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A Pilot Study to Unveiling the Link Between Physical Fitness and Cognitive Health in Early Vs. Late Diagnosed Diabetic Patients

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ABSTRACT

Introduction: Diabetes mellitus is a common chronic health condition that adversely affects various organ systems. However, its influence on physical fitness and cognitive health has yet to be thoroughly investigated, especially the timing of diagnosis.

Material and Methods: For our analysis, we examined 40 diabetic patients and divided them into two groups based on how long they had been diagnosed: early (≤ 5 years) and late (≥ 6 years). Participants were subjected to a battery of physical fitness tests, including evaluations of upper and lower body strength, Coordination, and aerobic endurance. Additionally, cognitive assessments such as the Addenbrooke's Cognitive Examination, Mini-Mental State Examination, and Montreal Cognitive Assessment were administered. The data were analyzed by conducting independent sample T-tests to compare the two groups.

Results: The study revealed notable disparities between the groups diagnosed early and those diagnosed late. Individuals who were diagnosed later experienced less favorable results in physical fitness evaluations, including handgrip strength, 6-minute walk distance aerobic endurance, and heart rate variability, as well as lower scores in all cognitive assessments. These findings suggest that a prolonged period of untreated diabetes can have detrimental effects on both physical and cognitive health outcomes.

Conclusion: To preserve both physical and cognitive functions, it is crucial to diagnose and manage diabetes early. The significance of prompt intervention has the potential to shape future recommendations on the treatment and detection of diabetes to enhance health outcomes.

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INTRODUCTION

Diabetes is a chronic condition that has a profound impact on the body's metabolic functions, resulting in a variety of complications [1]. In addition to the widely recognized impact on cardiovascular health and neuropathy, recent studies indicate an emerging link between diabetes and cognitive decline [2,3]. Recent research has indicated a possible connection between diabetes and a decline in cognitive abilities, which has sparked concerns about the wider impact of this disease on mental well-being [4]. Diabetic patients often experience higher rates of memory problems, dementia, and other cognitive impairments.

Understanding the intricate relationship between physical fitness and cognitive function is of utmost importance in the ongoing investigation of the wide-ranging effects of diabetes on human health. Having a deep understanding of how diabetes impacts physical fitness and cognitive health, particularly when it is diagnosed, can provide valuable insights for developing more effective management strategies and enhancing patient outcomes. It is believed that maintaining physical fitness can help reduce the risk of diabetes-related complications and potentially contribute to maintaining cognitive health [5].

This Study seeks to assess physical fitness and its association with cognitive health among two groups of diabetic patients: those diagnosed at an early stage and those diagnosed at a later stage. Through an examination of the potential connection between physical fitness and cognitive function in individuals with type 2 diabetes, this pilot study seeks to provide insights into the influence of diagnosis timing and lifestyle choices on cognitive health outcomes.

MATERIAL AND METHODS

Study Design

This Study is a cross-sectional pilot study. The Study employs a range of assessments to evaluate Functional performance, Cardiopulmonary health, and Cognitive function in individuals diagnosed with type 2 diabetes mellitus (T2DM). Participants are divided into two categories: those who were diagnosed within five years and those who were diagnosed more than five years ago. The research was carried out in the Department of Physiology in collaboration with the Departments of Medicine/ Biochemistry/ Neurology.

Ethical Considerations

The study was conducted following the guidelines of the Declaration of Helsinki and received approval from the institutional ethics committee of AIIMS Raebareli. The study was assigned the code I.E.C. 2021-3-IMP-1 and reference number F.31 BIOETHICS/AIIMS-RBL/APPR/IM/2020/11, with a date of February 12, 2022. Every participant willingly gave their informed consent prior to taking part in the Study. Great attention was given to maintaining the confidentiality of the data throughout the research process.

Screening and Recruitment

Participants were recruited from the Outpatient Department (OPD) of AIIMS Raebareli. The selection process focused on individuals who met specific inclusion and exclusion criteria. This recruitment strategy aimed to ensure a representative sample of the diabetic population in the region. Criteria for Inclusion: Individuals between the ages of 18 and 70 who have been diagnosed with type 2 diabetes mellitus in AIIMS Raebareli O.P.D. Capable of giving informed consent. Exclusion Criteria: Individuals with a medical history of neurological or psychiatric disorders. Uncontrolled high blood pressure. A condition characterized by uncontrolled proliferation of blood vessels in the retina. Conditions that restrict physical function due to musculoskeletal issues.

Sample Size

Considering the preliminary nature of the Study, we plan to recruit a convenience sample of 40 participants (around 15-20% per group). We recruited 40 adults diagnosed with T2DM, evenly split into two groups - one with early diagnosis (≤ 5 years) (n=20) and the other with late diagnosis (≥ 6 years) (n=20) depending on when their disease was identified.

Data Collection

The data collection was carried out by trained professionals from the Departments of Physiology, Medicine, Biochemistry, and Neurology at AIIMS Raebareli. This interdisciplinary approach ensured the accuracy and reliability of the data collected. Assessing functional performance in clinical settings typically entails a battery of tests that aim to evaluate different facets of physical health and capabilities. *Assessing Functional Performance: Evaluating Upper Body Strength*: Maximal grip strength is evaluated using a dynamometer in order to assess participants' strength. *Assessing Lower Body Strength*: The chair-sit-and-reach test is utilized to evaluate the flexibility and strength of the lower body.

Participants are required to reach toward their toes while seated on a chair, enabling a comprehensive assessment. *Coordination tests* involve the 8-foot up-and-go test (Time Up-and-Go test, TUG). This test measures the time it takes for an individual to transition from a seated position, walk around a cone positioned 8 feet away, and then return to sitting. This test evaluates an individual's mobility and balance. Participants can undergo tandem walking to assess their Coordination and balance. This involves walking heel-to-toe in a straight line.

Testing Aerobic Endurance: The 6-Minute Walk Test (6 M.W.T.) evaluates aerobic capacity and endurance by measuring the distance a participant can walk on a flat, hard surface within a six-minute period. *VO2 Max*: This test measures the maximum volume of oxygen an individual can use during intense exercise and is typically conducted using a bicycle ergometer. It is a crucial measure of cardiovascular fitness.

Cardiopulmonary Testing: Heart Rate Variability (H.R.V.) testing involves analyzing the time intervals between heartbeats to evaluate autonomic nervous system function and cardiovascular health. This test evaluates lung function by measuring the volume and speed of inhaled and exhaled air. This assessment tool is essential for identifying respiratory conditions. These tests give a complete assessment of a person's functional health, providing valuable information about their physical fitness, cardiovascular endurance, and overall physical abilities.

Measuring Grip Strength Involves the Use of a Dynamometer to Assess Upper Body Strength [6]**:** Participants maintained a posture with their shoulders adducted and the arm being tested held close to their body while ensuring that the elbow was fully extended. They were given verbal encouragement to exert their maximum grip strength (M.G.S.). At first, two tries were made, with each one involving a 2-4 second intense contraction followed by a 30-second break between attempts. If the M.G.S. measurements from these attempts were within 10% of each other, there was no need for any additional attempts. Furthermore, multiple attempts were made until two reliable M.G.S. readings were obtained. We used the highest value from these consistent trials for analysis. Next, the same procedure was performed on the other arm, with the initial side selected randomly.

Assessing flexibility and lower body strength has been done through a chair-sit-and-reach test [7]: Participants were seated at the edge of a chair that was securely positioned against a wall. They positioned one leg in front, with the knee straight and the heel firmly planted on the ground, while the other foot stayed flat on the floor. They interlocked their hands with fingers perfectly aligned, took a deep breath, and gracefully extended their reach towards their toes as they exhaled. Their bodies gracefully bent at the hip, maintaining a straight back and a lifted head. The movements were executed with fluidity, devoid of any jarring motions, and the stretching was done with care, avoiding any discomfort. The reach was maintained for 2 seconds, and the distance from the fingertips to the toes was carefully measured. The test was conducted twice for each leg, and the scores were meticulously recorded to the nearest half-inch.

Co-ordination: a. The Time Up-and-Go (TUG) 8-Foot Test [8]: A chair was positioned next to a wall to ensure safety, and a marker was placed 8 feet away. The space in between was cleared. Participants started the experiment by sitting down, placing their hands on their knees, and keeping their feet flat on the ground. As soon as the command "Go" was given, the timer began counting. Participants stood up, walked around the marker, and returned to sit down as efficiently and safely as they could. The test was conducted twice, and the most accurate time was recorded to the nearest tenth of a second; **b.** Assessing participants' walking ability involves observing their performance as they walk heel-to-toe in a straight line**.** Participants were given clear instructions on how to walk in a specific manner. They were asked to place the heel of one foot directly in front of the toes of the other foot while keeping their arms by their sides. Ensure safety involved by staying nearby and providing assistance in case of any balance issues. The observer carefully analyzed the participant's gait, paying close attention to the rhythm, base width, pelvic shift, and knee flexion.

Assessing Aerobic Endurance (6 Minute Walk Test) [9]**:** A rectangular walking course was carefully marked with cones at regular intervals. Participants were given the opportunity to walk for a duration of six minutes at their own pace, with the freedom to take breaks and rest whenever necessary. The distance covered was carefully measured and accurately recorded.

Maximum Cardiopulmonary Exercise Testing (CPET) [10]**:** This were evaluated through the use of a bicycle ergometer, performed by highly skilled individuals. Participants gradually increased their speed on a treadmill until they reached their limit after warming up. The speeds were gradually increased, first every two minutes and then every minute. The exhaled gases were collected during the test and analyzed for oxygen and carbon dioxide fractions. The VO2 max is the highest average oxygen consumption recorded over a minute.

Heart Rate Variability **Testing:** ***Heart Rate Variability (H.R.V.)*** [11] was measured from 5-minute E.C.G. recordings in the lead II while participants were in a relaxed and supine position using the Powerlab data acquisition system, A.D. Instruments. Frequency domain indices of H.R.V. were computed to evaluate autonomic nervous system function, revealing the activities of the sympathetic and parasympathetic systems. H.R.V. indices were calculated by analyzing the very low frequency (VLF) power, low frequency (L.F.) power (0.04-0.15 Hz), and high frequency (H.F.) power (0.15-0.4Hz). A measure of sympathovagal balance was determined by calculating the ratio of L.F. to H.F. power. When analyzing the frequency domain, L.F.'s power reveals a combination of sympathetic and parasympathetic influences on heart rate, with a greater emphasis on the sympathetic aspect. On the other hand, H.F. power represents the parasympathetic regulation of heart rate [12].

***Cognitive Function Assessment*:**

We administer a well-established cognitive assessment battery to evaluate different cognitive domains, including memory, attention, executive function, and processing speed. Cognitive function was assessed using a battery of standardized neuropsychological tests, including Initial Screening of Cognition assessment was measured with Addebbroke Cognitive Examination (ACE-III), Mini-mental state

Table 1. Measurement of Functional Performance in Early and Late Diagnosed Diabetic Patients

Parameter	Early Diagnosis (≤ 5 years)	Late Diagnosis (≥ 6 years)
Upper Body Strength		
Hand Grip strength		
Dominant (Kgf)	32.29±1.76	24.63±1.73*
Non-dominant (Kgf)	27.36±1.12	22.65±1.25*
Lower Body Strength		
Chair-sit-and-reach test (Inches)	4.70±0.48	3.40±0.33*
Coordination		
8-foot up-and-go test (Second)	2.77±0.27	3.95±0.57*
Heel-to-toe test	Performed	Performed
Aerobic Endurance		
6MWD (m)	469.50±16.46	362.90±21.83*
6 MWw X10^3 (Kg.m)	34.65±7.32	20.43±5.47*
VO_2 Max (mL/kg/min)	14.52±2.08	9.63±1.42*
Heart Rate Variability Testing		
VLF (%)	26.19±0.22	27.93±1.35
LF (%)	59.29±3.31	73.63±2.73*
HF (%)	17.85±1.52	11.53±1.02*
LF/ HF	1.32±0.22	1.81±0.21*

VO_2Max - Maximum Oxygen Consumption, 6MWD -6-Minute Walk distance, *6MWw*- 6-Minute Walk Work (Body weight x distance product), *Significant differences observed ($p < 0.05$)

Examination (MMSE), and Montreal Cognitive Assessment (MoCA). The Addenbrooke's Cognitive Examination III (ACE-III) is a widely used assessment tool in the field of cognitive evaluation. The ACE-III is an improved version of the ACE-II and ACE-R, providing a slightly more thorough cognitive evaluation in comparison to the MMSE and MoCA. It assesses various cognitive domains, such as memory, language, fluency, attention, and visuospatial abilities, with a maximum score of 100. Individuals with lower scores on the ACE-III may indicate the presence of memory deficits and other cognitive impairments. Mini-Mental State Examination (MMSE): The MMSE is a brief cognitive screening tool that covers ten different categories. It is commonly used to evaluate cognitive functions and has established standards for various levels of dementia severity. A score of 30 is considered the highest possible, while scores of 23 or lower often suggest cognitive impairment. Montreal Cognitive Assessment (MoCA): This tool evaluates cognitive functions in eight different areas, including visuospatial and executive functioning, naming, memory, attention, language, abstraction, delayed recall, and orientation. Every accurate answer will earn you a point, which will add up to a maximum score of 30. Scoring 30 indicates no cognitive impairment, while a score below 26 is often linked to mild dementia. However, there are no specific thresholds to differentiate mild from moderate dementia.

Analysis of Data

The analysis was performed using SPSS software, version 20.0, which is based in Chicago, US. Mean and standard deviation (Mean +/- S.D.) were calculated for all variables. Using the independent sample 't' test, we compared the means of different variables between the two groups. A p-value of 0.05 or lower was considered to indicate statistical significance.

RESULTS

Measuring Functional Outcome

Based on Table 1 shows when assessing *Upper body strength,* it is vital to consider (Hand grip strength). In this case, the dominant hand exhibited an average strength of 32.29 kgf, while the non-dominant hand recorded 27.36 kgf. After careful examination, it was discovered that the strength of the dominant hand had decreased to 24.63 kg, while the non-dominant hand's strength was measured at 22.65 kg. These values show a significant decline when compared to the group that was diagnosed early, indicating a gradual decrease in muscular strength over time ($p < 0.05$). *Lower Body Strength (Chair-Sit-and-Reach Test)*: Early Diagnosis: Demonstrated an average of 4.70 inches, suggesting a baseline level of flexibility. After a late diagnosis, there has been a significant decrease in flexibility, with a drop to 3.40 inches. This reduction is statistically significant, with a p-value of less than 0.05. *Coordination: (8-Foot Up-and-Go Test)*: Early Diagnosis: Achieved with an average completion time

Table 2. Measurement of Blood Glucose and Cognition in Early and Late Diagnosed Diabetic Patients

Parameter	Early Diagnosis (≤ 5 years)	Late Diagnosis (≥ 6 years)	Reference Values
Gender	Male - 14 (70%) Female-06 (30%)	Male -17 (85%) Female-03 (15 %)	
Hb A_{1C} Level	6.85±0.67	9.69±0.29*	[4-6%]
Blood Sugar- Fasting	87.28±3.40	108.65±2.12*	[70-110mg/dl]
Blood Sugar- PP	107.07±1.80	121.35±2.18*	[70-140mg/dl]
BMI (Kg/m^2)	21.63±1.03	22.76±0.92	
Age	35.87±2.95	48.67±3.24*	
Duration of diabetes	2.83±1.06	7.96±1.33*	
Cognitive Assessment 1. Addenbrooke's Cognitive Examination (ACE-III)	88.38±1.25	84.65±2.56*	88 ≥ Cognition Intact, 83-87- Inconclusive or mild Cognitive Impairment, < 83- Severe Cognitive Impairment
2. Mini-Mental State Examination (MMSE)	26.60±1.37	21.56±1.40*	24-30- Cognition Intact, 18-23-Mild Cognitive Impairment, 0-17-Severe Cognitive Impairment
3. Montreal Cognitive Assessment (MoCA)	31.72±1.24	26.35±2.43*	30 ≥- Cognition Intact, 26-30- Inconclusive or mild Cognitive Impairment, < 26- Severe Cognitive Impairment

*Significant differences observed ($p < 0.05$)

of 2.77 seconds. Delayed Diagnosis: Demonstrated slower Coordination with an average of 3.95 seconds, which was significantly higher than the group that received an early diagnosis ($p < 0.05$). Both groups were able to successfully complete the Heel-to-Toe test, with no notable variations between them. *Measured Aerobic Endurance (6-Minute Walk Test and VO2 Max)*: The distance covered in early diagnosis individuals was 469.50 meters, with a work output of 34.65 kg.m and a VO2 max of 14.52 mL/kg/min. With a deep understanding of the body's functions, the diagnosis revealed that the late diagnosis individual was only able to cover a distance of 362.90 meters. Their work output was measured at 20.43 kg.m, and their VO2 max was significantly reduced to 9.63 mL/kg/min. Hence, the aerobic endurance parameters in patients diagnosed later were found to be significantly lower compared to those diagnosed early ($p < 0.05$). *Cardiopulmonary Testing: Heart Rate Variability (H.R.V.) and Pulmonary Function*. Upon a late diagnosis, significant changes were observed in the percentages of low-frequency (L.F.) and high-frequency (H.F.), as well as the LF/HF ratio. There was no significant alteration in the very low frequency (VLF).

Assessment of Cognitive Health Outcomes (Glycemic and Cognitive Assessments)

Based on Table 2 shows an understanding of *HbA1C and Blood Sugar Levels*: Patients who were diagnosed late showed significantly higher HbA1C levels and both fasting and post-prandial blood sugar levels, indicating poorer glycemic control ($p < 0.05$). Assessment tools commonly used to evaluate cognitive function include the Addenbrooke's Cognitive Examination, Mini-Mental State Examination, and Montreal Cognitive Assessment. There was a significant difference in scores between the late diagnosis group and the early group, suggesting a link between a longer duration of diabetes and decreased cognitive abilities ($p<0.05$). Demographics: The group that received a late diagnosis had a greater proportion of males and an average age that was significantly higher in comparison to the early diagnosis group.

DISCUSSION

These findings shed light on the negative impacts of late detection of diabetes on both physical and cognitive well-being. It is evident that individuals who are diagnosed with diabetes at a later stage experience a notable decline in physical fitness indicators, including hand grip strength, lower body flexibility, and aerobic endurance. This implies that the initial phases of diabetes may result in gradual but significant deterioration in muscular and aerobic capabilities. This decline may be due to the progressive nature of complications related to diabetes, which can negatively affect muscular strength and cardiovascular health [13, 14].

When it comes to Coordination, the slower times observed in the 8-foot Up-and-Go test for the late diagnosis group highlight the possible decrease in motor control and balance, which are essential for carrying out everyday tasks. It is clear that early interventions are crucial in preserving motor functions in diabetic patients [15,16]. These findings emphasize the susceptibility of the cardiovascular and pulmonary systems to prolonged hyperglycaemic states, as evidenced by the altered heart rate variability (H.R.V.) [17,18]. Understanding the relationship between H.R.V. and the autonomic nervous system can provide valuable insights into the potential cardiovascular risks faced by patients diagnosed with diabetes later in life. This highlights the crucial role of timely diabetes management in mitigating these risks.

The late-diagnosed group showed significantly more pronounced cognitive impairments, as evidenced by significant reductions in scores across all cognitive tests administered (Addenbrooke's Cognitive Examination, Mini-Mental State Examination, and Montreal Cognitive Assessment). It is in line with previous research that connects long-term high blood sugar levels with an increased likelihood of cognitive decline [19–21]. This could be attributed to damage to the small blood vessels and the subsequent reduction in blood flow to the brain [3]. In addition, the demographic data reveals a higher percentage of older males in the late diagnosis group, which could indicate that this particular demographic may be more prone to delayed diagnosis or potentially overlook early symptoms of diabetes.

Overall, these findings highlight the crucial significance of early diagnosis and intervention in diabetes. Through early detection and effective disease management, it is possible to prevent or reduce the long-term complications linked to diabetes. This helps in preserving both physical and cognitive functions. This study provides strong support for the continued improvement of early screening and diagnosis strategies, with a particular focus on populations at risk of being diagnosed late.

CONCLUSION

The noticeable decreases in upper and lower body strength, aerobic endurance, and Coordination in individuals who were diagnosed late highlight the negative impact of uncontrolled diabetes as time goes on. In addition, the cognitive decline observed in these patients emphasizes the broader impact of diabetes on overall health and functionality. These findings highlight the importance of detecting diabetes early to minimize the negative impacts of the disease. Understanding the importance of early diagnosis, one can appreciate the significance of timely management strategies. By placing emphasis on early diagnosis and proactive management, healthcare systems have the potential to enhance the quality of life for individuals with diabetes and alleviate the burden of this chronic condition on both individuals and society as a whole.

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

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