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Unraveling the Biochemical and Hematological Pathways of Cognitive Decline: A Case Study of Emerging Biomarkers Linking Type 2 Diabetes Mellitus and Alzheimer's Disease

Khadija Batool and Ambreen Ilyas

ABSTRACT

BACKGROUND

Individuals with type 2 diabetes are more likely to experience modest types of cognitive dysfunction, dementia, including Alzheimer's disease (AD), and cognitive impairment. According to current diabetes recommendations, people with diabetes and cognitive impairment should get diabetes management advice, and groups at high risk should be screened for cognitive impairment. However, there is currently no cure for the condition, and significant uncertainties surround the processes producing cognitive deterioration linked to diabetes. For milder and more severe types of diabetes-related cognitive impairment, these pathways are probably complex and distinct.

OBJECTIVE

To explore the significant association of AD (cognitive dysfunction) with diabetes mellitus and to investigate abnormal blood occurrences in AD patients compared to healthy individuals.

METHODS

Novel biomarkers of certain dementia etiologies, brain parenchymal damage, and cerebral blood flow and metabolism have been discovered in recent years as a result of research on dementia, brain aging, diabetes, and vascular disease. These indicators provide insight into the mechanisms behind cognitive impairment linked to diabetes, have obvious uses in ongoing studies and, more and more, in clinical diagnosis, and may eventually direct focused therapy. The Lahore District will be used to collect random samples of AD patients and healthy people in order to look for abnormal blood occurrences. Case-control training was conducted to observe the widespread occurrence of irregular blood HbA1c levels in patients with AD. The stages of Hemoglobin, RBC, WBC, thrombocytes, neutrophils, lymphocytes, MCV, MCH, MCHC, PVC (HCT), and HbA1c, were determined from the DHQ Teaching Hospital Lahore lab.

RESULTS

A t-test was applied to get the importance of the difference between individual patient assemblages (Alzheimer's disease, AD) through the control category for individual CBC, HbA1c, and then vitamin B12 boundary. A total number of 500 persons were involved in this learning. The mean time of life of the patients is 60 years, ranging from 25 to 94, in which the minimum age of patients is 44 and the maximum age is 90. Patients are more likely to be female (69%) than male (31%). Every patient group's average scores for each variable were below the acceptable range. T-test results show substantial differences (p-value 0.0001) in each variable for the control group vs. AD patients.

CONCLUSION

The study emphasized the significant association of cognitive dysfunction, AD, and diabetic mellitus. The substantial differences observed in CBC parameters, HbA1c, and vitamin B12 levels between AD patients and healthy controls indicate a potential link between metabolic and hematological alterations and cognitive decline. The statistically significant p-value (0.0001) across all variables supports the hypothesis that abnormal blood profiles, particularly elevated HbA1c levels and altered hematological indices, may contribute to or reflect the underlying pathophysiological processes of AD in diabetic individuals. These findings highlight the importance of regular metabolic and hematological screening in elderly diabetic populations for early detection and intervention in cognitive impairment. The predominance of female patients (69%) also suggests a possible gender-based vulnerability that warrants further investigation.

Keywords: Alzheimer's disease, Type 2 diabetes mellitus, Cognitive impairment, Hematological indices, Insulin dysregulation

Introduction

There is growing recognition that cognitive impairment is a prevalent comorbidity and consequence of both type 1 and type 2 diabetes.^{1,2} Diabetes has been linked to subtle cognitive changes in people of all ages, but those 60 and older are more at risk for overt dementia and cognitive impairment.³ The effects of cognitive decline are widespread. A higher risk of cardiovascular events and mortality, as well as a higher frequency of severe hypoglycemic episodes, are linked to worse diabetes control.^{4,5} In order to prevent hypoglycemia and increase compliance, diabetes guidelines advise screening for cognitive impairment in those over 65 with diabetes and recommend that therapy for those with cognitive impairment be customized.⁴⁻⁶

Therefore, the focus of diabetes-related cognitive impairment has shifted from research to therapeutic treatment. But there are still significant issues. The causal relationship between diabetes and certain alterations in the brain is unclear. Furthermore, nothing is known about the underlying processes. For instance, the burden of Alzheimer's disease (AD) neuropathology does not seem to be higher in people with diabetes, despite strong epidemiological evidence that diabetes increases the incidence of dementia, including AD.^{7,8} Furthermore, diabetes does not seem to be the main cause of the elevated risk for dementia,⁹ despite the fact that it is linked to cerebrovascular illness and an increased risk of stroke.¹⁰ Other pathways, some of

which may be directly related to the diabetic condition, are being discovered.

Additional mechanisms are being identified, including some that might be directly linked to the diabetic state, such as brain amylin buildup and insulin resistance.¹⁰ Because of this, cognitive impairment in diabetes is probably caused by a variety of etiologies, some of which are unique to diabetes and many of which are not, resulting in mixed pathologies that vary significantly between individuals.¹⁰ The diagnosis, prevention, and treatment of cognitive impairment linked to diabetes are complicated by this finding. With an emphasis on type 2 diabetes, this review demonstrates how biomarker techniques might help clarify the intricate etiology of diabetes-associated cognitive impairment.

Cognitive dysfunction or AD stands a neurological condition that is prevalent in the elderly. Various degrees of memory, behavioral, and cognitive impairment exist in people. The majority of those who have the condition gradually lose their capacity to remember things, think clearly, and even complete simple tasks. In those who have the late-onset type of the disease, symptoms start to show in their mid-sixties. Approximately 18% of the world's population is affected by neuropsychiatric disorders. Their cognitive, memory, emotional, and social functioning decline. AD is to blame for 70% of dementia cases worldwide.^{11–13} AD has a variety of causes, including deficits in vitamins, diabetes, persistent alcohol misuse, psychiatric illnesses, subdural hematomas, neurological disorders, sadness, infections (HIV), and mental dysfunction brought on by chemotherapy.¹⁴ Early-stage AD progressively becomes worse and is ignored. The patient frequently loses track of time and is disoriented. The symptoms are clearer and more visible to the caregivers on the middle face. They describe symptoms such as difficulty swallowing and ingestion, stability issues, verbal and dialogue problems, memory loss that causes them to forget names of people or things, adjustments in conduct, uneasiness, wandering, and persistent questioning, and amnesia of recent events and names. They frequently needed extra assistance with concentration, communication, and problem-solving. The penultimate phase is characterized by memory disturbance. People are unable to recognize local relatives, locations, or activities. There is hostility, sobbing, or fury.^{15–17} Hallucinations, nervousness, despair, anxiety, impulsive behavior, elation, laziness, irritability, delusions, abnormal motor activity, and changes in food or sleep are a few of the behavioral and psychological signs of AD. Due to the disease's protracted effects, which include hospital stays and medical costs, AD patients typically have poor outcomes. It involves drug abuse as well as the agitation or discomfort of the patients and the caregivers. Patients might experience multiple symptoms at once or just one.¹⁸

Diabetes mellitus (DM) is categorized by chronic hyperglycemia and abnormalities in the uptake of celluloses, fats, and proteins. It is raised by an inadequacy in insulin secretion and/or action, either completely

or in part. The two principal types of diabetes are type 1 diabetes mellitus (T1DM), an insulin-dependent type of diabetes, and non-insulin-dependent diabetes mellitus type 2 diabetes mellitus (T2DM). The most typical kind of diabetes, T2DM, affects 90–95% of all diabetic patients.¹⁹ Type 1 diabetes is mostly a hereditary problem that manifests in adolescence, whereas type 2 diabetes is primarily a diet-related condition that appears over time. In persons with type 1 diabetes, their immune structure is violent and ends the insulin-producing cells inside the human pancreas.²⁰ T2DM symptoms include hyperglycemia, glucose intolerance, and a comparative lack of insulin. These results from decreased insulin susceptibility of muscle, hepatic, and adipocytes (also called insulin resistance). In general, the pancreas increases its synthesis of insulin right after eating. Insulin targets the muscle strength, adipose, hepatic, and acellular. Insulin boosts sugar from the blood and helps glycol genesis by restricting glycogen synthesis. Islet amyloid polypeptide in humans (hIAPP, amylin), which causes pancreatic β cell malfunction, is another characteristic of diabetes. Chronic hyperglycemia is the direct source of numerous diabetic indications, including retinopathy, peripheral neuropathy, and nephropathy, as a result of the ensuing metabolic disruption.^{21–23} The interplay of genetic, environmental, and other risk factors primarily causes T2DM. Additionally, diminished first-phase insulin release, aberrant baseline pulsatile insulin excretion, and elevated glucagon production all hasten the onset of Form II DM.²⁴

Type 2 diabetes is linked to AD virus, the most frequent condition of dementia. Various researchers who have studied massive populations for so many decades suggest that those with type 2 diabetes may be further prone to grow AD. Some individuals refer to AD as “type 3 diabetes.” Along with malfunction, the action of glucose engagement in the neurons for liveliness manufacture in T2DM is highly associated with cognitive impairment, according to substantial epidemiological evidence. The complicated connection between T2DM and AD is influenced by oxidative stress, inflammation, glycogen synthase kinase 3 β (GSK3 β) signaling, amyloid beta ($A\beta$) production from amyloid precursor protein (APP), the development of neurofibrillary tangles, and modulation of acetylcholine esterase activity. Due to common devices of T1DM, T2DM, and AD, scholars established the term “type 3 diabetes.” The goal of the review article is to talk about cellular and molecular associations between diabetes and AD, which are destined for type 3 diabetes.^{25–27} The terminology was proposed by some scientists because they think dementia is brought on by insulin imbalance in the brain. The supposed AD gene mutation APOE4 appears to get in the way of the use of insulin by brain cells, potentially leading to starvation and death. It is mentioned as type 3 diabetes informally.²⁸ AD rates may have increased because of the epidemic of insulin resistance, pre-diabetes, and type 2 diabetes. According to recent studies, there is a clear association between AD and sugar imbalance.²⁹ APP, amyloid- β (APP- $A\beta$) deposit,

cell loss, a lot of neurofibrillary tangles, dystrophic neuritis, amplified beginning of pre-death genetic factor and signing pathway, impaired energy metabolism, mitochondrial flawed, long-term oxidative trauma, also DNA injury are all hallmarks of AD. A framework that mechanistically connects all these occurrences is necessary to better understand AD pathogenesis. There is currently a rapid expansion of research pointing to insulin conflict and deficit as mediating factors in AD-type neurodegeneration, but there are many unclear as well as conflicting theories about potential functions of T2DM, the metabolic disorders, and other conditions in this deluge of updated information and obesity in AD pathogenesis. In this article, we analyze the data showing that:

1. Type 2 diabetes mellitus results in cognitive impairments, oxidative stress, and brain insulin sensitivity, although its overall consequences are significantly short to imitating AD.
2. The majority of the molecular, biochemical, and histological abnormalities in AD may be caused by widespread disruptions in head insulin and insulin-like growth factor (IGF) signaling structures, which constitute initial and progressive abnormalities.
3. Numerous characteristics of AD are present in chronic cerebral diabetes brought upon with intravenous infusion hyperglycemia delivery of streptozotocin, involving mental impairment and abnormalities in acetylcholine homeostasis.
4. Insulin sensitizer therapies, or medications already prescribed to treat T2DM, can be used to treat experimental brain diabetes.

We come to the conclusion that AD is described as a category of diabetes. It possesses molecular and biological features and is uniquely associated with the brain with both type 1 diabetes mellitus and T2DM. The term “type 3 diabetes” correctly captures this.^{30–33} We have elaborated on the possible biological pathways linking T2DM and AD. Specifically, we discussed the roles of insulin resistance, chronic hyperglycemia-induced oxidative stress, and inflammation in neuronal damage and impaired glucose metabolism in the brain. In clinical practice, it is preferable to categorize these patients’ symptoms in order to estimate prognosis, treatment response, and illness natural cores. Some of these elements apply to them. The greatest risk factor is age. As people age, their symptoms get worse. A larger risk exists for first-degree relatives of AD patients. Other risk factors include dietary habits, diabetes, and hypertension, as well as the level of mental activity over the course of a lifetime.³³ Reduced glucose utilization is a common aspect of AD, and insulin therapy has been revealed to improve memory. According to reports, IRs and insulin levels in AD patients are lower than in normal persons; hence, raising insulin levels can enhance cognition. Clinical studies have shown that administering insulin along with other anti-diabetic drugs will lessen plaque buildup and enhance reasoning piece

in AD patients with DM. The current investigation will highlight a strong relationship between insulin dysregulation in the mind and AD.³⁴ Low stages of B12 might create high homocysteine levels, which can affect some brain cells. Your brain messages become distorted as a result, resulting in mood changes and even anxiety. Potential AD treatments that stop the fundamental disease processes have been made possible by our increased understanding of how the illness affects the brain. Future AD treatments might involve a combination of drugs, much like how HIV/AIDS or cancer treatments might involve more than one therapy.

Research Objectives

To evaluate the hematological profile of AD and diabetes patients.

To investigate how insulin dysregulation in the brain causes AD.

To control the higher risk of AD by controlling diabetes.

Research Methodology

Study Strategy

Samples numbering 300 will be collected from AD patients and healthy individuals as a control group from the Lahore District of Punjab to determine the frequency of aberrant blood indices and insulin dysregulation in AD patients.

Inclusion Criteria

Both the AD patients and the control group of healthy persons will enroll in Punjab. The following categories of AD patients will be listed: Lahore District residents with diabetes and AD.

Questionnaire

The questionnaire contains all the suggestions that will be helpful in examining or researching AD. In comparison to males, AD affects women more frequently than it does males. The majority of those who have the condition gradually lose their capacity to remember things, think clearly, and even complete simple tasks. In those who have the late-onset type of the disease, symptoms start to show in their mid-sixties.

Exclusion Criteria

Malignant patients are unwilling to take part in the research.

Blood Sampling

Blood samples will be taken from AD patients in the DHQ Teaching Hospital in Lahore. Blood samples from unharmed volunteers will also be taken at the DHQ Teaching Hospital in Lahore.

Laboratory Testing

The blood tasters were delivered on the way to the DHQ Teaching Hospital’s laboratory in Lahore. The level of hemoglobin, erythrocytes, leukocytes, platelets, neutrophils, lymphocytes, MCV, MCH, MCHC, PVC(HCT), vitamin B12, and HbA1c were assessed by

the complete blood count (CBC), HbA1c, and vitamin tests in the normal and patients' group, respectively. Biochemistry laboratory tests were also performed to measure the serum electrolytes (Sodium & Potassium).

Data Collection and Analysis

Age, gender, location, medication use, and diabetes status will all be collected in the data. Using PRISM 5.01, the descriptive statistics will be examined, including frequencies, means, minimum and maximum values, and so on. Each CBC, HbA1c, and vitamin B12 parameter will be compared to the normal ranges.

Tools Used in Data Collection

A data collecting form is divided into three sections. The socio-demographic details, such as age, gender, place of residence, marital status, and diabetes, are involved in the first section. The second unit includes elements associated with sickness, such as questions related to memory, orientation, functional ability, visuospatial, and language. The third part of the study contains the comparison of the levels of hematological indices [Hb, RBC count, WBC count, Platelets count, Neutrophils, Lymphocytes, MCV, MCH, MCHC, and PVC (HCT)], Vitamin B12 and HbA1c levels between AD patients and control groups.

Table 1 Socio-demographic characteristics of AD				
		Presence of AD		Total
		Yes	No	
Age	25–34	0	92	92
	35–44	15	75	90
	45–54	87	34	121
	55–64	83	49	132
	65–74	42	0	42
	75–84	11	0	11
	85–94	12	0	12
Total		250	250	500

Ethical Approval

Just before the study began, authorization from the public health authorities, the Faculty of Graduate Studies at DHQ Teaching Hospital, Lahore, and the Institutional Review Board (IRB) were all obtained in order to protect participants' safety and advance the study. Following affirmative consent and discussion of the study's goals and procedures, only participants who agreed to take part were counted.

Hematological Profile

The DHQ Teaching Hospital in Lahore's laboratory will receive the blood samples. The complete blood count (CBC) test will be used to detect the levels of hemoglobin, RBC count, WBC count, platelets count, Neutrophils (poly), Lymphocytes, Monocytes, Eosinophils, Basophils, MCV, MCH, MCHC, PCV (HCT), and ESR in mutually the patient group and the control group.

Insulin Determining Index

A test to find out the level of insulin in the body is an insulin blood test (HbA1c), often known as a fasting insulin test. It is also used to monitor insulin fighting and the treatment of aberrant insulin levels. The HbA1c test is used to determine the blood's insulin content.

Statistical Analysis

PRISM 5.01 and Microsoft Excel 2010 were used to analyze all data. Variables that were normally distributed were provided as standard deviations and means in the descriptive statistic (SD). A t-test will be performed to assess the significance of the variations in each of the CBC, HbA1c, and vitamin B12 parameters between every group of AD patients and the control group. The outcome is important if the p-value is <0.050.

Results and Discussion

Socio-Demographic Characteristics of AD

In this study, 500 people were enrolled. This depicts the patients' socio-demographic traits. The patient ages range from 25 to 94, with a mean stage of development of 58 years (Table 1, Graph 1).

Age and Presence of AD

Table 1 Showed the Socio-demographic characteristics of Alzheimer disease.

Graphical Analysis

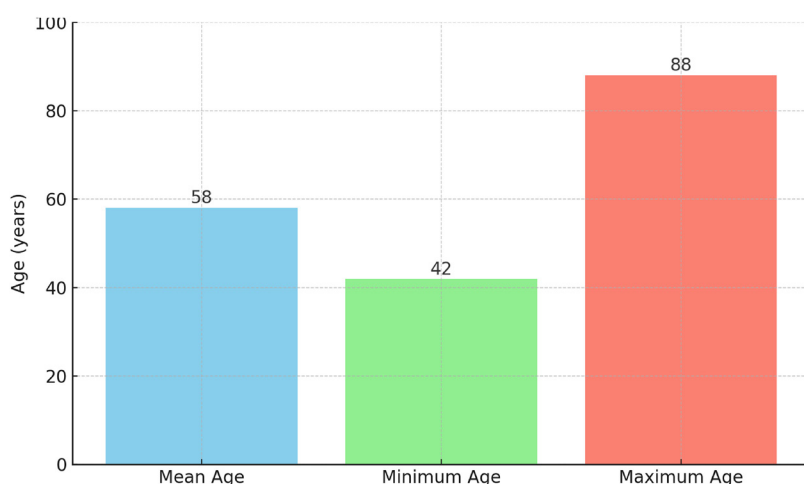
The graphical analysis is shown in Graph 1.

Gender Distribution

The study reveals the demographic status of gender distribution among males and females. This shows the majority of patients were females (68.85%) as compared to male patients (31%) (Table 2, Graph 2)

Gender and Presence of AD

Patients seem to be more likely to be female (68.8%) than male (31%). The significant majority of patients come from rural regions.



Graph 1 | Mean age of the AD patients is 58 years, in which the minimum age of patients is 42 and the maximum age is 88

Graphical Analysis

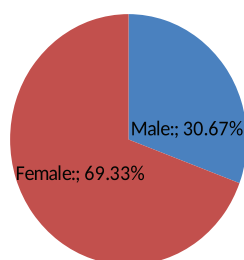
The graphical analysis is shown in Graph 2.

Hematological Indices

This study reveals the mean values, standard deviation, and significant differences of AD patients in comparison with the control group. The mean $\pm$ SD (10.8 $\pm$ 2.51234) of the hemoglobin parameters of AD patients is lower than the normal range. In accordance with the t-test, important changes (p-value < 0.0001) exist in hemoglobin levels in the control group vs. AD patients. The mean $\pm$ SD (4.2 $\pm$ 0.29) of the RBC parameter of AD patients is lower than the regular range. Significant

Table 2 Gender distributions of AD patients				
		Presence of AD		Total
		Female	Male	
Gender	25–34	0	0	0
	35–44	23	09	32
	45–54	66	14	80
	55–64	55	08	63
	65–74	15	07	22
	75–84	35	06	41
	85–94	07	05	12
Total		201	49	250

Gender Ratio of Alzheimer Patients



Graph 2 | Relative ratio of AD among genders. The ratio of female patients (68.85%) is more as compared to male patients (31%)

differences (p-value 0.0001) are found via the t-test in RBC levels in the control group vs. AD patients. The mean $\pm$ SD (7.5 $\pm$ 1.6) of the WBC parameter of AD patients is lower than the regular variety. Important alterations (p-value < 0.0413) exist, according to the t-test, in WBC levels in the control group vs. AD patients. The mean $\pm$ SD (208.25 $\pm$ 83.24) of the platelet parameter of AD patients is lower than the normal range. Given the t-test, noteworthy differences (p-value < 0.0001) exist in platelet levels in the control group vs. AD patients. The mean $\pm$ SD (54.25 $\pm$ 10.156) of the neutrophil parameter of AD patients is lower than the normal range. T-test, significant differences (p-value < 0.0001) exist in neutrophil levels in the control group vs. AD patients. The mean $\pm$ SD (31.6067 $\pm$ 9.0767) of the lymphocyte parameter of AD patients is lower than the normal range. According to the t-test, significant differences (p-value < 0.0060) exist in lymphocyte levels in the control group vs. AD patients.

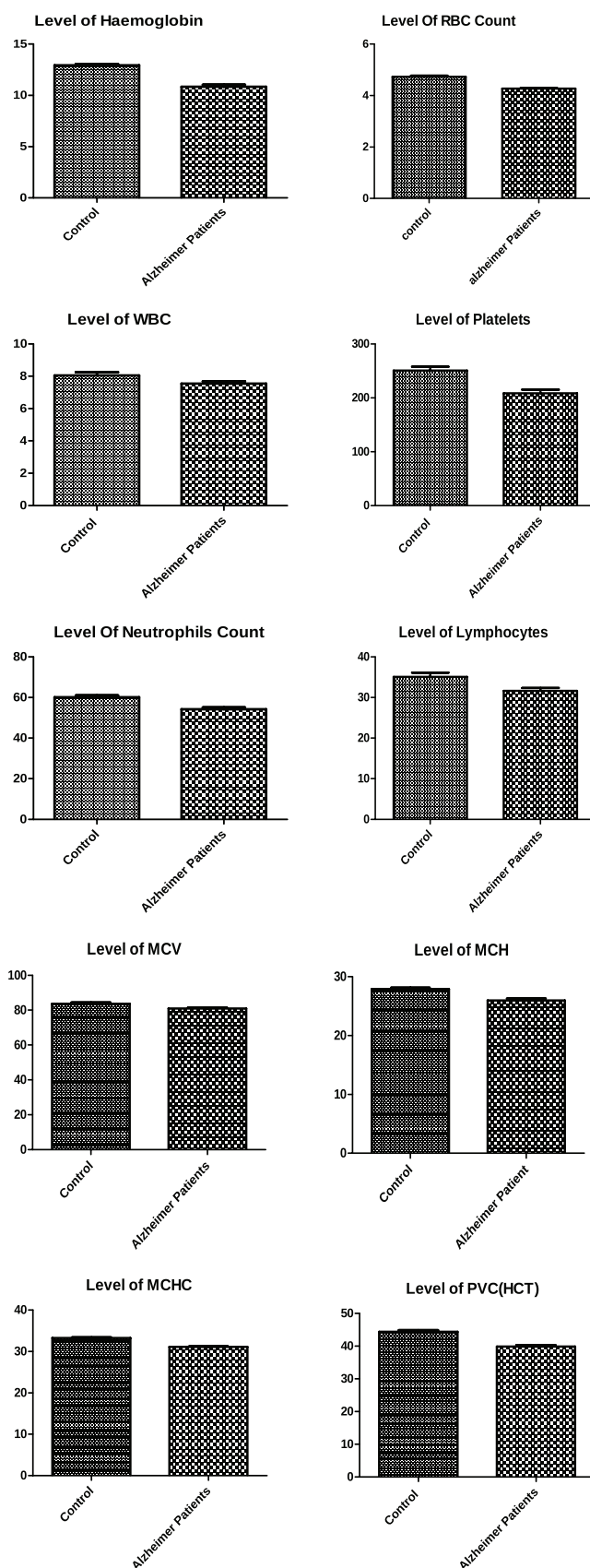
The mean $\pm$ SD (80.92 $\pm$ 8.0377) of the MCV parameter of AD patients is less than the standard range. Weighty changes (p-value < 0.0042), according to the t-test, exist in MCV levels in the control group vs. AD patients. The mean $\pm$ SD (25.98 $\pm$ 3.77) of the MCH parameter of AD patients is lower than the normal range. T-test, important alterations (p-value < 0.0001) exist in MCH levels in the control group vs. AD patients. The mean $\pm$ SD (31.31 $\pm$ 2.035) of the MCHC parameter of AD patients is lower than the normal range. According to the t-test, significant differences (p-value < 0.0001) exist in MCHC levels in the control group vs. AD patients. The mean $\pm$ SD (39.87 $\pm$ 4.84) of the PVC (HCT) parameter of AD patients is lower than the normal range. According to the t-test, significant differences (p-value < 0.0001) exist in PVC (HCT) levels in the control group vs. AD patients (Table 3)

Nearly all parameters in the control group were within normal limits, but in the AD patient group, every parameter's mean value was outside of this range. Indicators of hematology in all AD patients were found to be at low levels (Table 3, Graph 3)

Table 3 Significant association of level of hematological indices in AD patients in comparison with control group						
Indices	AD Patients		Control Group		t-Test	P-Value
	Mean	Std. Deviation	Mean	Std. Deviation		
Hemoglobin	10.8306	2.51234	12.915	1.58613	8.592	<0.0001
RBC	4.268	0.292483	4.72667	0.589012	8.542	<0.0001
WBC	7.546	1.62297	8.04667	2.51393	2.049	0.0413
Platelets	208.253	83.2428	250.507	87.07	4.296	<0.0001
Neutrophils	54.24	10.1563	60.1267	10.9926	4.817	<0.0001
Lymphocytes	31.6067	9.07678	35.0867	12.4415	2.767	0.0060
MCV	80.9267	8.03774	83.7267	8.74846	2.887	0.0042
MCH	25.98	3.77286	27.92	2.69855	5.122	<0.0001
MCHC	31.1	2.03575	33.24	2.22155	8.698	<0.0001
PVC(HCT)	39.8733	4.84151	44.34	6.9936	6.431	<0.0001

Graphical Analysis

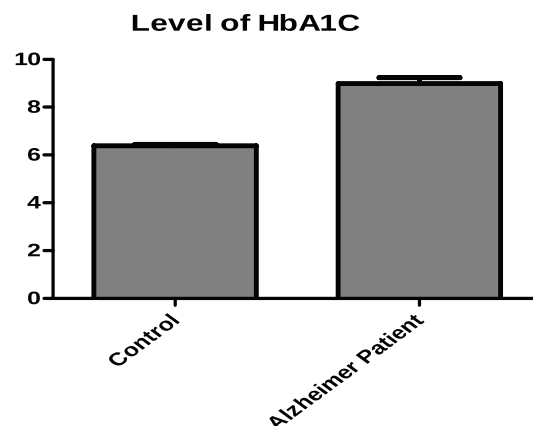
The graphical analysis is shown in Graph 3.



Graph 3 | Levels of relationships between AD patients and controls that are independent of each other. The table shows a significant association of $p < 0.050$

Table 4 | Levels of HbA1c among AD patients and control group. This shows a significant association of insulin levels among AD patients

Indices	AD Patients		Control Group		t-Test	P-Value
	Mean	Std. Deviation	Mean	Std. Deviation		
HbA1c	8.994	3.103	6.388	0.693587	10.04	<0.0001



Graph 4 | Associations among controls and AD patients that are not dependent on one another. The measured value of frequency is shown by the height or length of the bar

Insulin Determining Index

Descriptive Analysis

The study reveals the mean value, standard deviation, and significant difference of AD patients in comparison with control group. The mean $\pm$ SD (8.99 ± 3.1) of the HbA1c parameter of AD patients is higher than the normal range. AD patients' HbA1c levels differ significantly (p -value 0.0001) from those of the control group using the t-test (Table 4, Graph 4)

Graphical Analysis

The graphical analysis is shown in Graph 4.

Discussion

A total number of 300 persons were included in this study. That shows the socio-demographic characteristics of the patients. The average oldness of the patients is 58 years, ranging from 25 to 94. Graph 1 shows the mean time of life of the AD patients is 58 years, in which the minimum age of patients is 42 and the maximum age is 88. The study reveals the demographic status of gender distribution among males and females. There are more female patients (68.85%) in comparison to male patients (31%). Graph 2 shows the relative ratio of AD among genders. The ratio of female patients (68.85%) is higher compared to male patients (31%).

This study reveals the mean values, standard deviation, and significant difference of AD patients in comparison with control group. The mean $\pm$ SD (10.8 ± 2.51234) of the hemoglobin parameters of AD patients is lower than the normal range. On the basis of

the t-test, noteworthy changes (p -value < 0.0001) exist in hemoglobin levels in the control group vs. AD patients. The mean $\pm$ SD (4.2 ± 0.29) of the RBC parameter of AD patients is lower than the normal range. On the basis of the t-test, important modifications (p -value < 0.0001) exist at the RBC levels in the control group vs. AD patients. The mean $\pm$ SD (7.5 ± 1.6) of the WBC parameter of AD patients is lower than the normal range. On the basis of the t-test, weighty alterations (p -value < 0.0413) exist at WBC levels in the control group vs. AD patients. The mean $\pm$ SD (208.25 ± 83.24) of the platelet parameter of AD patients is lower than the normal range. On the basis of t-test, noteworthy modifications (p -value < 0.0001) exist in platelets levels in the control group vs. AD patients. The mean $\pm$ SD (54.25 ± 10.156) of the neutrophil parameter of AD patients is lower than the normal range. According to the t-test, significant differences (p -value < 0.0001) exist in neutrophil levels in the control group vs. AD patients. The mean $\pm$ SD (31.6067 ± 9.0767) of the lymphocyte parameter of AD patients is lower than the normal range. From the t-test, noteworthy transformations (p -value < 0.0060) exist in lymphocyte levels in the control group vs. AD patients. The mean $\pm$ SD (80.92 ± 8.0377) of the MCV parameter of AD patients is lower than the normal range. From the t-test, noteworthy differences (p -value < 0.0042) exist in MCV levels in the control group vs. AD patients. The mean $\pm$ SD (25.98 ± 3.77) of MCH parameter of AD patients is lower than the normal range. According to the t-test, significant differences (p -value < 0.0001) exist in MCH levels in the control group vs. AD patients. The mean $\pm$ SD (31.31 ± 2.035) of the MCHC parameter of AD patients is lower than the normal range. On the basis of t-test, significant changes (p -value < 0.0001) exist in MCHC levels in the control group vs. AD patients. The mean $\pm$ SD (39.87 ± 4.84) of the PVC (HCT) parameter of AD patients is lower than the normal range. From the t-test, important differences (p -value < 0.0001) exist in PVC (HCT) levels in the control group vs. AD patients. Table 2 shows the significant association of levels of hematological indices in AD patients in comparison with control group. The control group takes the usual values of almost all limits; however, in the patients' group (AD), the average value of each parameter is less than the normal range. Low levels were analyzed in hematological indices in all AD patients. Graphs shows the levels of relationships between AD patients and controls that are independent of each other. The table shows a significant association of $p < 0.050$.

The study reveals the mean value, standard deviation, and significant difference of AD patients in comparison with control group. The mean $\pm$ SD (8.99 ± 3.1) of the HbA1c parameter of AD patients is higher than the normal range. On the basis of the t-test, significant alterations (p -value < 0.0001) exist in HbA1c levels in the control group vs. AD patients. Table 3 shows the level of HbA1c among AD patients and control group. This shows a significant association between insulin levels among AD patients. The graph shows the relationships between AD patients and controls that are

self-regulating of each other. The tallness or distance of the bar designates the measured value of incidence.

This study reveals the mean value, standard deviation, and significant difference of AD patients in comparison with control group. The mean $\pm$ SD (8.99 ± 3.1) of the vitamin B12 parameter of AD patients is less than the normal range. From the t-test, significant changes (p -value < 0.0001) exist in vitamin B12 levels in the control group vs. AD patients. Table 4 shows the level of HbA1c among AD patients and control group. This shows a significant association between insulin levels among AD patients. The graph shows the relationships between AD patients and controls that are self-determining of each other. The altitude or dimension of the bar shows the controlled price of consistency. Further analysis of gender differences observed in hematological and biochemical parameters among AD and T2DM patients through hormonal differences, lifestyle factors, and differential disease progression between males and females could contribute to the disparities in our data. The limitation of not employing standardized cognitive scales like the Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment (MoCA) in our current study is acknowledged, and its inclusion in future research to validate clinical dementia diagnoses and better correlate hematological/metabolic changes with cognitive decline is suggested.

Conclusion

This study highlights a significant association between AD and diabetes mellitus, emphasizing the role of metabolic and hematological alterations in cognitive decline. The marked differences observed in CBC parameters, HbA1c, and vitamin B12 levels between AD patients and healthy individuals ($p < 0.0001$) suggest that disrupted blood profiles, particularly poor glycemic control, may contribute to the pathophysiological mechanisms underlying AD. The higher prevalence of AD among females and the abnormal hematological indices further reinforce the need for routine metabolic and blood parameter monitoring, especially in elderly diabetic populations. Early detection through such screenings could play a crucial role in preventing or delaying cognitive dysfunction. Future research should explore the gender disparities and complex biological pathways linking diabetes and AD for more targeted intervention strategies.

Limitations

Despite its important findings, this study has several limitations. Firstly, the sample size was confined to a specific geographic region, which may limit the generalizability of the results to broader populations. Secondly, the study design was observational and cross-sectional, which restricts the ability to establish causality between diabetes, hematological changes, and AD. Thirdly, the study did not control for potential confounding variables such as lifestyle factors, medication history, genetic predisposition, or comorbid conditions like hypertension or cardiovascular diseases, all of which can influence cognitive health.

Furthermore, the cognitive status of participants was not assessed using standardized neuropsychological tools, which could have provided more robust correlations. Lastly, the absence of longitudinal follow-up limits insights into disease progression and the temporal relationship between diabetes and cognitive decline.

Recommendations

Future studies should include larger, multi-center populations with longitudinal designs to establish causality and progression patterns. Integrating neuroimaging, genetic profiling, and detailed cognitive assessments would also enhance the understanding of the complex interplay between metabolic disorders and neurodegeneration.

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