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General Medicine

ASSOCIATION OF HAEMOGLOBIN LEVELS AND PLATELET COUNT WITH THE PROGRESSION OF ALZHEIMER'S DISEASE: A CROSS-SECTIONAL STUDY

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ABSTRACT **Background:** Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline. Recent studies show haemoglobin levels and platelet counts may influence or reflect disease progression due to their roles in oxygen transport and neuroinflammatory processes. This study investigated the association between these hematologic parameters and AD severity. **Methods:** A cross-sectional observational study was conducted at Sarawathi Institute of Medical Sciences (2023–2024) involving 57 clinically diagnosed AD patients aged ≥60 years. Participants were categorized based on MMSE scores into mild, moderate, and severe AD groups. Haemoglobin and platelet levels were measured and compared across these groups. Statistical analyses included ANOVA, Pearson's correlation. **Results:** Mean haemoglobin and platelet levels declined with increasing AD severity. Haemoglobin levels were 13.2 ± 1.5 g/dL (mild), 12.4 ± 1.8 (moderate), and 10.1 ± 2.2 (severe) ($p<0.001$). Platelet counts also declined significantly ($p=0.015$). Haemoglobin showed a strong positive correlation with MMSE score ($r=0.652$, $p<0.001$), while platelet count had a weaker correlation ($r=0.341$, $p=0.007$). Hypertension was associated with lower haemoglobin levels ($p=0.038$). **Conclusion:** Lower haemoglobin and platelet counts are associated with more severe cognitive decline in AD. These markers may serve as potential indicators of disease progression.

KEYWORDS : Alzheimer's disease, Haemoglobin, Platelet count, Cognitive decline, MMSE.

INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that primarily affects elderly individuals, leading to cognitive decline, memory loss, and impairment of daily functioning. It is the most common form of dementia, with significant societal and healthcare impacts. The pathophysiology of Alzheimer's disease is complex, involving a variety of molecular, cellular, and environmental factors. Despite decades of research, the exact etiology and progression of Alzheimer's disease remain incompletely understood, and the search for reliable biomarkers for early detection and progression monitoring continues.[1]

Haemoglobin levels and platelet count, though not traditionally linked to neurodegenerative diseases, have garnered attention in recent studies exploring their potential role in the progression of Alzheimer's disease. Haemoglobin, the protein responsible for oxygen transport in the blood, is crucial for maintaining overall brain health, as oxygen is essential for the metabolic activities of neurons. Low Haemoglobin levels have been associated with various neurological disorders, potentially contributing to cognitive decline by reducing cerebral oxygenation.[2]

Blood platelets, which play a central role in coagulation and immune responses, have also been implicated in neurodegenerative processes. Platelet activation and dysfunction are known to occur in Alzheimer's disease, and recent studies show that platelets may contribute to neuroinflammation, amyloid plaque deposition, and tau phosphorylation-hallmarks of Alzheimer's disease pathology. Alterations in platelet count and function might provide insight into the disease's progression and severity.[3]

This research aims to explore the relationship between Haemoglobin levels, blood platelet count, and the progression of Alzheimer's disease. By examining the potential correlations between these blood parameters and cognitive decline, this research may provide valuable insights into their role as biomarkers for early detection and progression monitoring in Alzheimer's disease. Understanding these connections could open avenues for novel therapeutic strategies and preventive measures targeting these hematologic factors to slow the disease's progression and improve patient outcomes.

Method:

This study was a cross-sectional, observational analysis designed to investigate the relationship between Haemoglobin levels, blood platelet counts, and the progression of Alzheimer's disease (AD). Conducted between 2023 and 2024 at the Department of General Medicine, Sarawathi Institute of Medical Sciences, the study aimed to explore these potential correlations to better understand their role in AD progression. The research received ethical approval from the institutional ethics committee, and all participants provided written informed consent before their inclusion in the study.

The study included 57 patients diagnosed with Alzheimer's disease, aged 60 years or older, who were either admitted to the hospital or attended outpatient clinics at the Sarawathi Institute of Medical Sciences during the study period. Participants were selected based on inclusion and exclusion criteria to ensure the focus remained on individuals with Alzheimer's disease and to minimize the impact of other factors. Inclusion criteria required a confirmed diagnosis of Alzheimer's disease, using clinical evaluation, cognitive assessments (e.g., Mini-Mental State Examination (MMSE) and neuropsychological testing), and neuroimaging (MRI or CT scan) based on DSM-5 criteria. Participants had to be aged 60 or above, of any gender, and willing to provide written informed consent. The exclusion criteria included individuals with other forms of dementia (such as vascular dementia or frontotemporal dementia), significant hematological disorders, acute illnesses, or those receiving treatments that might influence blood parameters (e.g., chemotherapy or anticoagulants).

A non-random convenience sampling method was used to select participants who met the inclusion criteria and were available for the study during the study period. A total of 57 participants were included in the study.

Data collection was carried out in two primary stages: clinical evaluation and laboratory investigations. Clinical evaluation involved the confirmation of Alzheimer's disease through cognitive assessments, including the MMSE score, which was used to assess the severity of cognitive impairment. Demographic details (age, gender, and comorbid conditions) and the duration of the disease were documented. Laboratory investigations involved the collection of venous blood samples to measure Haemoglobin levels and platelet counts. Haemoglobin was measured in grams per deciliter (g/dL) using an automated hematology analyzer, and platelet count was measured in cells per microliter ($\times 10^3/\mu L$). Routine blood tests, including total white blood cell count and red blood cell count, were also conducted to rule out any hematological abnormalities that could affect the study's results.

For data analysis, the collected data were entered into a computerized database and analyzed using SPSS software (version 22 or equivalent). Descriptive statistics, including means, standard deviations (SD), and frequencies, were calculated for demographic and laboratory parameters. To assess the relationship between Haemoglobin levels, platelet counts, and the severity of Alzheimer's disease, participants were grouped based on MMSE scores: mild AD (MMSE score 18–24), moderate AD (MMSE score 10–17), and severe AD (MMSE score 0–9).[4] The Haemoglobin levels and platelet counts across these groups were compared using one-way ANOVA, and post-hoc pairwise

comparisons were performed where significant differences were observed. Pearson's correlation coefficient was used to assess the relationship between Haemoglobin levels, platelet counts, and the MMSE score, with a p-value of < 0.05 considered statistically significant. Moreover, multiple linear regression analysis was employed to examine the predictive value of Haemoglobin levels and platelet counts for the severity of Alzheimer's disease, adjusting for potential confounders such as age, gender, and disease duration.

Ethical considerations were strictly followed throughout the study, adhering to the principles outlined in the Declaration of Helsinki. All participants were thoroughly informed about the study's purpose, procedures, and any potential risks, with the assurance of confidentiality. Informed consent was obtained from each participant and if not able then from their legal gardian, and all personal data were anonymized for data analysis and reporting. Participants were also given the right to withdraw from the study at any time without any repercussions to their care or treatment.

RESULT:

Table 1: Demographic And Clinical Characteristics Of Patients With Alzheimer's Disease

Characteristic	Mean ± SD	Range
Age (years)	68.3 ± 6.5	60–84
Gender (Male)	28 (49.1%)	-
Gender (Female)	29 (50.9%)	-
Duration of Alzheimer's Disease (years)	4.2 ± 2.3	1–12
Cognitive Impairment Severity (MMSE score)	16.3 ± 6.2	0–24
Comorbidities (Hypertension)	32 (56.1%)	-
Comorbidities (Diabetes Mellitus)	26 (45.6%)	-

The study included 57 patients diagnosed with Alzheimer's disease, with a mean age of 68.3 ± 6.5 years, ranging from 60 to 84 years. The gender distribution was nearly equal, with 28 males (49.1%) and 29 females (50.9%). The average duration of Alzheimer's disease was 4.2 ± 2.3 years, spanning from 1 to 12 years. Cognitive impairment severity, assessed by the Mini-Mental State Examination (MMSE), had a mean score of 16.3 ± 6.2, with scores ranging between 0 and 24, showing varying levels of cognitive decline among participants.

The most common comorbidities observed were hypertension, present in 32 participants (56.1%), and diabetes mellitus, affecting 26 participants (45.6%). This shows the prevalence of cardiovascular and metabolic conditions within the study population, which could potentially influence disease progression and outcomes.

Table 2: Haemoglobin Levels And Platelet Count Based On Alzheimer's Disease Severity

Alzheimer's Disease Severity	Haemoglobin Level (g/dL) (Mean ± SD)	Platelet Count ($\times10^3$/μL) (Mean ± SD)
Mild (MMSE score 18–24)	13.2 ± 1.5	218.4 ± 51.0
Moderate (MMSE score 10–17)	12.4 ± 1.8	215.0 ± 49.5
Severe (MMSE score 0–9)	10.1 ± 2.2	198.7 ± 60.3
Total	12.0 ± 2.0	211.5 ± 55.6
P value	<0.001*	0.045*

Patients with mild Alzheimer's disease (MMSE score 18–24) had the highest mean Haemoglobin level (13.2 ± 1.5 g/dL) and platelet count (218.4 ± 51.0 $\times10^3$/μL). In contrast, those with severe Alzheimer's disease (MMSE score 0–9) exhibited the lowest mean Haemoglobin level (10.1 ± 2.2 g/dL) and platelet count (198.7 ± 60.3 $\times10^3$/μL). The Haemoglobin and platelet levels of patients with moderate Alzheimer's disease (MMSE score 10–17) were intermediate, with values of 12.4 ± 1.8 g/dL and 215.0 ± 49.5 $\times10^3$/μL, respectively.

The differences in Haemoglobin levels and platelet counts across severity groups were statistically significant, with p-values of <0.001 for Haemoglobin and ranging of 0.045 for platelet count. These findings show a potential association between worsening Alzheimer's disease severity and declining Haemoglobin levels and platelet counts.

Table 3: Correlation Between Haemoglobin Level, Platelet Count, And MMSE Score

Variable	MMSE Score (r)	p-value
Haemoglobin Level (g/dL)	0.652	<0.001*
Platelet Count ($\times10^3$/μL)	0.341	0.007*

There was a moderate positive correlation between Haemoglobin levels and MMSE score, showing that higher Haemoglobin levels are associated with better cognitive function. Platelet count also showed a positive but weaker correlation with MMSE score.

Table 4: Comparison Of Haemoglobin Levels And Platelet Count Between Participants With And Without Comorbidities

Comorbid Condition	Haemoglobin Level (g/dL) (Mean ± SD)	Platelet Count ($\times10^3$/μL) (Mean ± SD)	p-value (Haemoglobin)	p-value (Platelet Count)
Hypertension (n = 32)	11.8 ± 1.9	210.2 ± 57.4	0.038*	0.215
Diabetes Mellitus (n = 26)	12.2 ± 2.0	218.6 ± 60.2	0.087	0.376
No Comorbidities (n = 25)	12.3 ± 1.7	212.1 ± 53.5	0.199	0.514

Haemoglobin levels were significantly lower in patients with hypertension compared to those without comorbidities, showing a possible association between hypertension and lower Haemoglobin levels. No significant differences were found for platelet count across the comorbidity groups.

Table 5: Analysis Of Haemoglobin Level And Platelet Count Based On Disease Duration

Disease Duration (years)	Haemoglobin Level (g/dL) (Mean ± SD)	Platelet Count ($\times10^3$/μL) (Mean ± SD)
1–3 years	12.6 ± 1.6	220.3 ± 59.1
4–6 years	11.8 ± 1.9	212.1 ± 53.7
7–12 years	10.9 ± 2.3	204.2 ± 62.1
P value	0.031	0.693

Haemoglobin levels was significantly lower in participants with a disease duration of 7–12 years compared to those with shorter durations, showing that prolonged Alzheimer's disease may be associated with changes in haemoglobin level. however, there was no difference in platelet counts with duration of disease.

DISCUSSION:

In the present study on the *Association of Hemoglobin Levels and Platelet Count with the Progression of Alzheimer's Disease*, the mean age of the participants was 68.3 ± 6.5 years (range 60–84), which is similar to previous findings on late-onset Alzheimer's disease (LOAD). Smirnov et al. (2021)[5] reported a bimodal age distribution for sporadic AD, with a separation at 63 years, while Walsh (1990)[6] found a mean age of symptom onset at 73.9 years and enrollment at 77.6 years. In contrast, studies on early-onset AD (EOAD) report lower mean ages; Balasa et al. (2011)[7] found an onset at 54.5 years (range 46–60), and autosomal dominant forms may manifest even earlier (Ryman et al., 2014). These comparisons support that our cohort primarily represents patients with LOAD.

In terms of gender distribution, our study observed near-equal representation with 29 females (50.9%) and 28 males (49.1%), whereas most large-scale studies show a higher female predominance. For example, Mouton et al. (2018)[8] reported 70.1% female patients in a French cohort (sex ratio 2.34), and Zissimopoulos et al. (2016)[9] found 48.8% women versus 28.8% men among Medicare beneficiaries. This discrepancy may be attributed to regional variations or sampling differences, though our sample supports the notion that both sexes are significantly affected.

The average duration of AD in our sample was 4.2 ± 2.3 years (range 1–12), which is comparable to previous studies. Larson et al. (2004)[10] found median survival of 4.2 years in men and 5.7 years in women, while Helzner et al. (2008)[11] reported survival ranging from 3.7 to 7.6 years across ethnic groups. Our findings fall within this range, supporting a moderate disease duration consistent with global data.

In evaluating cognitive severity through MMSE scores, our study recorded a mean MMSE score of 16.3 ± 6.2 (range 0–24), showing moderate cognitive impairment. This is similar to Bartos & Raisova (2016)[12], who noted MMSE means of 22 ± 5 in dementia patients and 25 ± 3 in mild cognitive impairment (MCI). Nelson et al. (2009)[13] also reported lower MMSE scores (10.7 ± 8.6) in AD compared to dementia with Lewy bodies, supporting the characteristic

cognitive decline in AD.

Regarding comorbidities, 56.1% of our patients had hypertension, and 45.6% had diabetes. These values contrast with Javanshiri et al. (2018)[14], where AD patients showed lower prevalence of hypertension and diabetes compared to vascular dementia patients. However, our findings resonate with Luchsinger et al. (2005)[15], who found that multiple vascular risk factors, including hypertension and diabetes, increased the risk of AD 3.4-fold. These findings underscore the ongoing debate regarding vascular risk in AD pathogenesis.

Similarly, platelet count also decreased with increasing AD severity- $218.4 \pm 51.0 \times 10^3/\mu L$ in mild AD to $198.7 \pm 60.3 \times 10^3/\mu L$ in severe cases ($p < 0.001$). Although Baskin et al. (2000)[16] showed declining platelet amyloid precursor protein (APP) ratios with cognitive decline, they did not measure absolute platelet counts. Our results show that decreased platelet counts, like hemoglobin, may correlate with cognitive deterioration, although further mechanistic studies are needed. Similar to our findings, Santos et al. study shows Hemoglobin and platelet levels were statistically lower in patients with AD. Whereas Wolters et al. shows U-shaped association between hemoglobin levels and dementia ($p = 0.005$), such that both low and high hemoglobin levels were associated with increased dementia risk.

CONCLUSION:

In conclusion, our study shows that hemoglobin and platelet levels are significantly associated with Alzheimer's disease severity and may serve as potential surrogate biomarkers. These findings extend the current literature and encourage future longitudinal studies to establish causality and evaluate underlying mechanisms.

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