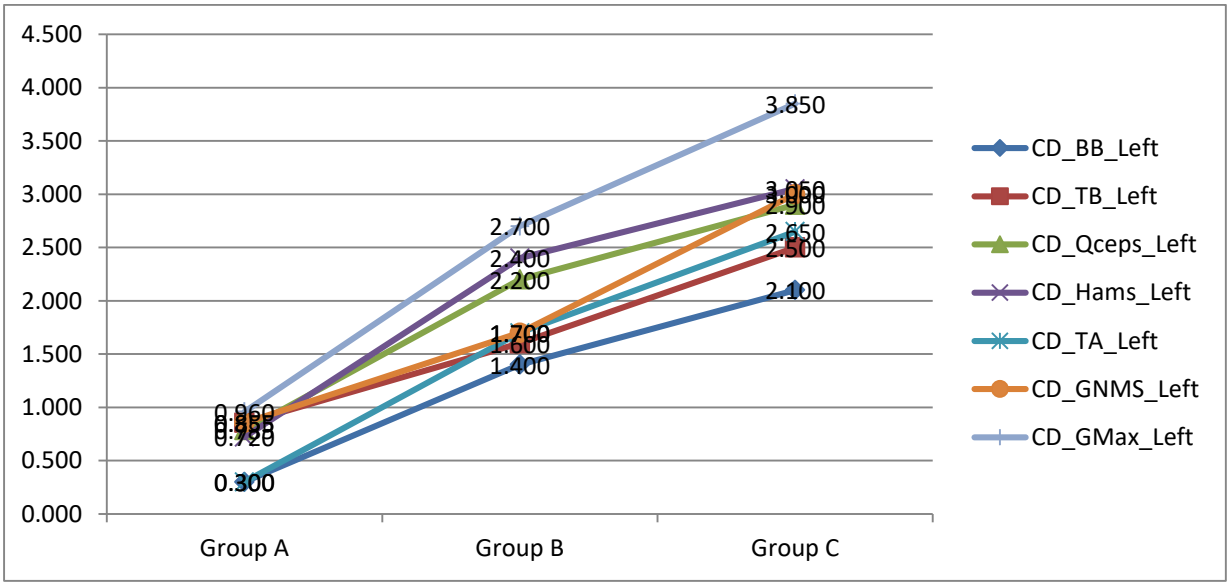

Figure 5 Chronaxie in left side muscles in each group.

4. DISCUSSION

Diabetic neuropathy is nerve damage caused by chronically elevated blood sugar content in the body leading to numbness (paraesthesia), and loss of sensation on feet, legs, or hands. Diabetes is one of the commonest causes of peripheral neuropathy. About 70% of T2DM develop peripheral neuropathy in their later years after the onset of DM. Researchers suggest that diabetic neuropathy is not only to extremities but also affected different parts of the body. With neuropathy, neural communication will be compromised and as a result, the sensation from every part of the body gets diminished leading to cuts, burns, or ulcers in the hands and feet.

The cost of untreated neuropathy can be lethal. Diabetic neuropathy symptoms are different in each person based on glycemic control. The symptoms of diabetic neuropathy include touch sensitivity, muscle weakness, proprioceptive deficits, balance problems, and falls (Bansal et al., 2006). These changes have happened slowly over the years. Because the changes are delicate and occur as they get aged, they have a propensity to overlook the signs of nerve injury, and thoughts of its component of aging. Researchers are stating that good diabetic control, control of blood pressure, regular physical activity or exercises, weight reduction for overweight or obese individuals, reduction or abstinence of alcohol, quitting smoking, proper medication, and diets can prevent or delay the nerve damage associated with diabetes (Suzanne et al., 2019).

The current study shows the symmetrical pattern of diabetic neuropathy in both proximal and distal muscle groups. The importance of this study of finding the difference in nerve excitability among T2DM is because south India has a 19.1% incidence rate of diabetic neuropathy (Ashok et al., 2002). Nearly 67% of T2DM have clinical or subclinical diabetic neuropathy. The subclinical diabetic neuropathy diagnosis includes electrophysiological studies, so the present study used Rheobase and Chronaxie value estimating after plotting the SD curve. The current study also classified Rheobase and Chronaxie in T2DM subjects based on the duration of diabetes (> 10 years and < 10 years), the reason is the increasing incidence of diabetic neuropathy from 7.5% to 50% at 25 years of follow-up and 40% prevalence after 10 years of T2DM (Riyas et al., 2022). 33.8% with T2DM less than 10 years and 68.6% with T2DM more than 10 years showed diabetic neuropathy in our study which shows a greater incidence rate after 10 years of T2DM.

Chronaxie and Rheobase from the SD curve will give the idea about nerve excitability in the clinical setting. These are conventional electro-diagnosis tests having easy administrative properties and reliable, non-invasive tests for identifying the innervation status. The present study shows higher Rheobase and Chronaxie values in T2DM subjects compared with non-diabetic groups. This indicates that T2DM subjects required more stimuli to elicit motor contraction in distal and proximal muscle groups following diabetic neuropathy. The study also shows higher Rheobase and Chronaxie values in T2DM with > 10 years duration than < 10 years. This shows the severity of diabetic neuropathy based on the duration and requires proper education of the subjects regarding future complications, the necessity of controlling the blood glucose level, and the importance of non-pharmacological and pharmacological intervention to improve the nerve health status.

The reason or pathophysiology behind diabetic neuropathic with or without pain is still under research and several hypotheses are postulated, which include Polyol pathway hyperactivity (Sheetz & King, 2002; Oates, 2002), oxidative and nitrosative stress (Brownlee, 2001; Giacco & Brownlee, 2010), microvascular changes (Arora et al., 2002, Doupis et al., 2009), channels sprouting (Dickenson et al., 2002; He et al., 2010), microglial activation (Suzuki et al., 2011; Crown, 2012), central sensitization (Chen & Pan, 2002; Maier et al., 2010), brain plasticity (Silva et al., 2013; Chen & Levine, 2001).

Our current research paper is investigating the changes in nerve excitability following T2DM with its duration and based on the neuropathy status, which will be helpful to identify the best physiotherapeutic intervention to manage diabetic neuropathy. We also found that there is no significant statistical difference between the Rheobase and Chronaxie value among the neuropathy and non-neuropathy subjects with less than 10 year duration and also in greater than 10 year duration. This open-up a wide scope of identifying the cause and further more detailed research in the area of nerve excitability in T2DM. We also recommend conducting similar kinds of studies on female subjects, based on the medications and also conducted with an advanced electro-diagnostic test like EMG, NCV, etc.

5. CONCLUSION

Males with T2DM have been found to experience significantly higher Rheobase and Chronaxie than non-diabetic male subjects. And also has higher values of Rheobase and Chronaxie in T2DM subjects with more than 10 years of duration. Diabetic neuropathic T2DM subjects also show higher Rheobase and Chronaxie values with an increase in the duration of diabetes.

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Authors Contribution

Conceptualization, Riyas Basheer K B and Dinesh K V N; Formal analysis, Riyas Basheer K B; Methodology, Riyas Basheer K B, Dinesh K V N, Subhashchandra Rai and Mohammed Arshak A T; Project administration, Riyas Basheer K B and Mohammed Arshak A T; Resources, Subhashchandra Rai and Mohammed Arshak A T; Supervision, Riyas Basheer K B; Writing – original draft, Riyas Basheer K B; Writing – review & editing, Dinesh K V N, Subhashchandra Rai and Mohammed Arshak A T.

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Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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