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Research Article

Alzheimer's disease Comorbidities and Inflammatory Parameters Correlate with Plasma GFAP: Conducting A Large-Scale Screening for AD

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Abstract

Background: Glial Fibrillary Acidic Protein (GFAP) is a major protein found in the astrocytic cells of the brain, and it is considered a marker of Alzheimer's disease. This study aimed to examine the most common comorbidities in AD and how they affect the clinical management of patients. Additionally, we will delve into the early detection and diagnosis of AD, highlighting certain physiological markers and evaluating the relationship between comorbidities and GFAP, emphasizing its significance in the advancement of AD.
Methodology: The research was conducted at General Hospitals Al Sader General Teaching in the province of Al-Najaf al-Ashraf and Karbala Hospital and external laboratories in Iraq. The study included sixty-three Iraqi individuals who underwent medical evaluations between September 2023 to May 2024. Thirty healthy adults without Alzheimer's disease or any other comorbidities or inflammatory disease were included.
Results: A total of 63 individuals diagnosed with AD participated in the study, including sixty-three AD patients and thirty controls. The median age of the AD participants was 73.14 ± 2.02 years, and the median BMI was 30.32 ± 1.53 kg/m^2. AD patients showed a significant decrease in HB and HCT compared to controls. Additionally, elevated ESR, Cr, urea, AST, and ALP levels were observed in the Alzheimer's disease group. IBS patients exhibited higher circulating GFAP concentrations (6.30 ± 2.09 pg/mL) than the healthy group. The area under the ROC curve was 0.893, and the GFAP cut-off was 0.517 pg/mL. Elevated GFAP concentrations were found to be correlated with higher ESR, CR, and ALP levels in AD patients.
Conclusion: The correlated GFAP and ESR levels in AD patients showed the potential connection of risk factors for AD and how they may be related to inflammatory mechanisms. Reduced kidney function was associated with increased levels of GFAP in AD patients. Furthermore, increased GFAP and ALP serum levels can be referred to as partly reflecting neuronal loss in Alzheimer's disease patients.

1. Introduction

Alzheimer's disease (AD) is a prevalent form of dementia marked by neuritic plaques and neurofibrillary tangles. The disease is caused by an accumulation of amyloid-β (Aβ) fibrils in the brain, which results in the formation of plaques and neurofibrillary tangles (NFTs),

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which in turn cause memory loss, behavioral abnormalities, and organ failure [1, 2]. In his eighth edition of the psychiatric textbook, Emil Kraepelin identified the ailment as Alzheimer's disease [3, 4].

Brain disorders such as Alzheimer's disease (AD) can cause a progressive loss of cognitive function. Other factors that can cause this include infections, intoxication, abnormalities in the pulmonary and circulatory systems that reduce the amount of oxygen reaching the brain, deficiencies in nutrition, a deficiency of vitamin B12, tumors, and more [5, 6].

In the diagnosis of Alzheimer's disease, patients are divided into three primary clinical stages: pre-clinical AD, mild cognitive impairment (MCI), and overt AD. These classifications are essential for understanding and addressing the progression of the disease [7]. The existing categorization method fails to take into account significant prognostic factors, such as concurrent illnesses. Coexisting conditions can influence the clinical condition and development of AD. Research indicates a connection between AD and long-term conditions such as diabetes, heart disease, depression, and inflammatory bowel disease [8–10].

Astrocytes comprise 30-40% of the central nervous system (CNS) cells. This demonstrates their crucial role in supporting and maintaining the CNS's functions [11]. Astrocytes are a key part of the blood-brain barrier and play a central role in the normal function of synapses and in maintaining axonal metabolic processes by regulating ion balance [12]. GFAP is the essential intermediate filament for astrocytes, playing a crucial role in their structure and function [13]. GFAP, a type-III intermediate filament, consists of 432 amino acids encoded by a gene on chromosome 17q21.1-q25. It is unequivocally expressed in mature astrocytes in various brain regions and Mueller cells in the retina. GFAP is expressed in non-neural cells such as Schwann cells, mature glial cells in the gut, and hepatic stellate cells in the periphery [14, 15].

In the realm of disease management for AD patients, the simultaneous existence of other medical conditions can prove to be disadvantageous. In this discussion, we will explore the most common comorbidities in AD and how they affect the clinical management of patients. Additionally, we will delve into the early detection and diagnosis of AD, highlighting certain physiological markers and evaluating the relationship between comorbidities and GFAP, emphasizing its significance in the advancement of AD.

2. Methods

2.1. Study Setting

The study was conducted at Al Sader General Teaching Hospital in Al-Najaf al-Ashraf, Karbala Hospital, and external laboratories in Iraq.

2.2. Participants

In the research, sixty-three Iraqi individuals underwent health assessments from September 2023 to May 2024. Additionally, thirty healthy adults without Alzheimer's disease or any other comorbidities or inflammatory disease were included.

2.3. Inclusion and Exclusion Criteria

Study participants underwent thorough health assessments and had to meet specific criteria. They were required to be between 65 and 80 years old and have been diagnosed with Alzheimer's disease. Furthermore, individuals were excluded from the study if they had HIV, COVID-19, or hepatitis infections, or if they had used antimicrobials within the previous month.

2.4. Assessment criteria

The participants underwent a thorough health evaluation, which involved analyzing their blood count (hemoglobin, red blood cell count, hematocrit, white blood cell count, and platelets), erythrocyte sedimentation rate (ESR), and blood chemistry (urea, creatinine, ALT, AST, and ALP). It is essential to remember the following information: Sixty-three adult individuals were diagnosed with Alzheimer's disease based on confirming memory loss and cognitive impairments using neurological tests, such as the Montreal Cognitive Assessment (MOCA) and Mini-Mental Status Examination (MMSE) [16, 17]. However, the ultimate AD diagnostic protocol can only be performed post-mortem to detect Aβ and tau NFTs in the brains of deceased patients [18].

2.5. BMI Calculation

BMI was determined by dividing a person's self-reported weight in kilograms by the square of their height in meters. BMI categories were based on the WHO physical status classification17 as follows: underweight (BMI $<$18.5 kg/m^2), normal weight (BMI 18.5-25 kg/m^2), overweight (BMI 25-30 kg/m^2), or obese (BMI $>$30 kg/m^2) [19].

2.6. Blood Sample Collection and Laboratory Analyses

Blood was obtained through venipuncture using sterile 5 mL syringes. After collection, each sample was promptly placed into specific tubes. Subsequently, the blood was left to coagulate at room temperature for 10 minutes before being centrifuged at 6000 rpm for 15 minutes. The resulting serum was then frozen and stored at -80 ºC for later laboratory analysis.

Each individual had a blood sample taken in an EDTA tube so that the full blood cell counts (Hb, RBC, WBC (total and subtypes), and platelet counts) could be determined. The procedure for storing blood samples was previously explained [20]. Westergren's method was employed to measure ESR. Male ESRs typically range from 0 to 15 mm/h, while female ESRs typically range from 0 to 20 mm/h. We have disregarded the variations in ESR values for gender differences in this investigation. In order to keep the statistical data analysis simple, this was done.

Serum levels of kidney function markers using colorimetric assays. Specific kits from Biolabo SA, France were used to determine serum urea and creatinine levels. ALT, AST, and ALP were quantified using enzymatic techniques and appropriate kits from Biolabo SA, France. We consistently measured the concentration of Glial fibrillary acidic protein (GFAP) using a validated enzyme-linked immunosorbent

assay (ELISA) kit. The assay had a detection limit of 400 ng/L, with intra- and inter-assay precision of less than 0.9% and less than 2.3%, respectively. All GFAP measurements were performed by investigators blinded to the patient's characteristics and outcomes.

2.7. Statistical Analysis

Version 26.0 of the Statistical Package for Social Sciences (SPSS) program was used to analyze the data. In order to compare patient and control subgroups, descriptive statistics like means and standard deviations have to be calculated as part of the significance testing process. The associations between markers and factors were assessed using Pearson and Spearman correlation coefficients. Excel 2016 for Microsoft Office was used to build data visualizations. A significance level of $P < 0.05$ was used for all statistical analyses.

3. Results

3.1. Patient Characteristics

The study included 93 individuals, with a 30-control group and 63 Alzheimer's disease patients group. The median age of AD patients was 73.14 ± 2.02 years, significantly higher than the control group's 28.5 ± 3.1 years. The BMI of AD patients averaged 30.32± 1.53, compared to 20.44 ± 0.91in controls. Among the AD patients, 30.8% were male and 69.2% were female, similar to the control group with an equal gender distribution Table 1.

Hematological parameters such as Hb, RBC, HCT, WBC, and PLT were comparable between AD patients and controls. Specifically, Hb levels were 11.92 ± 0.586 g/dL in AD patients, which is a significant decrease compared to 14.82 ± 0.306 g/dL in controls. RBC counts were 4.11 ± 0.212 × 10^6/µL in AD patients compared to 4.275 ± 0.085 × 10^6/µL in controls. In patients with AD, the HCT values showed a significant decrease to 35.771 ± 1.6 compared to 46.75 ± 1.49 in the control group. Patients with Alzheimer's disease had a white blood cell count (WBC) of 14.12 ± 2.28 × 10^3/µL, which was significantly higher than the WBC count of 5.15 ± 0.11 × 10^3/µL in the control group. PLT counts were 203.75 ± 28.80 × 10^3/µL in AD patients and 204 ± 32.632 × 10^3/µL in controls.

In patients with AD, the ESR levels showed a significant increase at 90.86 ± 7.008 g/dL compared to 11.25 ± 1.25 g/dL in the controls. These findings underscore the importance of further research in this area to better understand the relationship between ESR levels and Alzheimer's disease Table 1.

Renal function markers such as urea and creatinine showed a significant increase between groups, with AD patients recording urea levels of 79.8 ± 8.62 mg/dL and creatinine levels of 1.3 ± 0.15 mg/dL Table 1.

However, significant differences were observed in ALT, AST, and ALP levels. In AD patients, there was no significant difference found in ALT levels compared to the control group. While, AD patients had markedly higher AST (28.14 ± 1.77 mg/dL), and ALP (91.86 ± 10.85 mg/dL) compared to controls Table 1.

Table 1: Baseline clinical and laboratory characteristics of the study AD patients and control

Parameters	Patient (Mean±Se)	Control (Mean±Se)	P value <0.05
Age (year)	73.14 ± 2.02 *	28.5 ± 3.1	0.01
BMI (kg/m^2) Normal weight Overweight Obese	30.32± 1.53 * (14 %) (24.6 %) (61.4 %)	20.44 ± 0.91	0.002
Gender	Male (30.8%) Female (69.2%)	Male (50%) Female (50%)	
HB (g/dL)	11.92 ± 0.586*	14.82 ± 0.306	0.007
RBC (106 /µL)	4.11 ± 0.212	4.275 ± 0.085	0.589
HCT%	35.771 ± 1.6*	46.75 ± 1.49	0.002
WBC (10^3 /µL)	14.12 ± 2.28*	5.1 5 ± 0.11	0.018
PLT (10^3 /µL)	204± 32.632	203.75 ± 28.80	0.99
ESR (mm/hr)	90.86 ± 7.008*	11.25 ± 1.25	0.003
Urea (mg/dL)	79.8 ± 8.62*	24.525 ± 2.21	0.001
Creatinine (mg/dL)	1.3 ± 0.15*	0.38 ± 0.056	0.002
ALT (IU/L)	16.29 ± 1.61	18.5 ± 1.55	0.063
AST (IU/L)	28.14 ±1.77 *	17.25 ± 2.28	0.008
ALP (IU/L)	91.86 ± 10.85 *	53.25 ± 1.797	0.012

* P< 0.05 statistically significant with the control group

Smoking was less prevalent among patients with Alzheimer's disease (AD), with only 14.3% being smokers. Among AD patients, 57.1% had a history of stroke disease, and 28.6% had a history of epilepsy disease. Additionally, 89% of AD patients showed a high prevalence of hypertension. Moreover, diabetes had an impact on 71% of AD patients, and 38.7% of patients tested positive for CRP Table 2.

Table 2: The Impact of Comorbid Diseases on Alzheimer's Disease

Disease	YES	NO
Smoking	(14.3 %)	(85.7 %)
Stroke	(57.1 %)	(42.9 %)
Epilepsy	(28.6 %)	(71.4 %)
Hypertension	(89%)	(11 %)
Diabetic	(71%)	(29 %)
CRP+	(38.7%)	(61.3%)

3.2. Evaluation of biomarkers associated with AD

GFAP levels were assessed as a specific biomarker between the studied groups. Our data showed a significant increase ($p < 0.05$) in GFAP levels (6.302 ± 2.09 pg/mL) in patients diagnosed with AD compared to the healthy control group (0.427 ± 0.029 pg/mL). The statistical mean was not shown in the Figure 1. Interestingly, there was a significant increase in GFAP levels observed in patients with higher hypertension, and epilepsy and in female patients among individuals with AD. The statistical mean was not shown in the Figure 2.

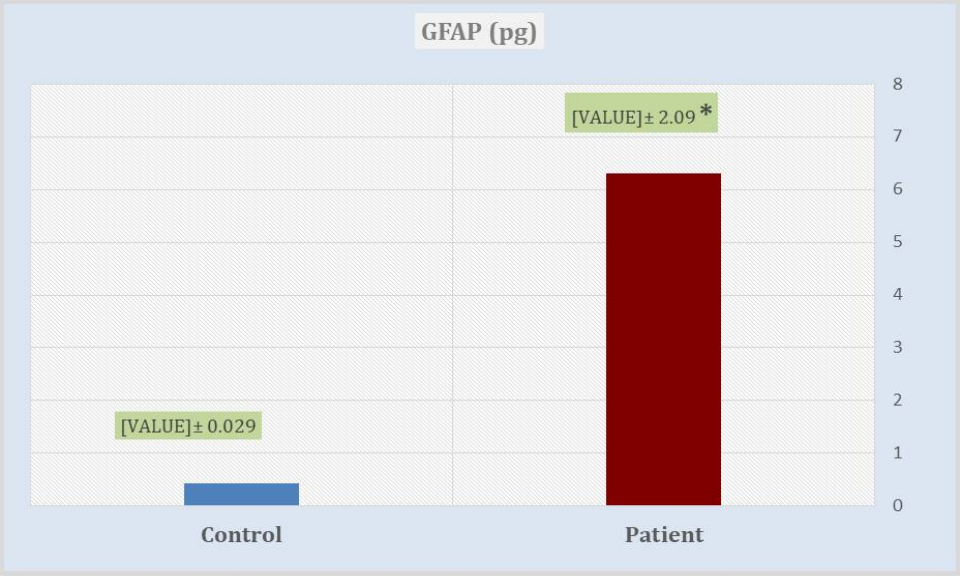


Figure 1: Comparison of the GFAP (pg) between Groups of Patients with AD and healthy group

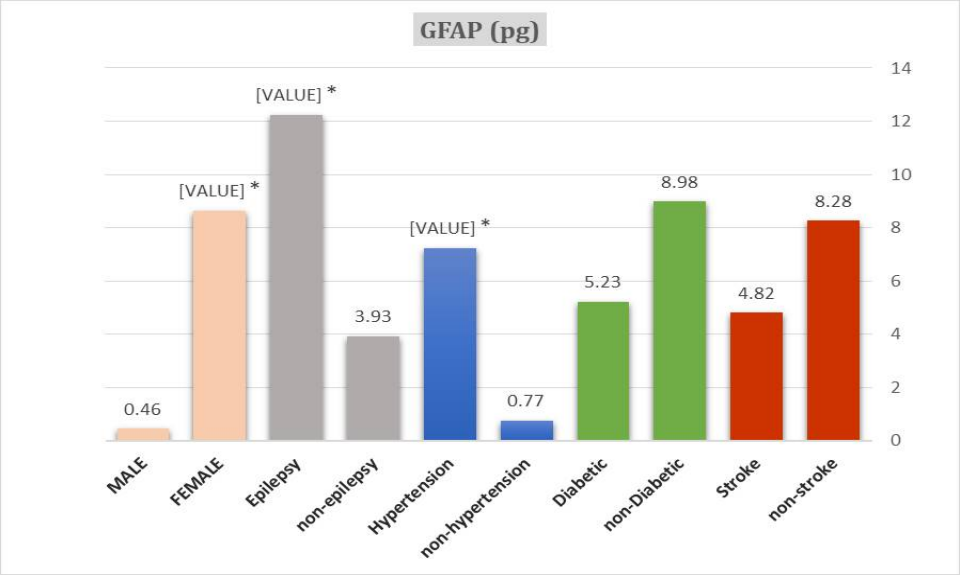
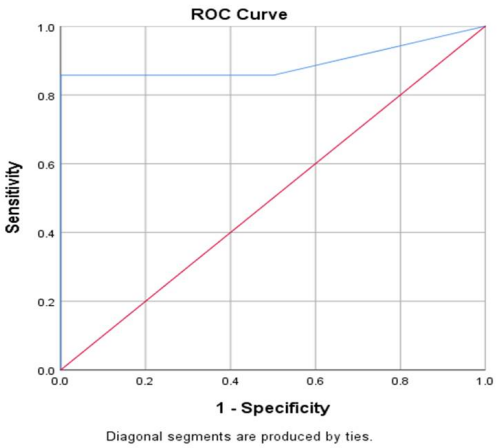


Figure 2: Comparison of the GFAP (pg) among Patients with Disease Comorbidities in Alzheimer's Disease

In the Receiver Operating Characteristic Area Under the Curve (ROC AUC) analysis, GFAP levels demonstrate a moderate ability to discriminate between subjects, with an AUC of 0.893 ± 0.108. This suggests that GFAP can distinguish between individuals with and

without AD-related characteristics. The cut-off value of 0.517 provides a practical threshold for identifying individuals based on their GFAP levels, as illustrated in Figure 3.



ROC AUC	Std. Error	Cut off value	SIG
.893	0.108	0.517	0.038

Figure 3: ROC curve for discrimination of the GFAP (pg) in all subjects

3.3. Correlation of Serum GFAP Levels with Clinical Biochemical Factors

The study also examined the association of GFAP with various parameters in patients with AD, focusing on the correlation with inflammation. The analysis revealed several significant correlations. There was a positive correlation between GFAP and ESR levels (r = 0.901, p = 0.006), indicating that higher GFAP levels are associated with higher ESR levels in AD patients. Additionally, GFAP showed a positive correlation with creatinine (r = 0.773, p = 0.041) and ALP (r = 0.930, p = 0.002). Other parameters, including age, BMI, Hb, HCT, WBC, PLT, urea, and AST, did not show significant correlations with GFAP levels Table 3.

Table 3: Pearson Correlation of Glial fibrillary acidic protein with other laboratory parameters in patients with AD

GFAP Correlations		
Parameters	**Pearson Correlation**	**P<0.05**
Age (year)	0.495	0.259
BMI (kg/m^2)	0.644	0.118
HB (g/dL)	-.255	0.581
RBC (10^6 /µL)	-0.170	0.716
HCT%	-0.250	0.589
WBC (10^3 /µL)	0.2403	0.236
PLT (10^3 /µL)	-0.514	0.238
ESR (mm/hr)	.901**	0.006
Urea (mg/dL)	0.547	0.204
Creatinine (mg/dL)	0.773*	0.041
ALT (IU/L)	-0.270	0.558
AST (IU/L)	-.206	0.657
ALP (IU/L)	0.930**	0.002

* Correlation is significant at the 0.05 level (2-tailed)

The study also examined the association of GFAP with various impact diseases in patients with AD. There was a positive correlation between GFAP and gender (r = 0.791, p = 0.034), indicating that higher GFAP levels are associated with females in AD patients. Additionally, GFAP showed a positive correlation with epilepsy (r = 0.789, p = 0.03) and CRP+ (r = 0.691, p = 0.025) Table 4.

Table 4: Spearman's Rho Correlation of Glial fibrillary acidic protein with other Impact of Disease in patients with AD

Disease	GFAP Correlations Spearman's Rho correlation	P<0.05
Gender	0.791*	0.034
Smoking	-0.204	0.661
Stroke	-.289	0.530
Epilepsy	0.789*	0.03
Hypertension	0.204	0.65
Diabetic	-0.158	0.735
CRP+	0.691*	0.025

* Correlation is significant at the 0.05 level (2-tailed)

4. Discussion

The most prevalent neurodegenerative disease in the world, Alzheimer's disease (AD), is linked to other comorbid conditions. Clinical and molecular research data indicates that many groups may be more susceptible to AD as a result of chronic illnesses such as diabetes, heart disease, depression, and inflammatory bowel disease [21]. Furthermore, demonstrated by our research These results were in line with the theory that one of the main risk factors for AD is age [22]. The prevalence of AD rises with age, reaching an estimated 19% in those 75–84 years old [23] and thirty to thirty-five and potentially even 50%, in people who are over 85 years old [24]. Therefore, in the cognitively healthy brain, as one age, the volume and weight of the brain decrease, the ventricles continue to grow, and certain parts of the brain experience an absence of neurotransmitters and dendrites which is followed by SP and new financial technology [25].

The current study encompasses a balanced male-female cohort, revealing significant biochemical differences between AD patients and controls. In line with previous studies, our results Table 1 indicate the median age and BMI of AD patients were higher than those of the control group. Aging is a significant risk factor for AD. An earlier study by [26] found that an elevated range of age and body mass index (BMI) in this text is associated with an increased risk of Alzheimer's disease. Additionally, the research advances our knowledge of the anemia linked to the pathogenesis of Alzheimer's [26]. According to studies, anemia was present in 6.1% of people and was linked to a 41% higher risk of AD. Due to variations in cerebral perfusion and white matter integrity, both low and high hemoglobin levels are linked to an increased risk of dementia, including AD [27].

Studies frequently concentrate on anemia and the lower range of hemoglobin levels, however there are a number of ways in which having a high hemoglobin level can be harmful or indicative of harmful conditions. First, higher readings in the presence of excess free iron and functional anemia may result from lysis of erythrocytes. Secondly, erythrocytosis arises as a result of systemic decreases in blood oxygenation, frequently brought on by heart failure, chronic renal disease, chronic obstructive lung disease, or smoking [28]. Although all of these are risk factors for dementia, the risk estimates for high hemoglobin were not affected when patients with common causes of erythrocytosis were excluded from our study. Third, hyperviscosity of the blood may be a risk factor for ischemia, as is commonly observed in polycythemia vera patients [29].

Our study revealed a significant increase in ESR levels in AD patients compared to healthy controls. Particularly in female patients over 50, we found a strong correlation between ESR and AD. Compared to control patients, female patients with unusually elevated ESR levels had a 2.31-fold increased risk of acquiring AD within a year after the lab test. This suggests that ESR is a risk factor for AD and might be examined in a prospective study to determine the prognosis of AD [30]. Although the very small sample size of the prior study prevented it from reaching significance, it did show an increasing trend for ESR in AD females [31]. Furthermore, we discovered that the elevated ESR in female patients with AD remains, indicating a potential involvement of inflammation in the etiology of AD [32], but we cannot completely rule out the possibility that its rise is attributable to AD medication.

The results of this research demonstrated that patients' (urea and creatinine) levels were significantly higher than those compared to the healthier category. It is acknowledged that there is a relationship between brain activity and renal function. Clinical research has shown that individuals with chronic kidney disease (CKD) are more likely to have cognitive impairment and Alzheimer's disease (AD) [33]. Consequently, it's possible that AD and CKD have similar risk factors and underlying mechanisms [21]. Undoubtedly, a number of risk factors are associated with both chronic kidney disease (CKD) and Alzheimer's disease (AD), including advanced age (>60 years), family history, lifestyle variables (such as poor food, smoking, and excessive alcohol use), and exposure to certain chemicals [34, 35].

Liver function is evaluated by measuring the levels of biochemical markers in peripheral blood, such as alkaline phosphatase, alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Liver damage is measured in routine clinical practice using AST and alanine aminotransferase (ALT) [36, 37]. and are elements linked to metabolic and cardiovascular illnesses [38, 39], established risk factors for dementia and Alzheimer's [40, 41].

Two potential processes, even the precise ones are still unknown, could account for the changed enzyme levels in AD. Reduced ALT levels first result in less pyruvate, which is needed for the liver's process of gluconeogenesis, which produces glucose, which is then dispersed throughout the body's tissues as an energy source [42], therefore affecting the equilibrium of energy. Second, changed levels of ALT and AST may have an impact on glutamate, a central nervous system excitatory neurotransmitter that is crucial for memory and synaptic transmission [43].

Higher alkaline phosphatase levels were found in AD patients, and there was a negative correlation between memory and aging and cognition [44]. In the liver, kidneys, and brain endothelial cells, alkaline phosphatase is an enzyme that is predominantly expressed [45]. Through its contribution to γ-aminobutyric acid metabolism, the neuronal form of alkaline phosphatase plays a role in activity-dependent cortical processes and developmental plasticity [46]. alterations in alkaline phosphatase plasma levels can result from damage to the central nervous system [47]. The damaging and toxic effects of electronic hookah vapours can worsen oxidative stress, particularly on liver tissue, and increase the likelihood of liver disease development over time [48].

Additionally, this study exhibited elevated GFAP levels in AD patients. The results aligned with the research conducted by [26, 49], which indicated a substantial difference in blood GFAP levels between those with Alzheimer's disease and the control group [26, 49]. One

indicator of astrogliosis is glial fibrillary acidic protein (GFAP). There have been reports of increased postmortem levels in AD patients' brains and AD patients' CSF [50, 51]. In a study of older persons who were cognitively normal, [52] discovered that GFAP was linked to a higher risk of dementia and a quicker rate of cognitive deterioration. Based on these findings, they concluded that GFAP has the potential to be a predictive blood-based biomarker for AD [52]. A different recent study found that individuals with early stages of AD had higher plasma GFAP levels, which may indicate that astrocytic reactivity or damage begins during the preclinical stage of AD [53].

Alzheimer's disease can result from irreversible cerebrovascular injury caused by hypertension (HT), which alters the structure and function of the cerebral microcirculation [54]. Similar to several neurodegenerative diseases and brain ischemia, hypertension causes a state of brain damage that increases GFAP expression and production. In addition to causing cerebrovascular alterations, cerebral hypertension can also result in dementia, neurodegeneration, and brain injury (vascular dementia) [55]. According to the research, GFAP may be involved in the early stages of cardiac hypertrophy in hypertension, although there appears to be more to this action than just blood pressure [56].

Also, the moderate ROC AUC (0.893) for GFAP levels suggests that this biomarker could be useful in distinguishing AD patients from healthy controls, offering a moderate discriminatory potential. Moreover, a positive correlation was found between GFAP and (ESR, Creatinine, ALP, gender, Epilepsy, and CRP+) in AD patients. The results indicate that there may be a confounding effect on plasma concentrations, such as lower kidney function leading to somewhat higher biomarker concentrations, particularly for GFAP, as the creatinine level was positively correlated with GFAP levels. This could explain the association between plasma biomarker concentrations and creatinine [57].

Women have been found to have greater amounts of GFAP in several studies [58, 59], and our investigation confirmed these findings. Sex hormones may be linked to neuroinflammation and the astrocyte response [60], which in turn may be linked to GFAP levels [61]. The serum GFAP level is a new diagnostic tool that can be used to distinguish between psychogenic attacks and epileptic seizures [62].

Previous studies have demonstrated a correlation between an elevated blood C-reactive protein (CRP) and an increased risk of Alzheimer's disease (AD) [63]. Systemic inflammation is caused by chemicals or injuries that trigger the production of CRP, a protein whose levels rise with age [64]. Age-related macular degeneration, post-stroke inflammation, and cardiovascular disease are among the chronic diseases linked to aging that have been linked to CRP etiology [65–67].

Type 2 diabetes and cardiovascular disease, two conditions that are linked to an increased risk of Alzheimer's disease, have been connected to peripheral chronic inflammation [68]. Age-related GFAP overexpression and release from aged astrocytes occur when oxidative stress and persistent low-grade inflammation cause astrocytes to become reactive [69].

These findings underscore the role of GFAP and ESR in the pathophysiology of AD and related Comorbidities disorders, suggesting that targeting these cells and their signaling pathways could provide new therapeutic avenues. In summary, the study found that GFAP levels in AD patients are significantly correlated with, ESR, creatinine, and ALP levels, as well as correlated with female gender and CRP levels, suggesting potential pathways through which GFAP may influence or reflect AD pathology.

5. Conclusion

In conclusion, our findings support the notion that AD is a multifaceted condition influenced by various factors, including age, gender, BMI, and metabolic health. The correlated GFAP and ESR levels in AD patients showed the potential connection of risk factors for AD and how they may be related to inflammatory mechanisms. GFAP levels were higher in AD individuals with reduced renal function. In clinical translation, kidney function should be taken into account since it may have an impact on the precision of blood biomarkers associated with dementia.

Furthermore, increased GFAP and ALP serum levels can be used as suitable biomarkers for the diagnosis of AD disease progression and may partly reflect neuronal loss. However, further research is needed to understand the mechanisms linking these circulating biomarkers to AD.

Article Information

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Informed Consent: Informed consent was obtained from all participants involved in the study.

Data Availability Statement: The data supporting the findings of this study are available from the corresponding author.

Clinical Trial Registration: Not applicable.

Reporting Guidelines Statement: This observational study was conducted in accordance with the STROBE reporting guidelines.

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

References

[1] R. Cacabelos. Pharmacogenomics of Alzheimer's and Parkinson's diseases. *Neuroscience letters*, 726:133807, 2020.

[2] U. Sehar, P. Rawat, A. P. Reddy, J. Kopel, and P. H. Reddy. Amyloid beta in aging and Alzheimer's disease. *International journal of molecular sciences*, 23(21):12924, 2022.

[3] M. Borri. Memory and Alzheimer's disease. *Medicina nei secoli: Journal of History of Medicine and Medical Humanities*, 34(2): 57–70, 2022.

[4] S. Heckers and K. S. Kendler. The evolution of Kraepelin's nosological principles. *World Psychiatry*, 19(3):381–388, 2020.

[5] T. Piekut, M. Hurła, N. Banaszek, P. Szejn, J. Dorszewska, W. Kozubski, and M. Prendecki. Infectious agents and Alzheimer's disease. *Journal of Integrative Neuroscience*, 21(2):73, 2022.

[6] Z. Breijyeh and R. Karaman. Comprehensive review on Alzheimer's disease: causes and treatment. *Molecules*, 25(24):5789, 2020.

[7] J. Zhou, M. Benoit, and M. G. Sharoar. Recent advances in pre-clinical diagnosis of Alzheimer's disease. *Metabolic Brain Disease*, 37 (6):1703–1725, 2022.

[8] J. A. Santiago and J. A. Potashkin. The impact of disease comorbidities in Alzheimer's disease. *Frontiers in aging neuroscience*, 13: 631770, 2021.

[9] S. Chatterjee and A. Mudher. Alzheimer's disease and type 2 diabetes: a critical assessment of the shared pathological traits. *Frontiers in neuroscience*, 12:383, 2018.

[10] P. Fu, M. Gao, and K. K. L. Yung. Association of intestinal disorders with Parkinson's disease and Alzheimer's disease: a systematic review and meta-analysis. *ACS chemical neuroscience*, 11(3):395–405, 2019.

[11] Y. Chen, C. Qin, J. Huang, X. Tang, C. Liu, K. Huang, others, and L. Zhou. The role of astrocytes in oxidative stress of central nervous system: A mixed blessing. *Cell proliferation*, 53(3), 2020. e12781.

[12] A. Verkhratsky, V. Parpura, B. Li, and C. Scuderi. Astrocytes: the housekeepers and guardians of the CNS. In *Astrocytes in psychiatric disorders*, pages 21–53. Cham: Springer International Publishing, 2021.

[13] A. M. Jurga, M. Paleczna, J. Kadluczka, and K. Z. Kuter. Beyond the GFAP-astrocyte protein markers in the brain. *Biomolecules*, 11 (9):1361, 2021.

[14] K. Goluba, L. Kunrade, U. Riekstina, and V. Parfejevs. Schwann cells in digestive system disorders. *Cells*, 11(5):832, 2022.

[15] H. K. Saboowala. *Exploring the Clinical use of Blood GFAP as an emerging Biomarker in Brain/Spinal cord Disorders and Neurological Diseases*. 2023.

[16] A. Abdelhak, M. Foschi, S. Abu-Rumeileh, J. K. Yue, L. D'Anna, A. Huss, others, and H. Tumani. Blood GFAP as an emerging biomarker in brain and spinal cord disorders. *Nature Reviews Neurology*, 18(3):158–172, 2022.

[17] T. C. Pinto, L. Machado, T. M. Bulgacov, A. L. Rodrigues-Júnior, M. L. Costa, R. C. Ximenes, and E. B. Sougey. Is the Montreal Cognitive Assessment (MoCA) screening superior to the Mini-Mental State Examination (MMSE) in the detection of mild cognitive impairment (MCI) and Alzheimer's Disease (AD) in the elderly? *International psychogeriatrics*, 31(4):491–504, 2019.

[18] M. Nikolac Perkovic, A. Videtic Paska, M. Konjevod, K. Kouter, D. Svob Strac, G. Nedic Erjavec, and N. Pivac. Epigenetics of Alzheimer's disease. *Biomolecules*, 11(2):195, 2021.

[19] D. Eratne, S. M. Loi, S. Farrand, W. Kelso, D. Velakoulis, and J. C. Looi. Alzheimer's disease: clinical update on epidemiology, pathophysiology and diagnosis. *Australasian psychiatry*, 26(4):347–357, 2018.

[20] A. D. Ware. The complete blood count and white blood cell differential. In *Contemporary practice in clinical chemistry*, pages 429–444. Academic Press, 2020.

[21] Santiago J. A. and J. A. Potashkin. The impact of disease comorbidities in Alzheimer's disease. *Frontiers in aging neuroscience*, 13: 631770, 2021.

[22] M. V. F. Silva, C. D. M. G. Loures, L. C. V. Alves, L. C. De Souza, K. B. G. Borges, and M. D. G. Carvalho. Alzheimer's disease: risk factors and potentially protective measures. *Journal of biomedical science*, 26(1):33, 2019.

[23] A. N. Abbas, R. A. Al-Masaoodi, S. Hassan, and M. K. Al-Shemery. The relationship between hormonal levels and hematological parameters in cystic ovarian syndrome. *Journal of Medicine and Life*, 16(6):937, 2023.

[24] D. A. Kadhim and A. N. Al-Dujaili. Estimation of nephrin level in sickle cell anemia patients associated with nephropathy. In *In AIP Conference Proceedings*, volume 2290. AIP Publishing, 2020.

[25] R. A. Al-Masaoodi, S. H. Alwaid, and M. K. Al-SHEMERY. DETERMINATION THE EFFECT OF IRON OVERLOAD ON VITAMIN D AND THE PERCENTAGE OF EACH BLOOD GROUPS IN PATIENTS WITH THALASSEMIA. *Periódico Tchê Química*, 17(36), 2020.

[26] M. K. Al-Shemery and A. N. Al-Dujaili. Estimation of Procollagen Type III Peptide (PIIIP) Level in Thalassemia Patients. *SCOPUS IJPHRD CITATION SCORE*, 10(7):653, 2019.

[27] F. J. Wolters, H. I. Zonneveld, S. Licher, and L. G. Cremers. Heart Brain Connection Collaborative Research Group, Ikram, M. K., ... Ikram, M. A. (2019). Hemoglobin and anemia in relation to dementia risk and accompanying changes on brain MRI. *Neurology*, 93(9): e917–e926, 2019.

[28] M. J. Cascio and T. G. DeLoughery. Anemia: evaluation and diagnostic tests. *Medical Clinics*, 101(2):263–284, 2017.

[29] D. W. Shin, J. Y. Gu, J. S. Kim, J. S. Jung, D. Y. Shin, Y. Koh, others, and H. K. Kim. Increased plasma viscosity in plasma cell dyscrasia and whole blood viscosity in polycythemia vera. *Clinical Hemorheology and Microcirculation*, 70(1):59–67, 2018.

[30] N. Vale, M. Pereira, and R. A. Mendes. Systemic Inflammatory Disorders,Immunosuppressive Treatment and Increase Risk of Head and Neck Cancers—A Narrative Review of Potential Physiopathological and Biological Mechanisms. *Cells*, 12(17):2192, 2023.

[31] X. Li, X. Zhu, W. Zhang, F. Yang, J. Hui, J. Tan, others, and Z. Yang. The etiological effect of a new low-frequency ESR1 variant on Mild Cognitive Impairment and Alzheimer's Disease: a population-based study. *Aging (Albany NY)*, 10(9):2316, 2018.

[32] N. Akdogan, S. Dogan, P. Incel-Uysal, E. Karabulut, C. Topcuoglu, B. Yalcin, and N. Atakan. Serum amyloid A and C-reactive protein levels and erythrocyte sedimentation rate are important indicators in hidradenitis suppurativa. *Archives of dermatological research*, 312 (4):255–262, 2020.

[33] C. Y. Zhang, F. F. He, H. Su, C. Zhang, and X. F. Meng. Association between chronic kidney disease and Alzheimer's disease: an update. *Metabolic Brain Disease*, 35 :883–894, 2020.

[34] D. M. Kelly and P. M. Rothwell. Disentangling the relationship between chronic kidney disease and cognitive disorders. *Frontiers in Neurology*, 13:830064, 2022.

[35] G. D. Stanciu, D. C. Ababei, V. Bild, W. Bild, L. Paduraru, M. M. Gutu, and B. I. Tamba. Renal contributions in the pathophysiology and neuropathological substrates shared by chronic kidney disease and Alzheimer's disease. *Brain Sciences*, 10(8):563, 2020.

[36] S. Sookoian, G. O. Castaño, R. Scian, T. F. Gianotti, H. Dopazo, C. Rohr, others, and C. J. Pirola. Serum aminotransferases in nonalcoholic fatty liver disease are a signature of liver metabolic perturbations at the amino acid and Krebs cycle level. *The American journal of clinical nutrition*, 103(2):422–434, 2016.

[37] S. Sookoian and C. J. Pirola. Alanine and aspartate aminotransferase and glutamine-cycling pathway: their roles in pathogenesis of metabolic syndrome. *World journal of gastroenterology: WJG*, 18(29):3775, 2012.

[38] R. A. Armstrong. Risk factors for Alzheimer's disease. *Folia neuropathologica*, 57(2):87–105, 2019.

[39] J. Leszek, E. V. Mikhaylenko, D. M. Belousov, E. Koutsouraki, K. Szczechowiak, M. Kobusiak-Prokopowicz, others, and G. Aliev. The links between cardiovascular diseases and Alzheimer's disease. *Current neuropharmacology*, 19(2):152–169, 2021.

[40] C. Y. Santos, P. J. Snyder, W. C. Wu, M. Zhang, A. Echeverria, and J. Alber. Pathophysiologic relationship between Alzheimer's disease, cerebrovascular disease, and cardiovascular risk: a review and synthesis. *Alzheimer's Dementia: Diagnosis, Assessment Disease Monitoring*, 7:69–87, 2017.

[41] D. A. Kadhim and A. N. Al-Dujaili. Assessment of soluble receptor for advance glycation end product level in patients suffering from sickle cell anemia related with nephropathy. In *AIP Conference Proceedings (Vol*, number 1, 2398, 2022. AIP Publishing.

[42] K. Qian, S. Zhong, K. Xie, . D. Yu, R. Yang, and D. W. Gong. Hepatic ALT isoenzymes are elevated in gluconeogenic conditions including diabetes and suppressed by insulin at the protein level. *Diabetes/metabolism research and reviews*, 31(6):562–571, 2015.

[43] D. A. Kadhim and A. N. Al-Dujaili. Assessment of Tumor Necrosis Factor Related Weak Inducer of Apoptosis (TWEAK) level in Systemic Lupus Erythematosus patients (nephritis patients). In *BIO Web of Conferences, 108*, 2024. Article 04004.

[44] V. Boccardi, V. Bubba, I. Murasecco, M. Pigliautile, R. Monastero, R. Cecchetti, others, and ReGAL 2.0 Study Group. Serum alkaline phosphatase is elevated and inversely correlated with cognitive functions in subjective cognitive decline: results from the ReGAl 2.0 project. *Aging clinical and experimental research*, 33(3):603–609, 2021.

[45] K. Makris, C. Mousa, and E. Cavalier. Alkaline phosphatases: biochemistry, functions, and measurement. *Calcified tissue international*, 112(2):233–242, 2023.

[46] Y. Liang, Y. Mao, W. Liang, L. Liang, M. Suo, J. Xue, and H. Yang. Association of serum alkaline phosphatase and depression in US adults: a population-based cross-sectional study. *Frontiers in psychiatry*, 14, 2023. Article 1131105.

[47] S. H. Alwaid, M. K. Al-Shemery, and R. A. Al-Masaoodi. Prevalence Of Metabolic Syndrome And It's Complications Among Patients With Rheumatoid Arthritis. *International Journal of Pharmaceutical Research*, 09752366, 2020.

[48] R. S. Nima and D. Z. Aziz. The Oxidative Stress Induced by the Vapours of Electronic-Hookah on Mice Liver Tissues. *Systematic Reviews in Pharmacy*, 11(9):420–3, 2020.

[49] K. Y. Kim, K. Y. Shin, and K. A. Chang. GFAP as a potential biomarker for Alzheimer's disease: a systematic review and meta-analysis. *Cells*, 12(9):1309, 2023.

[50] P. Oeckl, S. Halbgebauer, S. Anderl-Straub, P. Steinacker, A. M. Huss, H. Neugebauer, others, and M. Otto. Glial fibrillary acidic protein in serum is increased in Alzheimer's disease and correlates with cognitive impairment. *Journal of Alzheimer's Disease*, 67(2): 481–488, 2019.

[51] C. Cicognola, S. Janelidze, J. Hertze, H. Zetterberg, K. Blennow, N. Mattsson-Carlgren, and O. Hansson. Plasma glial fibrillary acidic protein detects Alzheimer pathology and predicts future conversion to Alzheimer dementia in patients with mild cognitive impairment. *Alzheimer's research therapy*, 13(1):68, 2021.

[52] I. M. Verberk, M. B. Laarhuis, K. A. van den Bosch, J. L. Ebenau, M. van Leeuwenstijn, N. D. Prins, others, and W. M. van der Flier. Serum markers glial fibrillary acidic protein and neurofilament light for prognosis and monitoring in cognitively normal older people: a prospective memory clinic-based cohort study. *The lancet Healthy longevity*, 2(2):e87–e95, 2021.

[53] P. Chatterjee, S. Pedrini, E. Stoops, K. Goozee, V. L. Villemagne, P. R. Asih, others, and R. N. Martins. Plasma glial fibrillary acidic protein is elevated in cognitively normal older adults at risk of Alzheimer's disease. *Translational psychiatry*, 11(1):27, 2021.

[54] J. Klohs. An integrated view on vascular dysfunction in Alzheimer's disease. *Neurodegenerative Diseases*, 19(3-4):109–127, 2019.

[55] O. V. Kuryata, Y. S. Kushnir, V. S. Nedzvetsky, V. V. Korsa, and A. A. Tykhomyrov. Serum levels of the biomarkers associated with astrocytosis, neurodegeneration, and demyelination: Neurological benefits of citicoline treatment of patients with ischemic stroke and atrial fibrillation. *Neurophysiology*, 53(1):2–12, 2021.

[56] D. A. Kadhim and A. N. Al-Dujaili. Estimation of S100 calcium binding protein A8/calgranulin A (S100A8) level in Systemic Lupus Erythematosus patients (nephritis patients). In *BIO Web of Conferences, 108*, 2024. Article 04010.

[57] A. Pichet Binette, S. Janelidze, N. Cullen, J. L. Dage, R. J. Bateman, H. Zetterberg, others, and O. Hansson. Confounding factors of Alzheimer's disease plasma biomarkers and their impact on clinical performance. *Alzheimer's Dementia*, 19(4):1403–1414, 2023.

[58] A. L. Benedet, M. Milà-Alomà, A. Vrillon, N. J. Ashton, T. A. Pascoal, F. Lussier, others, and A. Stevensson. Differences between plasma and cerebrospinal fluid glial fibrillary acidic protein levels across the Alzheimer disease continuum. *JAMA neurology*, 78(12): 1471–1483, 2021.

[59] K. A. Maryam and N. A. Arshad. Estimation of osteoprotgrin level in B thalassemia patient. In *AIP Conference Proceedings*, volume 2144, 2019.

[60] N. C. Chisholm and F. Sohrabji. Astrocytic response to cerebral ischemia is influenced by sex differences and impaired by aging. *Neurobiology of disease*, 85:245–253, 2016.

[61] P. Chatterjee, S. Pedrini, E. Stoops, K. Goozee, V. L. Villemagne, P. R. Asih, others, and R. N. Martins. Plasma glial fibrillary acidic protein is elevated in cognitively normal older adults at risk of Alzheimer's disease. *Translational psychiatry*, 11(1):27, 2021.

[62] L. Simani, M. Elmi, and M. Asadollahi. Serum GFAP level: a novel adjunctive diagnostic test in differentiate epileptic seizures from psychogenic attacks. *Seizure*, 61:41–44, 2018.

[63] Q. Tao, T. F. Alvin Ang, S. C. Akhter-Khan, I. S. Itchapurapu, R. Killiany, X. Zhang, others, and Alzheimer's Disease Neuroimaging Initiative. Impact of C-reactive protein on cognition and Alzheimer disease biomarkers in homozygous APOE 4 carriers. *Neurology*, 97 (12):e1243–e1252, 2021.

[64] K. A. Walker, B. N. Ficek, and R. Westbrook. Understanding the role of systemic inflammation in Alzheimer's disease. *ACS chemical neuroscience*, 10(8):3340–3342, 2019.

[65] A. K. Shetty, R. Upadhya, L. N. Madhu, and M. Kodali. Novel insights on systemic and brain aging, stroke, amyotrophic lateral sclerosis, and Alzheimer's disease. *Aging and disease*, 10(2):470, 2019.

[66] L. K. Too, N. Hunt, and M. P. Simunovic. The role of inflammation and infection in age-related neurodegenerative diseases: lessons from bacterial meningitis applied to Alzheimer disease and age-related macular degeneration. *Frontiers in Cellular Neuroscience*, 15: 635486, 2021.

[67] L. Biscetti, E. Luchetti, A. Vergaro, P. Menduno, C. Cagini, and L. Parnetti. Associations of Alzheimer's disease with macular degeneration. *Front Biosci (Elite Ed)*, 9:174–191, 2017.

[68] Y. Chornenkyy, W. X. Wang, A. Wei, and P. T. Nelson. Alzheimer's disease and type 2 diabetes mellitus are distinct diseases with potential overlapping metabolic dysfunction upstream of observed cognitive decline. *Brain Pathology*, 29(1):3–17, 2019.

[69] M. Verkerke, E. M. Hol, and J. Middeldorp. Physiological and pathological ageing of astrocytes in the human brain. *Neurochemical Research*, 46(10):2662–2675, 2021.