Original Article

Effects of the Six Months of Programmed Exercise Therapy on Cardio-respiratory Endurance and Neurophysiological Variables in Asymptomatic Young Adults Diagnosed Newly With Type 2 Diabetes Mellitus – A Randomized Controlled Trial

Harpreet Kour*1, V. A. Kothiwale2 and Shivaprasad S. Goudar1

Departments of Physiology1 and Medicine2,
KAHER’s J.N. Medical College,
Belagavi

Abstract

Introduction: In the 21st Century, a large proportion of India’s population belongs to the younger age group that’s why called Young India. Before being diagnosed as diabetic, the individual goes through the pre-diabetic period or impaired glucose tolerance phase for almost 4-5 years which includes acute episodes of hyperglycemia and hypoglycemia. These acute episodes may lead to micro-vascular diseases resulting in deficits in cardiorespiratory endurance and neurophysiological variables. Targeting young Type 2 Diabetes Mellitus (T2DM) patients with exercise therapy may delay the onset and complications and provide them with a better quality of life. Therefore, the present study has assessed, in a randomized manner, the impact of exercise therapy on cardiorespiratory endurance and neurophysiological functions in young adults of age group 20-45 years with T2DM.

Objectives: To study the effects of six months structured exercise therapy on cardiorespiratory endurance and neurophysiological variables in young adults of age 20-45 years with newly diagnosed T2DM on dietary control and anti-diabetic drug of age group

Material & Methods: The study was conducted in the Research Laboratory, Department of Physiology on newly diagnosed asymptomatic patients with type 2 diabetes mellitus of age group 20-45 years. Study participants were recruited from the OPD, Department of Medicine, KLE’s Dr. Prabhakar Kore Hospital and Research Centre. Recruitment started from the period of April 2017 ended in October 2018 Ethical approval was obtained from the institutional ethical committee. Written Informed consent was obtained from all participants. The patients were enrolled as per inclusion criteria and then randomly divided into diabetic controls and Interventional group. The interventional group was given six months of structured exercise program consisting of aerobic and resistance exercises. The primary study variables were Cardio-respiratory Endurance variables viz; Physical Fitness Index (PFI) and Maximal oxygen uptake (VO2 maximum) and Neuro-Physiological Variables viz; Nerve Conduction Velocity (NCV) and Audio-Visual Reaction Time (ART and VRT). The data were collected at baseline and 6th months for both groups and 2nd, 4th month for the interventional group.

*Corresponding author :
Dr. Harpreet Kour, Assistant Professor, Department of Physiology, J.N. Medical College, KLE Academy of Higher Education and Research, Nehru Nagar, Belagavi, Karnataka – 590 010 (India); E-mail : harpreet.kour@yahoo.co.in
(Received on Aug. 10, 2019)
Introduction

Type 2 Diabetes mellitus (T2DM) is a diverse group of disorders related to inappropriate metabolism of carbohydrate, fats, and protein causing either impaired insulin secretion or impaired action of insulin on target tissues and finally resulting in chronic hyperglycemia (1). Various studies reported an increased prevalence of type 2 diabetes mellitus is due to rapid urbanization, physical inactivity, more junk food consumption, sedentary lifestyle, obesity, etc. and documented it as lifestyle disorder (2-3). The trend of increasing prevalence is seen evidently from the last two decades accounting for almost one-third of all new cases of diabetes diagnosed in young adults (4). Diabetes can have catastrophic effects on all the systems of the body including macro and microvascular complications and results in increased morbidity and mortality.

The battery of papers have documented decreased cardiorespiratory fitness among the diabetic population and included it as one among the main independent determinants of mortality in diabetic patients (5-6). The studies have also reported decreased maximal oxygen uptake among patients when compared with healthy individuals. The lack of physical activity and sedentary lifestyles in the young generation has been a matter of concern in recent days. Physical fitness index (PFI) and Maximal oxygen uptake (VO2 maximum) are important criteria to assess the cardiopulmonary endurance of an individual (7-8).

Diabetic neuropathies are also one among commonly seen microvascular complications of diabetes accounting for 28% among all other complications of diabetes mellitus.

The diabetic neuropathies are silent killers due to slow progression and asymptomatic stage for a long quiescent period. Bansal et al have reported the decrease in nerve conduction velocity to indicate damage of myelin sheaths (9-10). Few studies have also reported an association between glycated hemoglobin and nerve conduction velocity as they found decreases in nerve conduction velocity with the increasing levels of glycated hemoglobin (10). Nerve conduction study (NCS) is considered as the gold standard for measurement of diabetic neuropathy. Along with this, the function of sensory and motor association of individual performance is measured by reaction time. The best tool to measure sensory-motor association is auditory reaction time and visual. The studies have reported altered auditory and visual reaction time in patients with type 2 diabetes mellitus (11-12).

It has been reported that complications of type 2 diabetes mellitus can be prevented by maintaining normal blood glucose through diet, exercise, or medication. Recently result of a randomized controlled trial established that aerobic exercise

Results: The median physical fitness index of subjects in the control group was 48.84 (IQR 40.11 to 54.55), and in the intervention group it was 69.59 (IQR 64.52 to 74.38) at the end of 6 months following the intervention. (p-value <0.001). The mean VO2 maximum of subjects in the diabetic control group was 30.76±5.42, and in the intervention group, it was 39.16±4.59, at the end of 6 months post-intervention. (p-value <0.001). Out of the neurophysiological parameters, Auditory Reaction Time had shown no statistically significant difference between the two groups at 6 months follow up period. Median Visual reaction time was significantly lower (200 Vs 234, p-value <0.001) in the intervention group, as compared to the diabetic control group. Nerve conduction velocity was significantly higher (49 vs 48, p-value 0.004) in the intervention group, as compared to the diabetic control group at 6 months post-intervention.

Conclusion: The exercise program implemented in the current study is simple, scientific, inexpensive, and is amenable for large scale adaptation in a wide variety of settings, ranging from primary to tertiary level care facilities.
improves physical fitness, glycemic control, and insulin sensitivity in people with diabetes (13-14).

A large proportion of India’s population belongs to the younger age group. Before being diagnosed as diabetic, the person goes through the pre-diabetic period or impaired glucose tolerance phase which includes acute episodes of hyperglycemia and hypoglycemia. These acute episodes may lead to microvascular diseases, resulting in deficits in cardiorespiratory endurance and neurophysiological variables. Targeting young type 2 diabetic patients with exercise therapy may delay the onset and complications and provide them with a better quality of life. Therefore, the present study has assessed, in a randomized manner, the impact of exercise therapy on cardiorespiratory endurance and neurophysiological functions in young adults of age group 20-45 years with T2DM.

It is hypothesized that exercise therapy along with dietary control and anti-diabetic medication will have a positive influence on cardiorespiratory endurance and neurophysiological functions compared to counseling for exercise, diet control and anti-diabetic agents.

Objectives of the study:

Primary:

To study the effects of six months structured exercise therapy on cardiorespiratory endurance and neurophysiological variables in young adults of age group 20-45 years with newly diagnosed T2DM on dietary control and anti-diabetic drug.

Secondary:

To study the effects of six months structured exercise therapy on glycated Hemoglobin (HbA1C) in young adults of age group 20-45 years with newly diagnosed T2DM on dietary control and anti-diabetic drug.

Material and Methods

The study was undertaken by the Department of Physiology in Research Laboratory, on newly diagnosed asymptomatic patients with type 2 diabetes mellitus of age group 20-45 years. The patients were recruited from OPD, Department of Medicine, KLE’s Dr. Prabhakar Kore Hospital and Research Centre. The recruitment started from April 2017 and ended in October 2018. The study was started after obtaining approval from the Institutional Ethical Committee. Informed consent was obtained from patients before the start of the study.

Inclusion Criteria:

Newly diagnosed T2DM clinically asymptomatic patients aged 20–45 years in whom the duration of diabetes was less than one year (ADA Guidelines) treated with only diet and oral anti-diabetics.

Exclusion Criteria:

Subject with history of Diabetes more than a year or Type 1 DM or having known vascular complication of diabetes, such as coronary artery disease, stroke, nephropathy, retinopathy, and polyneuropathy, other chronic diseases restricting physical activity or with prior regimen of physical exercise and alcoholics or smokers.

Sample Size:

The patients aged 20-45 years who were eligible as per the inclusion criteria were enrolled. Sex, age and education level matched healthy individuals were taken into study as normal controls. The sample size was calculated by using below mentioned formula

$$\frac{(Z_{1-\alpha} + Z_{1-\beta})^2 (SD_1^2 + SD_2^2)}{(X_1 - X_2)^2}$$

Where, $Z_{1-\alpha} = \text{at } 95\%, \text{ Confidence Interval } = 1.96$, $Z_{1-\beta} = \text{at } 80\%, \text{ Power of the test } = 1.64$, Mean and SD from review of literature for study and control groups were taken : 29.3±0.84 and 28.7±1.69, $X_1 - X_2 = \text{Expected impact size } n = (1.64±1.96)^2 \cdot \frac{(0.8426152^2 + 1.6970562^2)}{(29.3 - 28.7)^2} = 130$, Accounting drop out cases as 10%, then the calculated sample size was $132/0.9 = 144.4$ - rounded to 146.
Study Design and Groups:

An Interventional randomized controlled trial. A total of 148 patients got enrolled in the study. Patients were randomly divided into Diabetic control group (DC; n=74) and Interventional Group (IG; n=74) by computer-generated, randomized number sequence placed in Opaque Sealed Envelopes. Sex and age matched healthy normal subjects (NC; n=74) were also enrolled in the study to compare the various variables at baseline. Diabetic controls were only on dietary control and anti-diabetic medication whereas patients in Interventional Group were on structured exercise therapy along with dietary control and anti-diabetic medication.

Initially, the normal controls were compared with enrolled diabetics at Baseline. Then the randomization was done for the diabetic population. Both Diabetic and Interventional group were evaluated at the end of six months. The interventional group was also evaluated at the end of 2nd and 4th month to see the timeline changes in study variables.

Programmed exercise Therapy:

The interventional therapy consists of six months of the individually designed exercise program of regular exercise consisting of aerobic and resistance exercises. The first 2 weeks of the regimen was consisting of supervised exercise training in Research Laboratory, Department of Physiology, J.N. Medical College, and Belgaum. Later on, the participants were advised to continue the exercise at their home regularly. The aerobic exercise is 30 min of activity 5 days/week, with no gap of more than 2 consecutive days without physical activity. Resistance exercise performed 3 times a week targeting all major muscle groups, progress to 3 sets of 8-10 repetitions at a weight that can’t be lifted more than 8-10 times. (Dumbbell flies, seated single leg extension, dumbbell shoulder press, dumbbell bent-over row, standing leg curls, dumbbell biceps curls, dumbbell upright row, dumbbell triceps kickbacks, and abdominal curls.) All the patients were provided with detailed instruction booklets describing each resistance training exercise and appropriate equipment (dumbbells) to perform resistance training (15).

Outcome Variables:

Primary: Cardio-respiratory Endurance variables viz; Physical Fitness Index (PFI) and Maximal oxygen uptake (VO2 maximum) and Neuro-Physiological Variables viz; Nerve Conduction Velocity (NCV) and Audio-Visual Reaction Time (ART and VRT)

Secondary: Glycated Hemoglobin (HbA1c)

Parameters assessed:

1. Age in years and Gender was noted.

2. Glycated Hemoglobin: HbA1c: was measured using a commercially available test kit according to the manufacturer’s recommendations with a laboratory method (Ion Exchange Resin method) using a semi-auto analyzer.

3. Physical Fitness Index (PFI): A platform of 20 inches height comprised of two steps i.e stepping up & down a step along with a metronome producing one beat every 2 seconds at a rate of 30 per minute was used. The subjects were asked to step up and down on the platform at a rate of 30 steps per minute for 5 minutes or until exhaustion. The total number of heartbeats was counted between 1 to 1.5 minutes after completing the task. Total test time in seconds for completing the task was noted. The Physical Index score was determined by the following equation (16):

\[
\text{Physical Fitness Index (PFI)} = \frac{100 \times \text{test duration in seconds}}{1.5 \times \text{pulse count between 1 and 1.5 minutes}}
\]

4. VO2 maximum: This test was done on a bicycle ergometer manufactured by Anand Agencies, Pune. The pulse rate was noted with the fingertip pulse oximeter manufactured by Nureca Inc. USA. After recording the resting pulse rate the subject was asked to do a warm-up ride without any load for 1-2 minutes. The subject was then asked to pedal the bicycle at a constant speed of 50 revolutions per minute with a load of 2 kgs. At the end of every minute pulse rate was noted. The subject was then asked to continue the work
for a minimum of 6 minutes. If the subject was able to perform this exercise, then the load was gradually increased by half kg and so on. The steady pulse rate which is achieved at 5th and 6th minutes were noted. If the pulse rate was differed by more than 5 beats/min at the end of 5th and 6th min, then the test was prolonged for 1-2 min until a steady state was achieved. The average of the last 2 min was designated as the maximum heart rate at that load. The VO2 maximum (maximum oxygen uptake) was calculated by using Astrand Nomogram. Correction of the age factor was done according to the table and multiplied by VO2 maximum score which gives the value of VO2max (L/min) (17).

\[
\text{VO2max (L/min)} \times 1000 = \frac{\text{VO2max (ml/min/kg)}}{\text{Body wt}}
\]

5. Nerve Conduction Velocity: Motor Nerve Conduction Velocity (MNCV) was assessed with the help of computerized equipment called “BIOPAC MP150” by using the traditional double stimulation technique. The subject was asked to sit on a wooden chair by keeping the dominant hand over the wooden table. The stimulating electrodes were placed at 5 cm below the medial epicondyle and at 5 cm above the medial epicondyle and the recording electrodes were placed over the abductor digiti minimi (ADM) muscle on the ulnar side of the hand i.e between the fifth metacarpophalangeal joint and the pisiform bone (18).

6. Audio-Visual Reaction time was done using click stimulus for auditory and red light stimulus for visual reaction time by using an audio-visual reaction time analyzer. (Anand Agency, Pune). The instrument has a built-in 4 digit chronoscope with a display accuracy of 1 milisecond. It features four stimuli, two response keys, and a ready signal. The time taken to respond to the stimulus was noted in msec. The player was asked to place his hands on the box in such a way that his thumbs rested on the response buttons. He was asked to respond to a given stimulus as soon as possible. The time required for the response was noted down. The mean of three trials was calculated for analysis (19).

Statistical Analysis:

The results are expressed as Mean±SD. Comparison was made between groups by unpaired ‘t’ test. The change in the quantitative parameters, before and after the intervention was assessed by paired t-test (In case of two periods) or one-way repeated measures ANOVA (In case of comparison across more than 2 time periods). One-way repeated measures ANOVA was used to assess the statistical significance of differences in the normally distributed quantitative variables, measured within the intervention group, at different periods. McNemar test was used to assess the statistical significance of the paired differences in categorical variables, within the intervention group, from baseline to different follow-up periods. P-value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

Results

Age and gender were comparable between normal controls and the diabetic population in the study, with no statistically significant difference.

There was statistically significant difference in Physical Fitness Index and VO2 maximum between normal controls and diabetic population (P-value <0.001). Diabetics had comparatively decreased nerve conduction velocity and visual reaction time as compared to normal controls (p<0.001). No significant difference was observed in auditory reaction time

| TABLE I: Comparison of baseline socio-demographic parameters between the study groups. |
|-----------------------------------------|---------------------------------|-----------------|--------|
| Parameter | Normal control | Combined diabetic population | p-value |
| Age (mean±SD) | 37.55±4.29 | 37.2±4.09 | 0.554 |
| Gender | | | |
| Male | 47 (63.51%) | 82 (55.40%) | 0.248 |
| Female | 27 (36.48%) | 66 (44.59%) | |
TABLE II: Comparison of study variables between Normal controls and combined Diabetic population at Baseline.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal control (N=74)</th>
<th>Diabetic population (N=148)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardio Respiratory Endurance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Fitness Index (Median IQR)</td>
<td>91.56 (80.23, 109.09)</td>
<td>49.59 (40.11, 54.55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VO2 maximum (ml/kg/min.)</td>
<td>59.12±5.52</td>
<td>30.53±5.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Neurophysiological</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auditory Reaction Time (msecs.)</td>
<td>192 (180, 198)</td>
<td>180 (176, 197)</td>
<td>0.004</td>
</tr>
<tr>
<td>Visual Reaction Time (msecs.)</td>
<td>192 (184, 200)</td>
<td>234 (210, 245)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nerve Conduction Velocity (m/sec.)</td>
<td>54 (49, 57)</td>
<td>46 (45, 48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Biochemical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>4.95±0.41</td>
<td>5.95±0.47</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

among two groups. The mean values of HbA1C% were significantly higher in diabetic patients in comparison to normal controls (p<0.001) (Table II).

TABLE III: Comparison of study variables after randomization between Diabetic Control Group and Intervention Group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diabetic control group (DC) (N=74)</th>
<th>Intervention group (N=74)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardio Respiratory Endurance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Fitness Index (Median IQR)</td>
<td>50.51 (40.11, 54.79)</td>
<td>48.85 (40.11, 54.55)</td>
<td>0.296</td>
</tr>
<tr>
<td>VO2 maximum (ml/kg/min.)</td>
<td>30.87±6.24</td>
<td>30.19±5.25</td>
<td>0.480</td>
</tr>
<tr>
<td><strong>Neurophysiological</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auditory Reaction Time (msecs.)</td>
<td>180 (176, 197.25)</td>
<td>224 (198, 243)</td>
<td>0.795</td>
</tr>
<tr>
<td>Visual Reaction Time (msecs.)</td>
<td>180 (176, 197)</td>
<td>235 (212.75, 249)</td>
<td>0.009</td>
</tr>
<tr>
<td>Nerve Conduction Velocity (m/sec.)</td>
<td>46 (45, 48)</td>
<td>47 (46, 49)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Biochemical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c %</td>
<td>5.93±0.46</td>
<td>5.97±0.48</td>
<td>0.542</td>
</tr>
</tbody>
</table>

No significant difference was found among two groups after randomization. This suggests that the two groups were comparable (Table III).
TABLE IV: Comparison of study variables between diabetes control group and intervention group at end of 6th months of Intervention Therapy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Diabetic control at the end of 6th month (DC)</th>
<th>Intervention group at the end of 6th month</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardio Respiratory Endurance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Fitness Index (Median IQR)</td>
<td>48.85 (40.11, 54.55)</td>
<td>68.97 (62.7, 73.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VO2 maximum (ml/kg/min.)</td>
<td>30.72±5.19</td>
<td>38.45±4.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Neurophysiological</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Auditory Reaction Time (msecs.)</td>
<td>180 (176, 196.25)</td>
<td>186 (180, 190)</td>
<td>0.355</td>
</tr>
<tr>
<td>Visual Reaction Time (msecs.)</td>
<td>234.5 (212, 249)</td>
<td>197 (192, 200)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nerve Conduction Velocity (m/sec.)</td>
<td>48 (46, 49)</td>
<td>49 (47, 51)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Biochemical</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c %</td>
<td>5.86±0.37</td>
<td>5.14±0.36</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Cardio-respiratory endurance parameters have shown statistically significant improvement at the end of six months of interventional therapy in patients with T2DM. Visual reaction time Nerve conduction velocity and glycated hemoglobin levels were also improved in interventional group as compared to the diabetic control group at the end of six months with intervention therapy (Table IV).

One-way repeated measures ANOVA was used to compute the statistical significance of differences in normally distributed quantitative variables at different follow up periods.

**Discussion**

The study population consisted of adult subjects aged 20-45 years newly diagnosed with T2DM. It is the most ubiquitous metabolic disorder and is one of the major health and socioeconomic problems globally. As the onset of diabetes mellitus is subtle, usually it remains undiagnosed in early conditions for almost 3-5 years. The nominal changes accountable for decreased cardio-respiratory endurance and microvascular complications are already present at the time of diagnosis of disease.

Cardio-respiratory endurance tests represent an important clinical tool to evaluate cardiorespiratory fitness and to predict future adverse cardiovascular events. Physical Fitness Index (PFI) and VO2 maximum are important criteria to assess the cardiopulmonary efficiency of subjects (18-20). Leila Jaafari et al. had done a study of anthropometric measures focusing on health indices and physical fitness and concluded that there was a significant negative association between most of the health-related anthropometric measures and physical fitness factors (21).

In the present study, it is observed that physical fitness index and VO2 maximum are decreased...
significantly in young adults freshly diagnosed with T2DM. At the end of six months of interventional therapy, significant improvement was observed in values of physical fitness index and VO2 maximum. Several studies have reported the correlation between insulin resistance and low cardio-respiratory fitness in non-diabetic patients. They have also suggested that the VO2 max can be considered as an early marker of insulin resistance. Earlier studies have also reported 20% lower cardiorespiratory fitness (VO2 maximum) in diabetics, as compared to normal age and sex-matched controls (22-24). The study by Kaplan et al has reported the role of insulin in the regulation of mitochondrial anion transporter during the Krebs cycle. A decrease in the number of mitochondria which is determined genetically, interprets the altered consumption of glucose and oxygen. This may lead to a negative impact on an individual's ability to achieve fitness level and thus have low VO2 maximum (25).

Many previous studies have reported similar findings, even though there were differences in the nature and intensity of exercise programs implemented. Few studies have explored the additional impact of the nature of diet on physical fitness. A review by Byrne H., et al. had concluded that self-directed exercise to be beneficial for improving cardiorespiratory fitness and functional parameters, in addition to various metabolic outcomes among type 2 diabetic patients (26). Kwon H. R., et al., in their study have compared the aerobic and resistance training program on various aspects, including aerobic capacity among women with Type 2 Diabetes mellitus. The average age of participants was about 57.0±6.8 years (27).

Mendes, R., et al. in their single group before-after evaluation study have assessed the impact of community-based supervised exercise program (Combination of aerobic, resistance, agility/balance with flexibility exercises), which was delivered as three, 70 minute sessions per week over 9 months period. The study had observed significant improvements 6-Minute Walk Test (8.20%), 30-Second Chair Stand Test (28.84%), Timed Up and Go Test (14.31%), and Chair Sit and Reach Test (102.90%) post-intervention (28). Larose, J., et al in their study have compared the impact of aerobic (A), resistant (R) and combined (C) on VO2 peak, workload, and treadmill time among type 2 diabetes patients. The comparison was also made between younger (39-54 years) and older (55-70 years) adults and both genders. As per the study VO2 peak had shown improvement by 1.73 and 1.93 units with A and A + R, respectively, as compared to C. There was no main effect of age or sex on training performance outcomes. A tendency for better improvement with combined exercise was observed in older adults (29). Taylor, J. D., et al. in their RCT had compared the physical therapist-directed exercise counseling and fitness center-based exercise training (experimental group) with laboratory-based, supervised exercise (comparison group). The authors could not find any significant difference in the improvement in exercise capacity between the two groups (30).

From the above discussion, it can be concluded that aerobic exercise training, whether delivered in a laboratory setting, through physical fitness center or self-directed can have a positive impact of physical fitness and exercise capacity of type II diabetic patients. The type of diet and age etc. can have a significant effect modification; hence have to be kept in consideration, while planning a structured exercise program.

Diabetic neuropathy is one of the protracted complications of Diabetes mellitus which develops early in the course of the disease and remains asymptomatic for years together and tends to deteriorate over time. Measurement of nerve conduction velocity is widely used for the assessment of diabetic neuropathy (31-32).

In the present study, there was a significant decrease in ulnar nerve motor conduction velocity in T2DM patient with no clinical features of neuropathy as compared to healthy controls. Among normal controls, the median nerve conduction velocity was 54 (IQR 49, 57) and it was 46 (IQR 45, 48) in the Diabetic control group (P-value <0.001). There was significant improvement observed in the nerve conduction velocity after the administration of structured exercise therapy. The study by Bertsman supported our findings and reported patients having...
the decline of motor nerve function in fairly controlled T2DM (33).

Our results are also consistent with earlier studies which showed that 18.1% of asymptomatic diabetic patients have median mononeuropathy without any evidence of polyneuropathy. They have also reported a decrease in conduction velocity in diabetes as compared to normal healthy controls. Few studies have reported that a decrease in nerve conduction velocity might be due to de-myelinating nature of diabetes mellitus and its abnormalities occurs sub clinically, hence patients remain asymptomatic (34-35).

A cohort study has reported approximately 0.5 m/sec. decrease in nerve conduction velocity annually in diabetic patients. The cumulative evidence suggested the multi-factorial pathogenesis of diabetic neuropathy where hyperglycemia is probably the main factor. Hyperglycemia could damage nerve cells due to increased glucose flux through the polyol pathway, non-enzymatic glycosylation of proteins, and oxidative stress (34-36).

Reaction time (RT), is defined as the elapsed time between the presentation of a stimulus of any modalities of sensory input and subsequent behavioral response to occur. For measurement of sensory-motor association, the auditory and visual reaction is considered as an ideal tool. We found increased duration of visual reaction time as compared to auditory reaction time in diabetics, in the present study. Among normal controls, the median auditory reaction time was 192 m.sec (IQR 180, 198) and it was 180 m. sec (IQR 176, 197) among the Diabetic control group (P-value 0.004). Among normal controls, the median visual reaction time was 192 (IQR 184, 200) and it was 234 (IQR 210, 245) in Diabetic control group (P-value <0.001). The possible mechanisms can be chemical changes involved in its occurrence (37-38). In the present study, there was a decrease in reaction time with six months of interventional therapy which indicates improvement in sensory-motor performance and could be due to enhanced processing ability of the CNS with exercise therapy.

The mean HbA1c (5.86±0.37 Vs 5.14±0.36. (P-value <0.001) was significantly lower in the intervention group, as compared to the control group, at the end of 6 months follow up period. Similar to current study findings, a study by Kadoglou, N. P., et al. has reported a significant reduction in HbA(1c) (P<0.05), following an exercise program (39-40). Majority of the parameters, which have shown statistically significant improvement within intervention groups, have done so in the first two months following the initiation of the intervention, with no statistically significant change after that. However, the improvement from the baseline value has persisted till the end of 6th month follow up period.

In summary, we found decreased cardio-respiratory and neuro-physiological functions in newly diagnosed patients with type 2 diabetes mellitus. Significant improvement was observed with structured exercise therapy consisting of aerobic and resistance exercises when compared to diabetic controls. However, our findings require validation with molecular studies to establish underlying mechanisms.

**Future Scope:**

A large-scale randomized clinical trial with a longer duration of structured exercise therapy is required to demonstrate and authenticate the use of structured exercise therapy as an effective non-invasive treatment of diabetic patients with neuropathy and Cardio respiratory endurance related disorders in patients with type 2 diabetes mellitus.

**Limitations of the study:**

We could not confirm relationship between glycated hemoglobin and decline in neurophysiological parameters possibly because of relatively strict metabolic control in our diabetic population.

**Strengths of the study:**

The key unique feature of the study is its focus on young adults about 35 years of age, which is usually a neglected population group, especially when
studying the Cardio-respiratory endurance and neurophysiological wellbeing. The exercise program implemented in the current study is simple, scientific, inexpensive, and is amenable for large scale adaptation in wide variety of settings, ranging from primary to tertiary level care facilities. Also, the programme can be implemented through well trained paramedical personnel, patient self-help groups, reducing the burden on the more qualified health care providers and the health care system. This may have an immense beneficial effect on health care systems, especially of high-volume, resource poor settings like India.

Acknowledgements

We are grateful to our Laboratory Assistants for all technical help and Ms. Prassana, statistician for helping in the data analysis.

Conflict of Interest:

No

Disclosure:

This Manuscript is a part of my project entitled “Evaluation of the effect of structured exercise therapy on neuro-physiological and cognitive functions of young adults with type 2 diabetes mellitus – A Randomized Controlled Trial”

Funding Sources:

We are grateful to the Indian Council of Medical Research for funding this project.

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