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RESEARCH ARTICLE

TO STUDY NERVE CONDUCTION PARAMETERS IN PREDIABETICS AND HEALTHY INDIVIDUALS

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Prediabetics, HbA1c, Neuropathy, American Diabetic Association, Impaired Glucose Tolerance

Abstract

Background: It has been found in various observational studies done till now that many micro and macro vascular complications start developing earlier to the diagnosis of T2DM. So, it becomes very important to diagnose this earlier stage of T2DM i.e. Prediabetes. It is at this stage when one can prevent progression of Pre diabetes to frank T2DM.

Objective:

Primiray Objective: To compare Nerve Conduction parameters in Prediabetics and healthy individuals (sensory and motor nerve).

Secondary Objective: To correlate HbA1c with nerve conduction parameters in Prediabetic individuals.

Material And Methods: A study on nerve conduction was conducted on the motor median, motor ulnar, motor tibial, sensory median and sural nerves. Prediabetic cases and healthy controls not associated with any pathology mentioned in exclusion criteria were included in the study. Their clinical history had taken and all routine and special investigations have carried out as per patient proforma. After collecting the blood samples, patients were referred from medicine to Physiology department for nerve conduction study, in which NCV parameters (Nerve conduction velocity and amplitude) were recorded.After explaining the purpose of the study and requisite details regarding the same, written informed consent was obtained from all patients as per ethical board guidelines.

Control Group (Group 1): comprise of 65 healthy individuals (NGT).

Prediabetic Group (Group 2): comprise of 65 individuals diagnosed with prediabetes (IGT).

Results: Ncv and Amplitude was reduced in prediabetics compared to healthy individuals.Significantnegativecorrelation was found between HbA1cand nerve conduction parameters in Prediabetic individuals.

Conclusion: By diagnosing it early in the course of prediabetes, morbidity and mortality secondary to neuropathy can be prevented. It may assist the physicians in early detection of nerve damage and to start timely intervention, if required to prevent further complications. So, it is suggested that nerve conduction study should be inducted in

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routine investigations of prediabetic cases for early diagnosis of cognitive decline.

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Introduction:-

Increasing obesity, unhealthy diets, and sedentary lifestyles have led to a global population that is more prone to diabetes mellitus and its complications. Diabetic neuropathy is a common complication seen in routine health care and is the most common form of peripheral neuropathy in the developed world.[1]

There is also increasing evidence to demonstrate a higher frequency of idiopathic polyneuropathy, painful sensory neuropathy and small Fiber neuropathy among pre-diabetic individuals with IGT.South Asians appear to be more prone to develop T2DM .[2]

Researches are going on to establish whether peripheral neuropathy can occur before the onset of established diabetes mellitus, i.e., in the prediabetes stage. This is an intermediate state of hyperglycaemia with glycaemic parameters above normal but below the diabetes threshold. The American Diabetes Association (ADA) has defined prediabetes as a state of intermediate hyperglycaemia using three specific parameters, impaired fasting glucose (IFG) defined as fasting plasma glucose (FPG) of 100 to 125 mg/dL (5.6-6.9 mmol/L) or impaired glucose tolerance (IGT) defined as 2h plasma glucose of 140-199 mg/dL (7.8-11.0 mmol/L) during 75 g OGTT or haemoglobin A1c (HbA1c) based criteria of a level of 5.7% to 6.4% (39-47mmol/mol).[3]

Prediabetics have shown nerve conduction velocities and reductions in compound muscle action potential (CMAP) in tibial nerve and sensory nerve action potential (SNAP) in sural nerve.[4] While another study observed that amplitude of sural SNAP and tibial CMAP was significantly lower in pre-diabetics whereas NCV of sural and tibial nerve is statistically nonsignificant.[5] In contrast, few studies observed no statistically significant difference in median, ulnar, sural nerves between the prediabetics and healthy control groups.[6] Both IFG and IGT patients when studied separately had shown significant nerve conduction abnormalities. The inverse correlations between sensory and motor NCV and HbA1C were observed.[7]

Therefore, in the present study, we attempt to study changes in nerve conduction velocity (NCV) and compound muscle action potential (CMAP) in motor and sensory nerve action potential (SNAP) in sensory nerves in prediabetes patients in a tertiary care institute.Westudy nerve conduction parameters on motor median, motor ulnar, motor tibial, sensory median and sural nerves. Thus, early diagnosis of abnormal nerve conduction parameters, early intervention and prompt management at pre-diabetic before development of symptoms prevents further complications. So, this study was designed to fill the lacuna in the current knowledge and try to establish that prediabetes patients may have altered nerve conduction.

Materials and Methods:-

Place of study:
Department of Physiology in collaboration with departments of General Medicine and Pathology at BPS Govt. Medical College for Women, Khanpur Kalan, Sonipat, Haryana.

Study Design:
It is a cross-sectional study.

Study period:
November 2023 to October 2024.

This observational cross-sectional study was conducted in the Department of Physiology in collaboration with the Department of Pathology and Department of General Medicine, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonepat. After Institutional Ethics Committee (IEC) approval, the patients attending the in-patient and out-patient services of department of General Medicine of the Institute, fulfilling the inclusion and exclusion criteria, were enrolled in the study after obtaining their written informed consent.

Selection criteria:
Prediabetic cases and healthy controls not associated with any pathology mentioned in exclusion criteria were included in the study. Their clinical history had taken and all routine and special investigations have carried out as per patient proforma. After collecting the blood samples, patients were referred from medicine to Physiology department for nerve conduction study, in which NCV parameters (Nerve conduction velocity and amplitude) were recorded.

After explaining the purpose of the study and requisite details regarding the same, written informed consent was obtained from all patients as per ethical board guidelines.
Control Group (Group 1) : comprise of 65 healthy individuals (NGT).
Prediabetic Group (Group 2) : comprise of 65 individuals diagnosed with prediabetes (IGT).

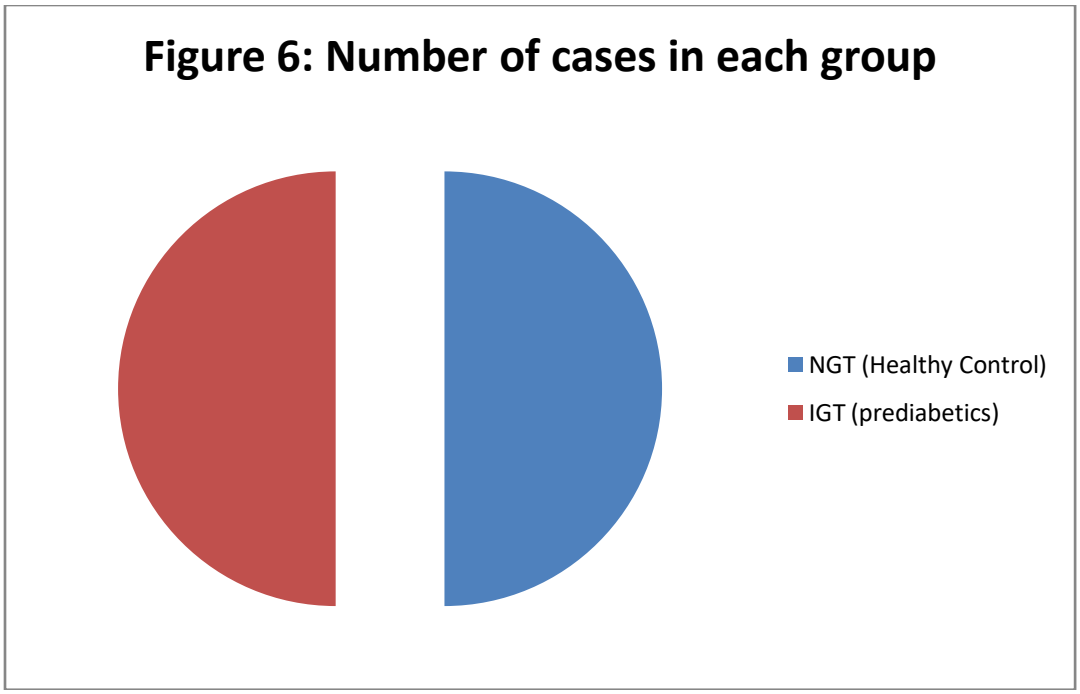
NCV parameters (nerve conduction velocity and amplitude)
The nerve conduction study was performed as per standard procedure by using Alleger EMG-NCV EP machine with the help of surface and ring electrodes and a stimulator in the Neurophysiology Lab of Physiology Department. The procedure explained to subjects in detail. Participants asked to remove any jewellery, hearing aids or other metal objects that may interfere with the procedure. NCV Tests were performed in a controlled environment, in an air-conditioned room maintaining ambient temperature between 26 to 28^0C in quite surroundings.Nerve conduction studies were performed on motor nerves e.g., median, ulnar, tibial and sensory nerves median and sural nerve bilaterally using the standardized technique. Filters were set at 2-5 Hz (low cut filter) to 10KHz (high cut filter) and sweep speed at 2-5 millisecond per division for motor study. For sensory study filters were set at 5-10 Hz (low cut filter) to 2-3 KHz (high cut filter) and sweep speed at 1-2 millisecond per division. Skin temperature was maintained at 34-37^0C.[8]

Placement of electrodes
Patients asked to lie down in supine position for the test. The electrodes were fixed on the skin overlying muscle supplied by nerve only after application of electrode jelly. The electrodes connected to the oscilloscope through the preamplifier. The Nerve conduction velocity test was done with 3 electrodes (active, reference and ground electrodes). For Motor NCV, the surface recording electrodes were commonly used and placed in belly tendon montage; keeping the active electrode close to motor point and reference electrode to the tendon. Ground electrode was placed between stimulating and recording electrodes. Motor nerve was then stimulated with supramaximal electrical stimulus at least at two points along its course by stimulator. An action potential known as compound muscle action potential (CAMP) was recorded. Whereas for sensory NCV, ring electrodes were used for median nerve and surface electrodes for sural nerve. Sensory NCV was measured by stimulating at a single stimulation site. Both active and reference electrodes were placed on nerve. An action potential known as sensory nerve action potential (SNAP) was recorded. The onset latency, nerve conduction velocity (NCV) and amplitude of compound muscle action potential (CMAP) in motor and sensory nerve action potential (SNAP) in sensory nerves were measured by the machine automatically for each nerve being tested.[9]

Results:-
It is a cross-sectional study conducted on 130 subjects (control-65 and prediabetics-65) to study nerve conduction parameters in prediabetics and healthy individuals. Both groups were age and sex matched and hence can be compared. We also correlate HbA1c with nerve conduction parameters in prediabetic individuals.

Table No. 2:- Showing distribution of cases.

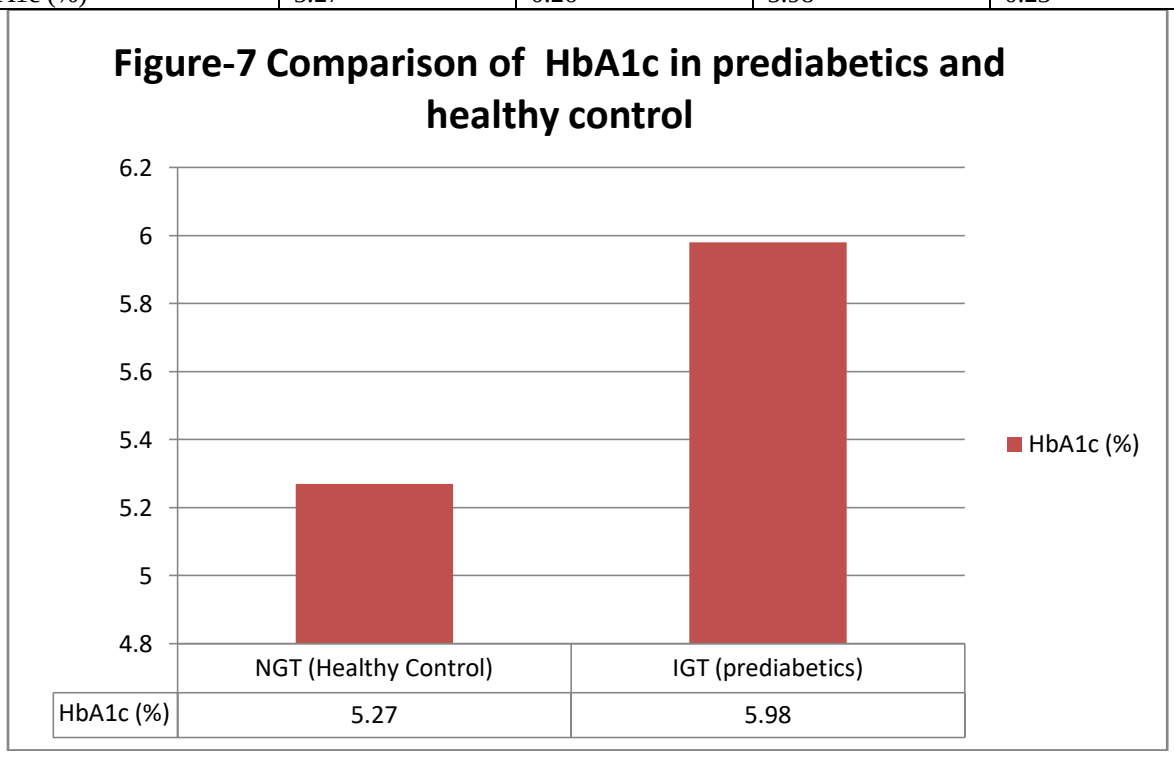
	Healthy control (NGT)	Prediabetics (IGT)
Number of cases in each group	65	65



In table 2 and figure 6:
Control Group (Group 1) : comprise of 65 healthy individuals (NGT).
Prediabetic Group (Group 2) : comprise of 65 individuals diagnosed with prediabetes (IGT).

Table No. 3:- Comparison of HbA1c in prediabetics and healthy control.

Comparisonof HbA1c in prediabetics and healthy control				
	Healthy control (NGT)		Prediabetics (IGT)	
	Mean	SD	Mean	SD
HbA1c (%)	5.27	0.26	5.98	0.23

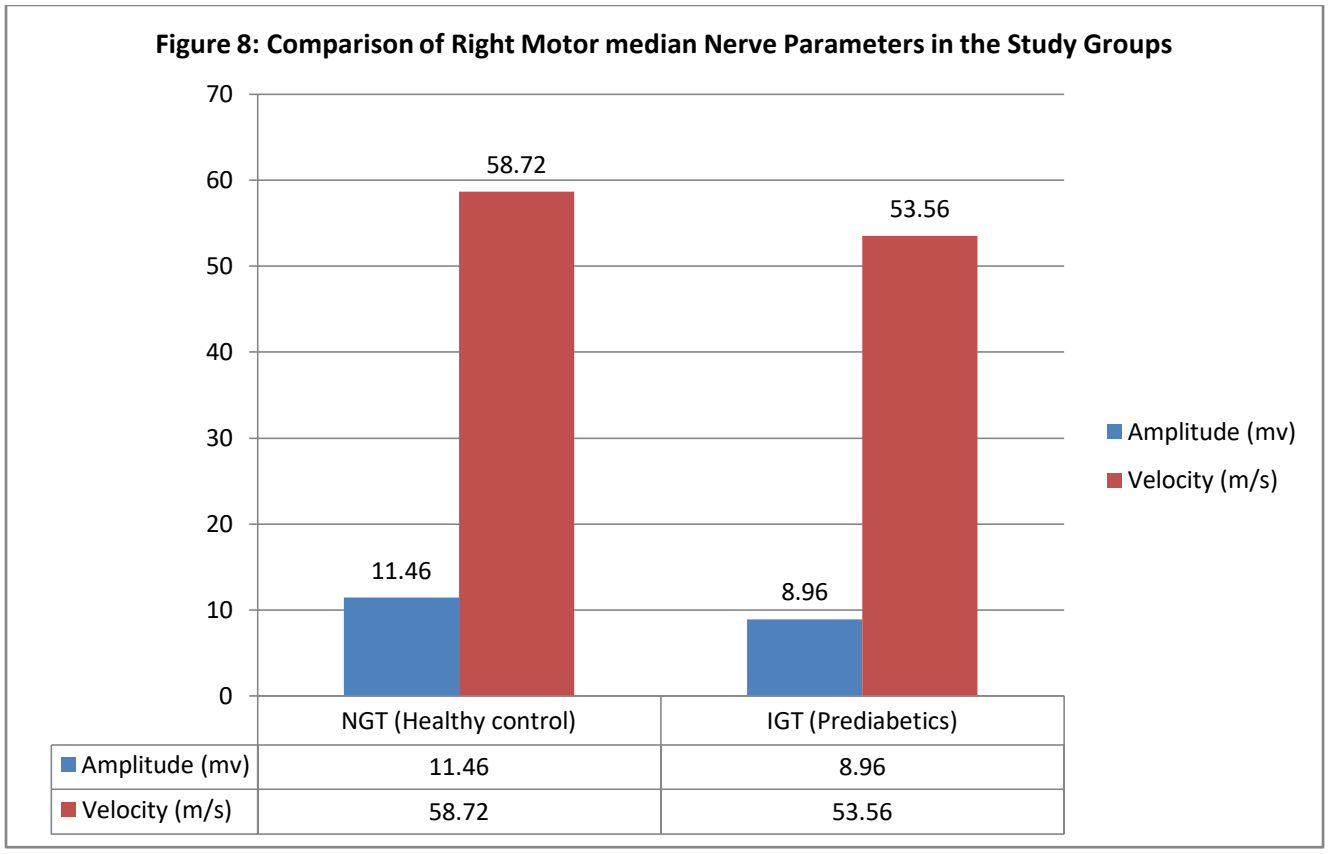


In table 3 and figure 7:

The mean HbA1c was significantly higher (P<0.001) in Prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group.

Table No. 4:- Comparison of Right Motor median Nerve Parameters in the Study Groups.

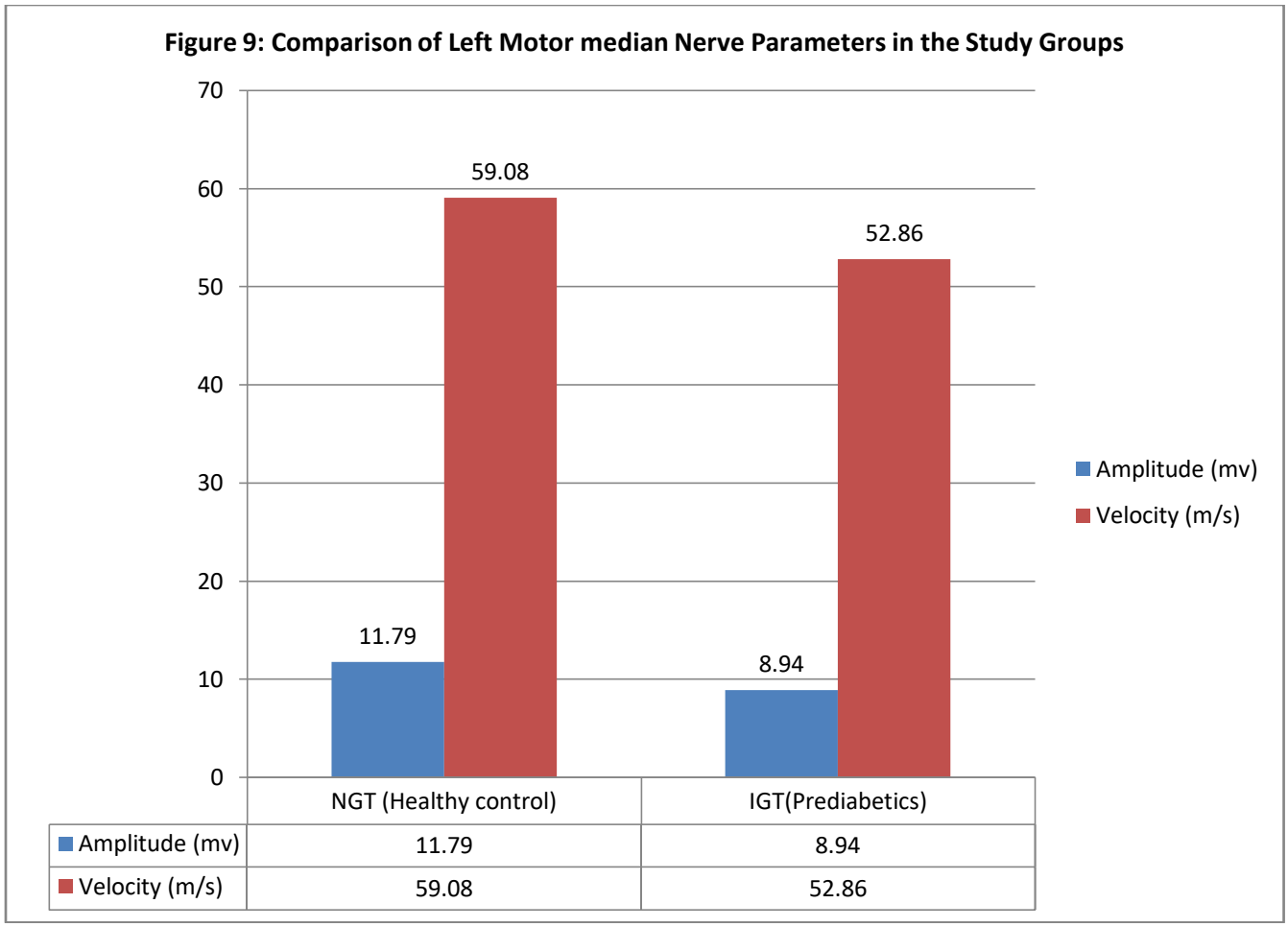
Comparison of Right Motor median (RMM) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT (Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (mv)	11.46	2.63	8.96	3.17	0.001
Velocity (m/s)	58.72	1.76	53.56	4.43	0.001



The table 4 and figure 8 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.001. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.928 and r value of amplitude is -0.731 which show negative association with HbA1c. This means that an increase in HbA1c would lead to decrease in nerve conduction parameters in prediabetic cases.

Table No. 5:- Comparison of Left Motor median Nerve Parameters in the Study Groups.

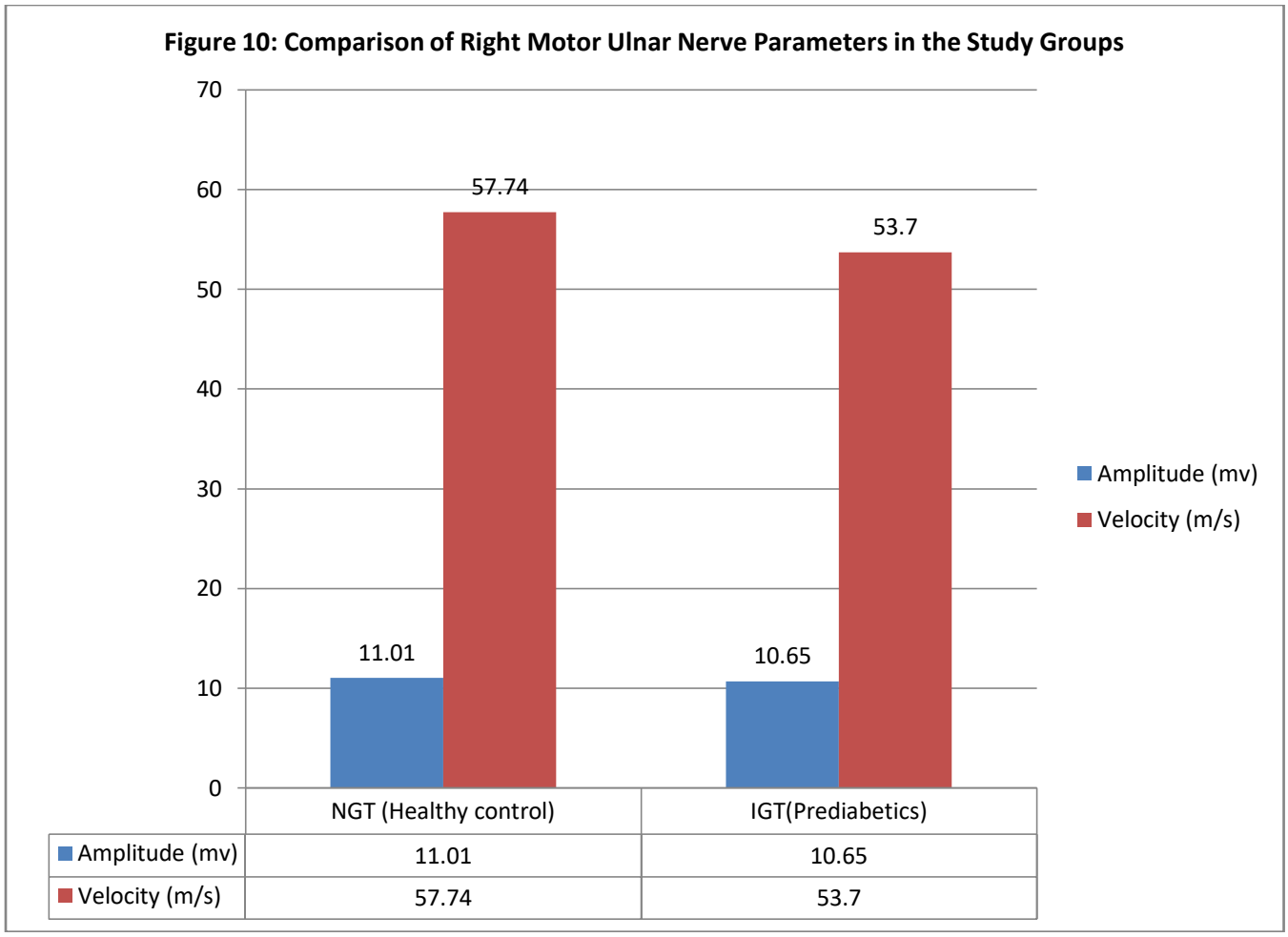
Comparison of Left Motor median (LMM) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT(Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (mv)	11.79	2.85	8.94	3.08	0.001
Velocity (m/s)	59.08	1.83	52.86	8.42	0.001



The table 5 and figure 9 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.001. There is significant difference in the mean NCV values between the healthy control and prediabetics group was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.492 and r value of amplitude is -0.664 which shows negative association with HbA1c. This means that an increase in HbA1c would lead to decrease in nerve conduction parameters in prediabetics cases.

Table No. 6:- Comparison of Right Motor Ulnar Nerve Parameters in the Study Groups.

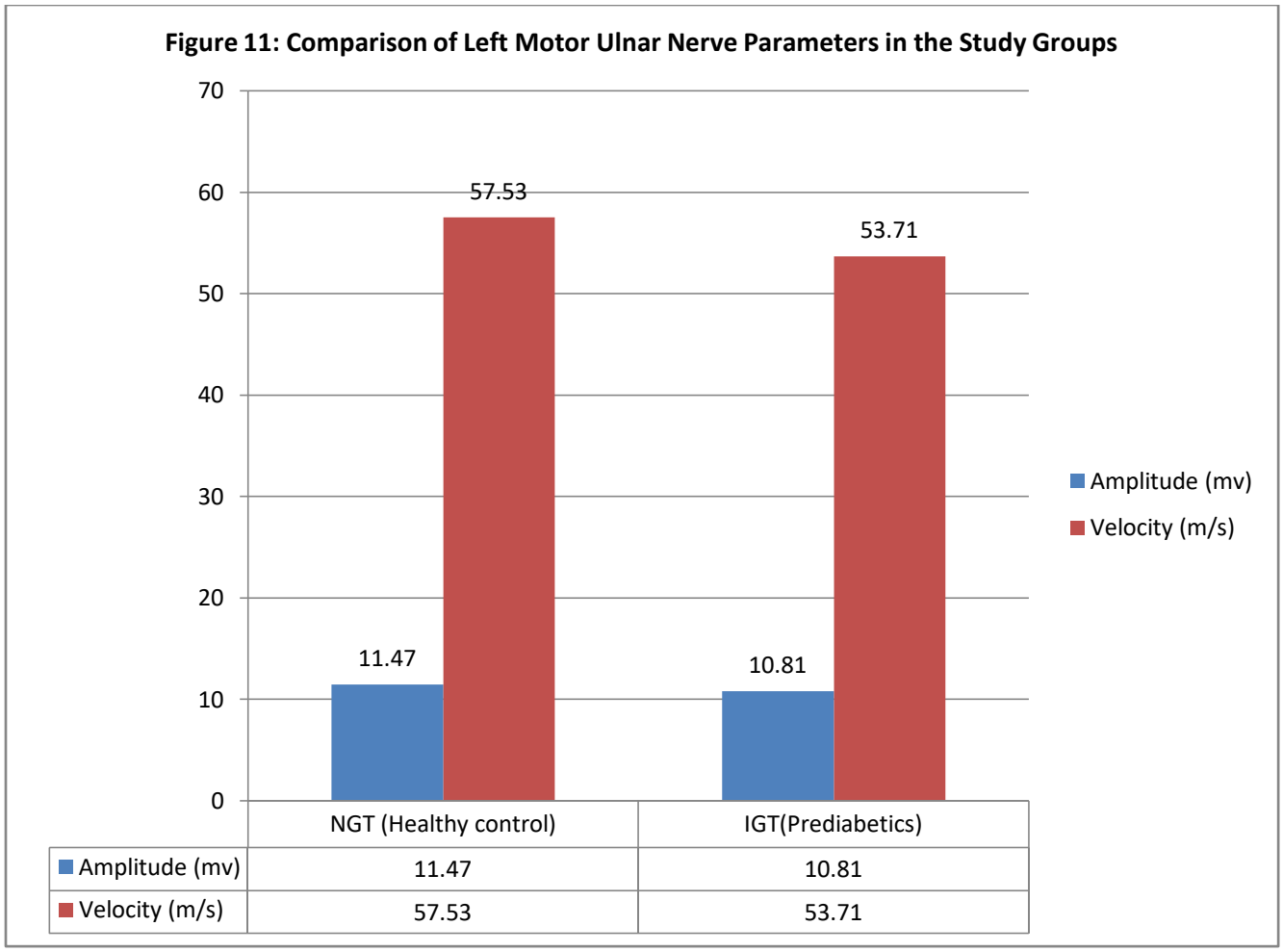
Comparison of Right Motor Ulnar (RMU) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT(Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (mv)	11.01	2.49	10.65	2.77	0.444
Velocity (m/s)	57.74	1.98	53.70	4.31	0.001



The table 6 and figure 10 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.444. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.838 and r value of amplitude is -0.670 which show negative association with HbA1c. This means that an increase in HbA1c would lead to decrease in nerve conduction parameters in prediabetic cases.

Table No. 7:- Comparison of Left Motor Ulnar Nerve Parameters in the Study Groups.

Comparison of Left Motor Ulnar (LMU) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT(Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (mv)	11.47	2.19	10.81	2.79	0.137
Velocity (m/s)	57.53	2.29	53.71	4.68	0.001

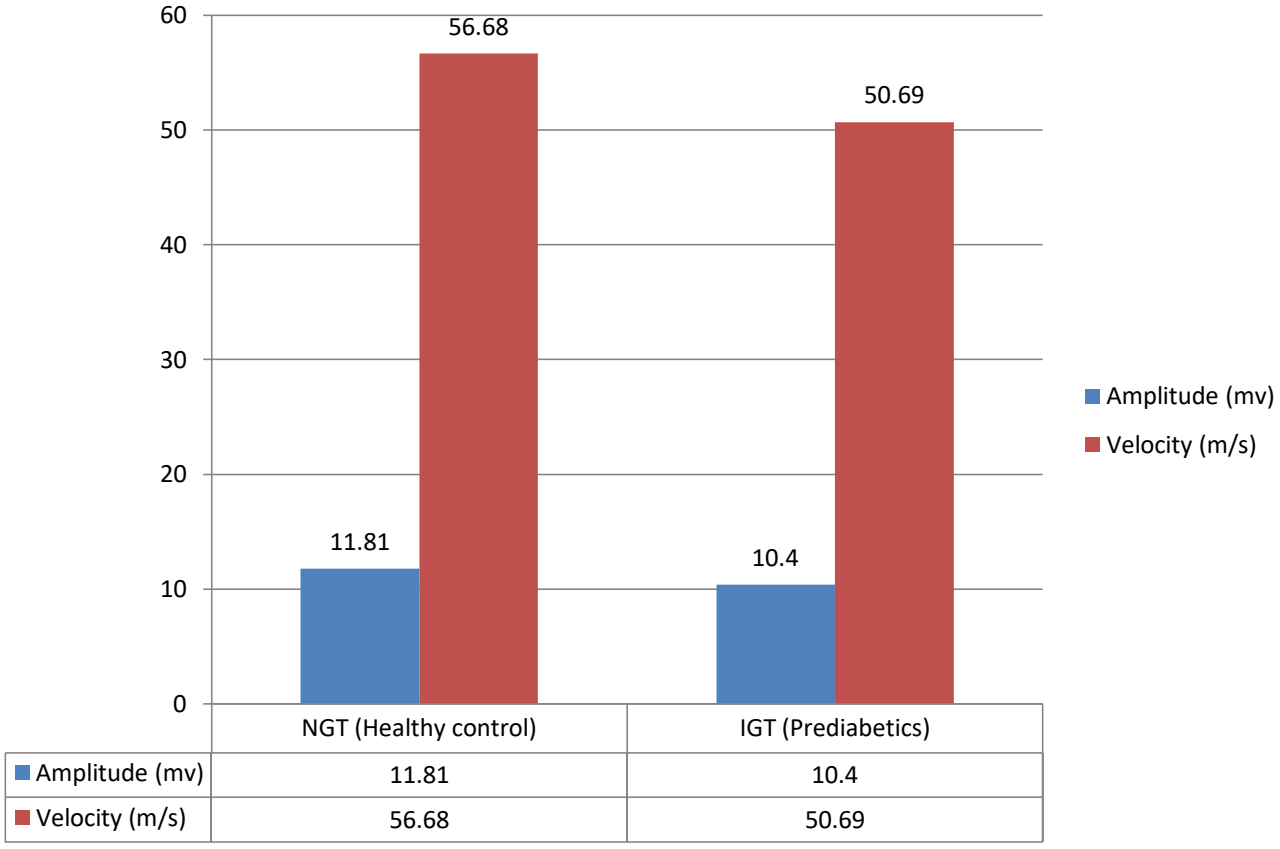


The table 7 and figure 11 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.137. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.863 and r value of amplitude is -0.572 which show negative association with HbA1c. This means that an increase in HbA1c would lead to decrease in nerve conduction parameters in prediabetic cases.

Table No. 8:- Comparison of Right Motor Tibial Nerve Parameters in the Study Groups.

Comparison of Right Motor Tibial (RMT) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT (Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (mv)	11.81	2.17	10.40	1.68	0.001
Velocity (m/s)	56.68	3.54	50.69	4.34	0.001

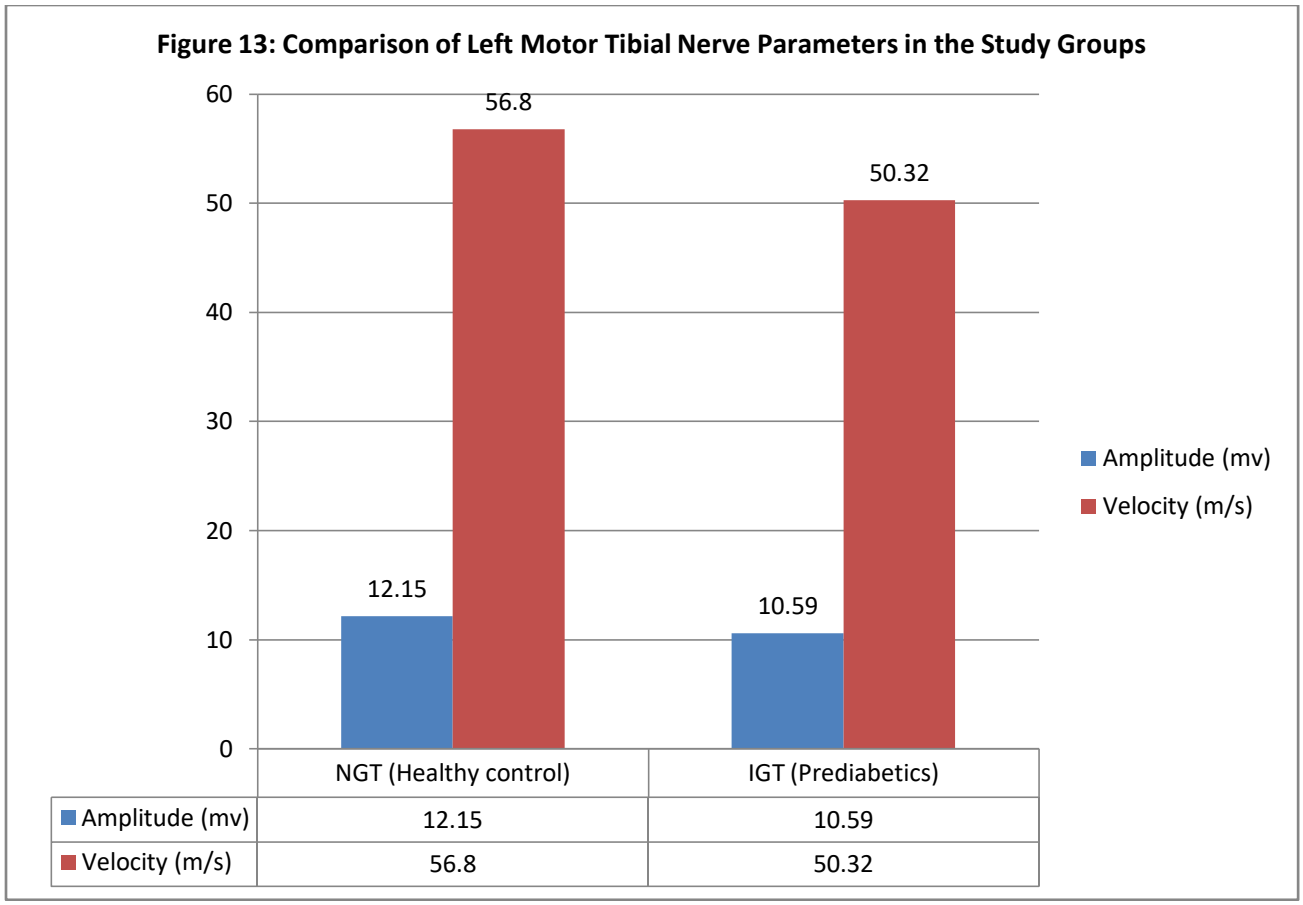
Figure 12: Comparison of Right Motor Tibial Nerve Parameters in the Study Groups



The table 8 and figure 12 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.001. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.692 and r value of amplitude is -0.428 which show negative association with HbA1c. This means that an increase in HbA1c would lead to decrease in nerve conduction parameters in prediabetic cases.

Table No. 9:- Comparison of Left Motor Tibial Nerve Parameters in the Study Groups.

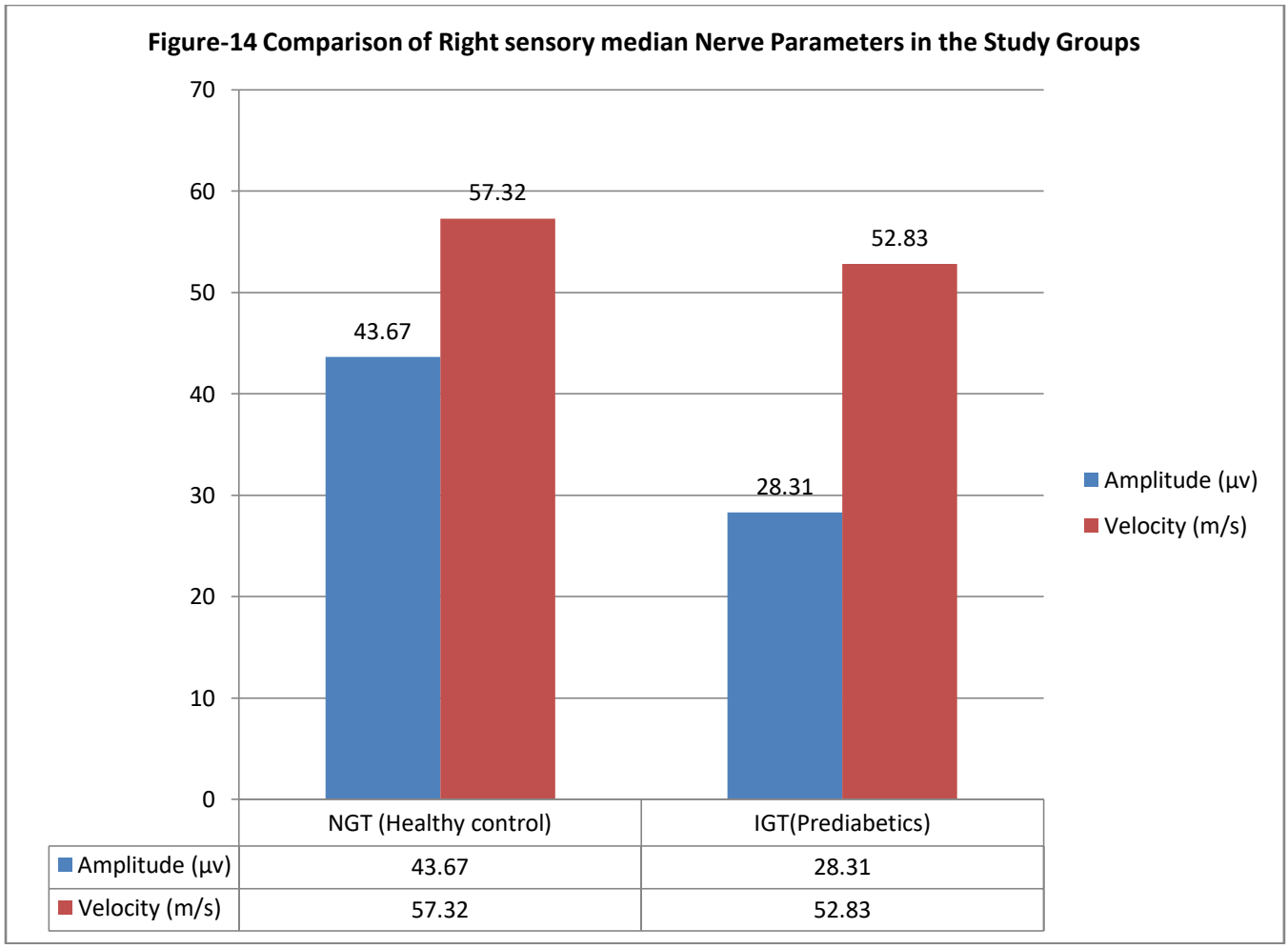
Comparison of Left Motor Tibial (LMT) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT (Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (mv)	12.15	1.85	10.59	1.81	0.001
Velocity (m/s)	56.80	3.80	50.32	4.57	0.001



The table 9 and figure 13 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.001. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.739 and r value of amplitude is -0.504 which shows negative association with HbA1c. This means that an increase in HbA1c would lead to decrease in nerve conduction parameters in prediabetic cases.

Table No. 10:- Comparison of Right sensory median Nerve Parameters in the Study Groups.

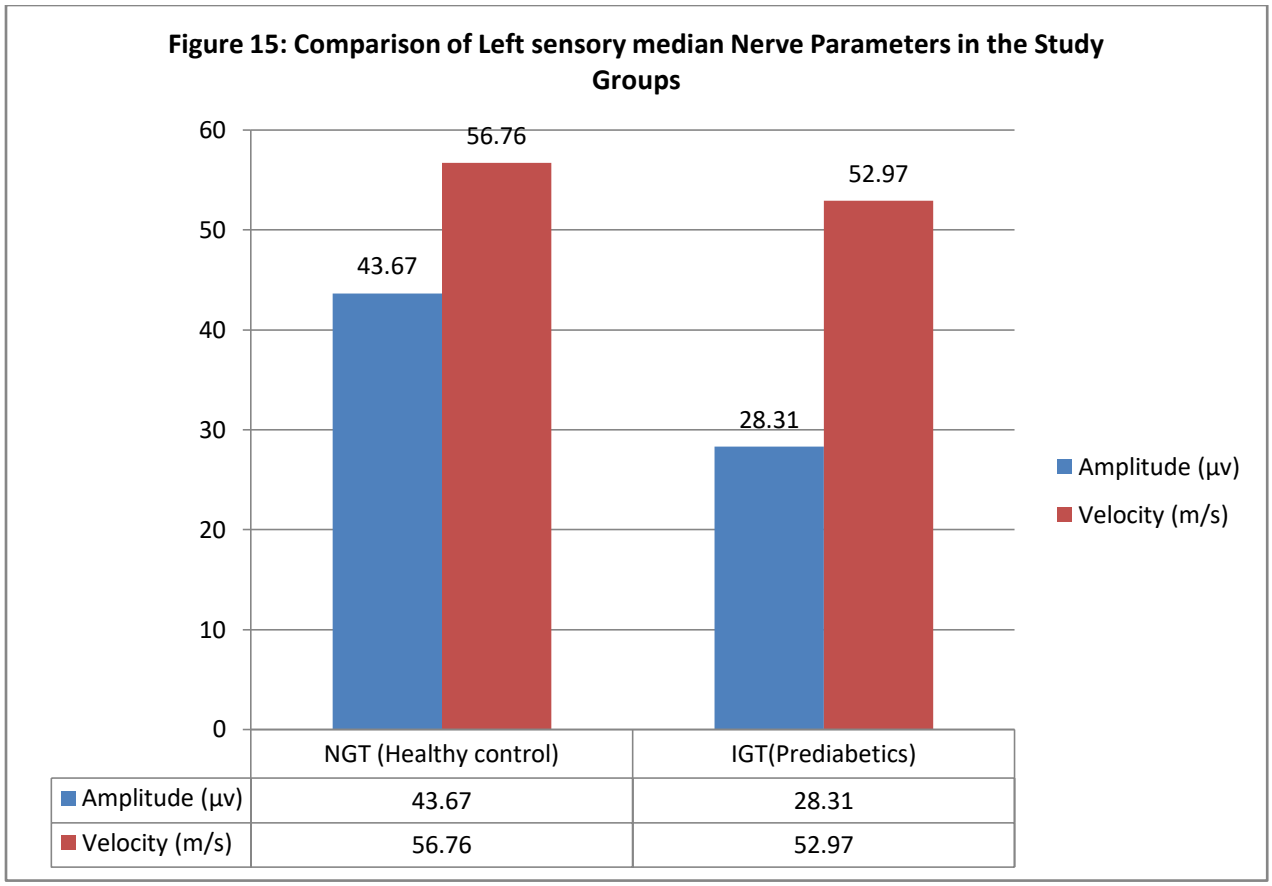
Comparison of Right sensory median (RSM) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT(Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (µv)	43.67	20.67	28.31	11.46	0.001
Velocity (m/s)	57.32	3.72	52.83	4.94	0.001



The table 10 and figure 14 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.001. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.796 and r value of amplitude is -0.588 which show negative association with HbA1c. This means that an increase in HbA1c would lead to a decrease in nerve conduction parameters in prediabetic cases.

Table No. 11:- Comparison of Left sensory median Nerve Parameters in the Study Groups.

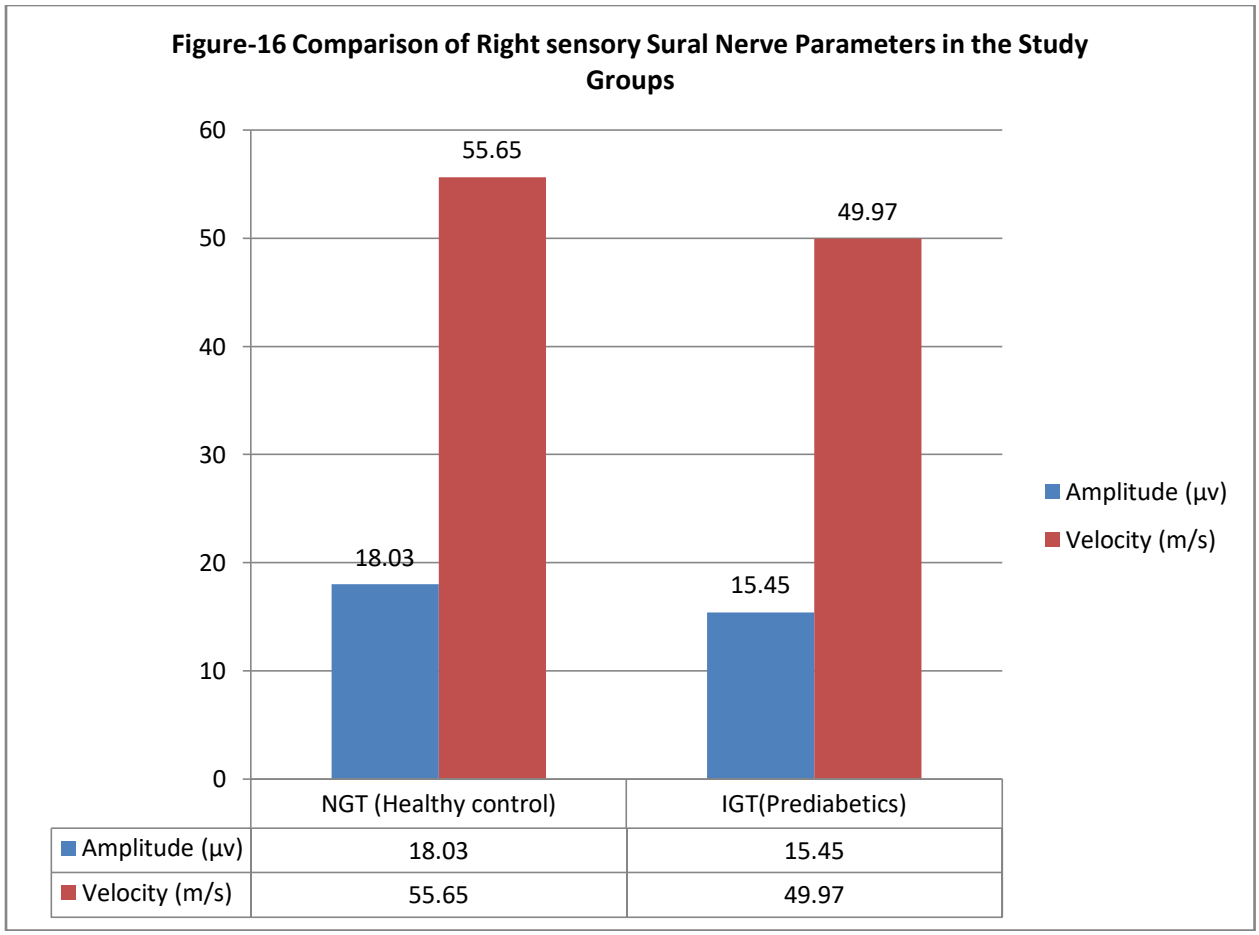
Comparison of Left sensory median (LSM) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT(Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (µv)	43.67	20.67	28.31	11.46	0.001
Velocity (m/s)	56.76	3.17	52.97	4.97	0.001



The table 11 and figure 15 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.001. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.729 and r value of amplitude is -0.667 which show negative association with HbA1c. This means that an increase in HbA1c would lead to a decrease in nerve conduction parameters in prediabetic cases.

Table No. 12:- Comparison of Right sensory Sural Nerve Parameters in the Study Groups.

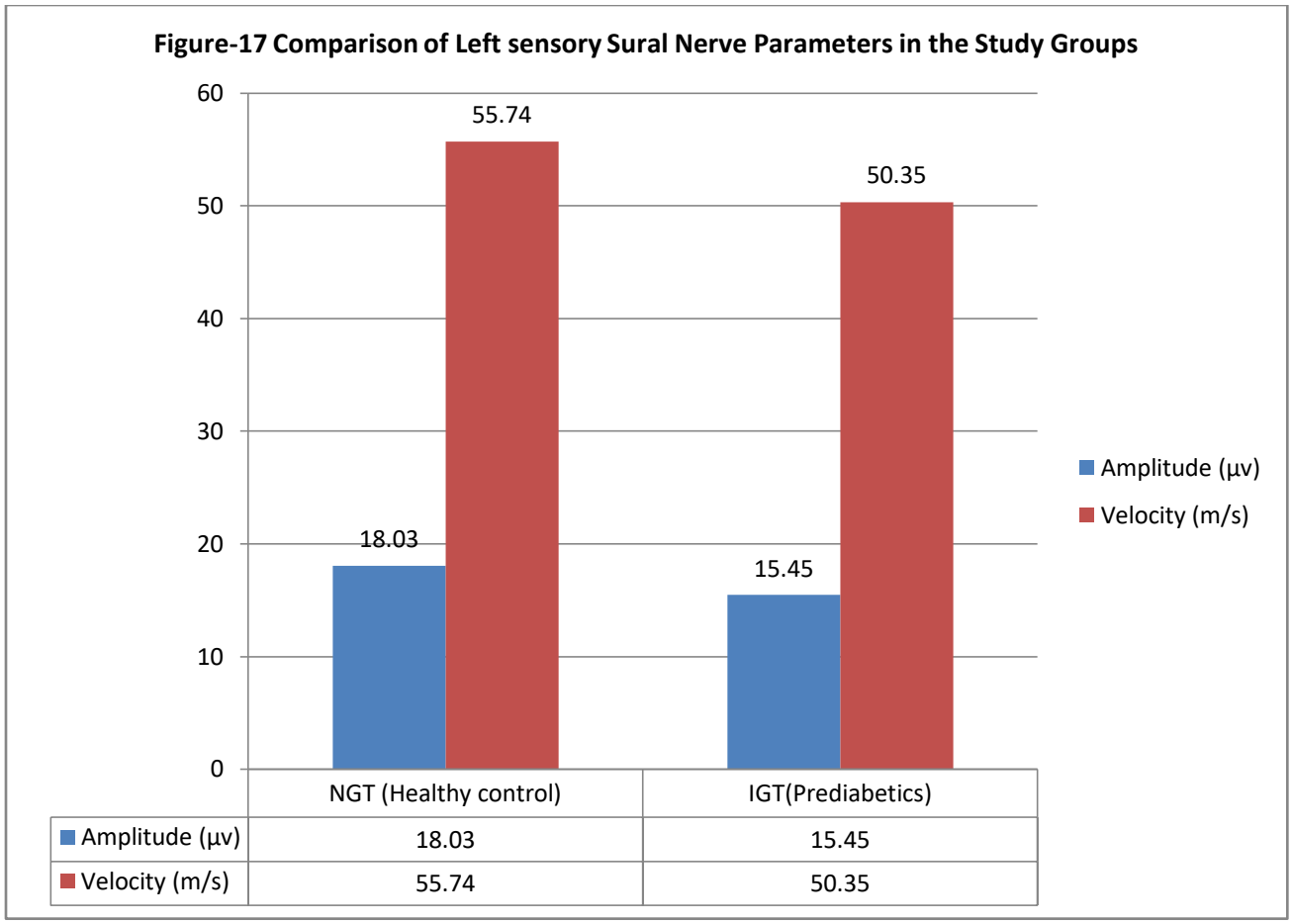
Comparison of Right sensory Sural (RSS) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT(Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (µv)	18.03	4.83	15.45	5.64	0.006
Velocity (m/s)	55.65	4.37	49.97	4.52	0.001



The table 12 and figure 16 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.006. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.517 and r value of amplitude is -0.522 which show negative association with HbA1c. This means that an increase in HbA1c would lead to decrease in nerve conduction parameters in prediabetic cases.

Table No. 13:- Comparison of Left sensory Sural Nerve Parameters in the Study Groups.

Comparison of Left sensory Sural (LSS) Nerve Parameters in the Study Groups					
	NGT (Healthy control)		IGT(Prediabetics)		
	Mean	SD	Mean	SD	p-value
Amplitude (µv)	18.03	4.83	15.45	5.64	0.005
Velocity (m/s)	55.74	3.58	50.35	4.66	0.001



The table 13 and figure 17 show that the mean HbA1c was significantly higher in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group (P<0.001). There was significant reduction in amplitude in prediabetics when compared with healthy control group with P value of 0.005. There is significant difference in the mean NCV values between the healthy control and prediabetics groups was noted with p value 0.001. The r value (Pearson correlation) of ncv is -0.512 and r value of amplitude is -0.617 which show negative association with HbA1c. This means that an increase in HbA1c would lead to decrease in nerve conduction parameters in prediabetic cases.

Discussion:-

In our study we recorded two nerve conduction parameters i.e. Velocity (NCV) and amplitude of all sensory and motor nerves using Allinger Scorpio Channel EMG-NCV machine with the help of surface electrodes and a stimulator. The nerve conduction parameters were evaluated for Median sensory (MS), Median Motor (MM), Ulnar Motor (UM), Tibial Motor (TM)and Sural Sensory (SS) nerves of both limbs. All study subjects underwent the nerve conduction studies in the department of Physiology. On comparing prediabetics with healthy individuals with various neuropathy parameters (nerve conduction velocity and amplitude), we observed a statistically significant reduced values in prediabetics and see inverse relationship (p<0.001) between HbA1c and nerve conduction study parameters in all the nerves. The mean HbA1c was significantly higher (P<0.001) in prediabetics (5.98 ± 0.23), when compared with the healthy control (5.27 ± 0.26), group.

The results of our study were in contrary to another study conducted on 50 subjects with prediabetes and 50 with normal glucose tolerance test. Median and ulnar nerves for both motor and sensory NCV along with sural and superficial peroneal nerves for sensory NCV were evaluated. There was no statistically significant difference between the two groups, for nerve conduction study parameters like amplitude, latency and nerve conduction velocity.[1]

Similarly, when other study compared 60 healthy subjects to 60 Pre-diabetics as a part of study and also observed that NCS of sural and tibial nerve is statistically nonsignificant.[6]

This is the findings of Eriksson et al, who showed that diabetes and not IGT was associated with peripheral nerve dysfunction.[10]

This is in accordance with the findings of Pour Hamidi K et al, whose extensive findings did not support the existence of neuropathy in a pre-diabetic stage.[11]

The results of our study were similar to another study conducted on 65 prediabetic cases with 65 control and found that the compound muscle action potential (CMAP) and nerve conduction velocity (NCV) of right tibial nerve were significantly reduced in the cases as compared to controls and were found to be statistically significant suggesting motor axonal neuropathy. The sensory nerve action potential (SNAP) and NCV of right sural nerve were significantly reduced in the cases as compared to controls which were find out to be statistically significant suggesting that cases had sensory axonal neuropathy.[4]

A study compared 50 prediabetic cases with control and found that the compound muscle action potential (CMAP) and nerve conduction velocity (NCV) were significantly reduced in the cases as compared to controls and were found to be statistically significant suggesting motor axonal neuropathy.[12]

One study observed that 50% prediabetic subjects had Impaired fasting glucose (IFG) of which 24.16% had significant nerve conduction abnormalities while 33.3% IGT patients had nerve conduction abnormalities.[7] Another study also found significantly affected NCV parameters in IGT patients. The inverse correlations between sensory and motor NCV with HbA1C were observed.[13]

Our study is also in accordance with study done by Viswanathan et al, who observed inverse correlation between sensory conduction velocity (SCV) and motor nerve conduction velocity (MCV) with HbA1c levels.[14]

Thus, the literature provides the contrasting results; some studies denoted clear cut significant changes in NCV tests in Prediabetics, other presented non-significant changes.Therefore, in the present study, we attempt to study the changes in nerve conduction study parameters in sensory and motor nerves in prediabetes patients in a tertiary care institute.

Thus, early diagnosis of abnormal nerve conduction study parameters, early intervention and prompt management at pre-diabetic before development of symptoms can prevents further complications. So, this study designed to fill the lacuna in the current knowledge and try to establish that prediabetes patients may have altered nerve conduction.

Limitation:
It is a hospital-based study and not society based. We completed this study only in one year and hence duration of the study was a limitation and so the individual subjects could not be followed up to assess the association between raised HbA1c and deterioration in nerve conduction study parameters.

Summary and Conclusion:-

The purpose of this study was to examine changes in nerve conduction parameters in individuals with early-stage glucose intolerance, or prediabetics. The current investigation was carried out in Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonipat. The study included 130 people in total, 65 of whom were prediabetics and 65 of whom were healthy individuals. A study on nerve conduction was conducted on the motor median, motor ulnar, motor tibial, sensory median and sural nerves. A1c was calculated. When comparing the prediabetic group to the healthy individuals, the prediabetic group's mean NCV and Amplitude level was significantly lower (p 0.001).

In addition, there was a significant difference (p 0.001) in the mean HbA1c between the prediabetic and healthy individuals groups and shows negative correlation with NCS parameters in prediabetics. The results of the investigation support the known hypothesis that NCV and Amplitude values in prediabetics participants are aberrant. prediabetic sufferers' slower mean NCS parameters suggests that these individuals should be screened for issues as soon as possible. The notion that prediabetic represents a pre-diabetic transitory state and the significance of nerve

conduction studies for early neuropathy identification were further bolstered by this work. By diagnosing it early in the course of prediabetes, morbidity and mortality secondary to neuropathy can be prevented. It may assist the physicians in early detection of nerve damage and to start timely intervention, if required to prevent further complications. So, it is suggested that nerve conduction study should be inducted in routine investigations of prediabetic cases for early diagnosis of cognitive decline.

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