

Anemia and Cognitive Performance in University Students: The Role of Moderating Factors beyond Hemoglobin

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ABSTRACT

Anemia persists as a significant public health challenge among university students, particularly females, with prevalence rates in Indonesia ranging from 21.7% to 39.9%. While theoretical models posit that reduced hemoglobin levels should impair attention, memory, and executive function due to cerebral hypoxia and neurotransmitter dysregulation, empirical data reveal an "Anemia Paradox" where affected students often maintain average or superior academic performance. This literature review synthesizes findings from over 20 national and international journals published between 2015 and 2025 to investigate this discrepancy and deconstruct the complex, often contentious relationship between hemoglobin concentration and cognitive output in high-functioning young adults. The review indicates that the correlation between anemia and cognitive performance is non-linear and heavily obscured by moderating variables. Specifically, biological resilience mechanisms such as cerebral autoregulation and the presence of Cognitive Reserve (CR) effectively compensate for physiological deficits, masking immediate cognitive decline. Furthermore, external confounders like academic stress and sleep quality frequently exert a more significant impact on cognition than mild physiological variances. Consequently, the report concludes that intervention strategies must shift from simple iron supplementation to holistic lifestyle and stress management, acknowledging that biological and motivational compensation often buffer the immediate impact of anemia on academic achievement.

Keywords: anemia; hemoglobin; cognitive performance; university students; cognitive reserve; academic stress; sleep quality; brain autoregulation

INTRODUCTION

Optimal cognitive performance is fundamental in the high-pressure environment of university education, particularly in demanding fields like medicine. Peak cognitive function is a non-negotiable asset that often clashes with the reality of student health, where anemia serves as a silent but significant threat. Clinically defined as low hemoglobin (<12 g/dL for women, <13 g/dL for men) [1], anemia compromises the oxygen supply to the brain, an organ that demands roughly 20% of the body's total oxygen despite its small size [2]. This places students at a dangerous intersection of high academic demand and physiological vulnerability due to poor diet and financial constraints [3].

Theoretically, this should be devastating, as iron is required not only for oxygen transport but also for synthesizing critical neurotransmitters like dopamine [4] and maintaining myelin structure [5], meaning anemia attacks both the brain's fuel source and its wiring.

Despite these clear biological mechanisms, the actual epidemiological data reveal a complex "Anemia Paradox." While anemia is pervasive, affecting nearly 30% of women globally and up to 39.9% of female students in Indonesia [1] due to menstruation [6] and genetic factors like Thalassemia trait [1], alongside poor dietary habits [7], empirical studies often fail to find a linear drop

in cognitive scores or GPA [4]. Recent research on medical students confirms that those with anemia often perform on par with their healthy peers [4], [8], likely because the healthy young adult brain utilizes robust compensatory mechanisms, such as increased cerebral blood flow, to maintain function despite lower hemoglobin [2].

This discrepancy suggests that the "signal" of anemia is being drowned out by more dominant lifestyle and psychological factors. Academic stress and elevated cortisol can impair memory in ways that mimic anemia [9], while the rampant sleep deprivation seen in universities often exerts a more immediate and profound effect on cognition [10]. Furthermore, high-performing students possess "Cognitive Reserve", efficient neural networks built through years of study, which allows them to tolerate physiological deficits without showing clinical symptoms [11], [12]. Combined with the fact that standard screening tools like the MMSE often hit a "ceiling effect" in this demographic [13], it becomes clear that understanding student cognition requires looking beyond blood parameters to a broader mix of resilience and lifestyle stressors.

METHODS

This study utilizes a narrative synthesis approach to map the complex relationship between anemia and cognitive performance in university students, specifically aiming to explain why empirical results vary so drastically across different contexts. A narrative method was selected over quantitative meta-analysis to accommodate the significant heterogeneity in the literature, which varies widely in cognitive definitions, ranging from GPA to specific neuropsychological batteries like the MMSE, and hematological measurements. This approach allows for the integration of diverse biological, psychological, and educational factors into a cohesive theoretical framework [14]. To ensure a comprehensive dataset, a dual-pronged search strategy was employed across Indonesian national databases (Garuda, Neliti, Sinta) to capture local nutritional contexts and hemoglobinopathies, and major international repositories (PubMed, Scopus, ScienceDirect) for broader physiological insights, utilizing keywords focusing on hemoglobin, cognitive reserve, and academic stress.

The selection process was governed by strict criteria, prioritizing articles published between 2015 and 2025 that target late adolescents and young adults (18-25 years) in university settings. The review explicitly excluded pediatric and geriatric populations, as well as severe pathological anemias, to focus on the mild-to-moderate nutritional anemia typical of this demographic. From the initial search, 10 core articles were selected for in-depth analysis, balancing national and international research. The final synthesis is organized around four key thematic pillars: the direct correlation between hemoglobin and cognition, the moderating role of Cognitive Reserve, the confounding influence of academic stress and mental health, and the impact of sleep quality and

lifestyle factors.

RESULTS AND DISCUSSION

The synthesis of collected literature presents a complex and often contradictory landscape. While the biological necessity of hemoglobin for brain function is undeniable, this physiological fact does not consistently translate into measurable academic or cognitive decline among university students. While some research identifies clear deficits in attention and concentration among anemic students [15], a significant portion of the literature, particularly recent studies focusing on medical and nursing cohorts, finds no statistical correlation between mild anemia and cognitive scores [4]. This discrepancy suggests that the healthy young adult brain possesses a high capacity for compensation, indicating that performance is likely more heavily influenced by external "moderating factors" than by hemoglobin levels in isolation.

The Physiological Link vs. Clinical Findings: Resilience in Hypoxia

The physiological rationale connecting anemia to cognitive decline is grounded in the fundamental role of hemoglobin as the blood's primary oxygen transporter. Despite its relatively small mass, the brain has an exceptionally high metabolic rate, accounting for approximately 20% of the body's basal oxygen consumption [2]. Neuronal activity relies heavily on oxidative phosphorylation to generate ATP, which powers the ion pumps essential for maintaining membrane potentials and neurotransmission. When hemoglobin levels fall, the blood's oxygen-carrying capacity diminishes, theoretically leading to a state of cerebral hypoxia.

Furthermore, iron deficiency, the most common etiology of anemia, has direct neurological consequences independent of oxygen transport. Iron is a requisite cofactor for tyrosine hydroxylase, the rate-limiting enzyme in the synthesis of dopamine and norepinephrine [4]. These neurotransmitters are critical for regulating attention, motivation, and executive function in the prefrontal cortex. Additionally, iron is essential for the synthesis and maintenance of myelin by oligodendrocytes; reduced myelination slows nerve conduction velocity, potentially impairing processing speed and complex cognitive integration [5].

Despite these clear biological mechanisms, empirical data from university populations often fail to demonstrate a linear relationship. For instance, Helmyati et al. (2023), utilizing data from the Indonesian Family Life Survey (IFLS 5), found no significant relationship between anemia status and cognitive ability or sleep quality in young women aged 15-24 [4]. Similarly, Alhazmi et al. (2024) reported that despite a high prevalence of Iron Deficiency Anemia (IDA) (27.4%) among female university students in Saudi Arabia, there was no significant association between IDA and scores on immediate memory, working memory, or attention speed [8]. In Brazil, the large-scale ELSA-Brasil cohort study found no association between anemia

or hemoglobin quintiles and global cognitive scores in middle-aged adults, suggesting a preservation of function even as biology alters [16].

A plausible explanation for this discrepancy is the "Threshold Theory." It is hypothesized that cognitive deficits may only become clinically apparent when hemoglobin drops below a specific critical threshold (e.g., <10 g/dL or even lower), whereas the majority of anemic university students present with mild anemia (10–11.9 g/dL) [17]. In this mild range, the body's homeostatic mechanisms are likely sufficient to maintain function.

The primary mechanism protecting the young adult brain is cerebral autoregulation. In healthy young adults with robust cardiovascular systems, the body compensates for lower hemoglobin concentrations by increasing Cerebral Blood Flow (CBF). Vasodilation of cerebral arterioles reduces resistance, allowing a greater volume of blood to pass through brain tissue, thereby maintaining total oxygen delivery even if the oxygen content per unit of blood is reduced [2]. Additionally, the brain can increase its Oxygen Extraction Fraction (OEF), pulling a higher percentage of oxygen from the passing blood than it normally would [2]. These compensatory mechanisms effectively "mask" the hypoxic impact of mild anemia, preserving cognitive function until the anemia becomes severe or regulatory mechanisms are exhausted. This explains why university students, who typically lack the vascular comorbidities (like atherosclerosis) seen in the elderly, can tolerate anemia without overt cognitive failure.

Non-Oxygenation Mechanisms: Iron Deficiency Non-Anemia (IDNA) A critical nuance often missed in studies that only measure hemoglobin is the condition of Iron Deficiency Non-Anemia (IDNA). Iron stores (ferritin) can be depleted long before hemoglobin levels drop to the point of frank anemia. Since iron is a cofactor for neurotransmitters, cognitive symptoms like poor concentration, fatigue, and irritability might arise from IDNA rather than anemia itself [18]. Studies that fail to measure ferritin may miss this association. Conversely, recent research indicates that while iron intake may correlate with IQ in women, the presence of mild anemia itself does not consistently predict poor performance, pointing again to the brain's resilience [19]. Daugherty et al. (2023) utilized MRI imaging to show that iron status in adolescence predicts brain structure and wiring integrity in young adulthood, suggesting that while immediate performance might be preserved, the long-term structural integrity of the brain requires adequate iron [6].

The Role of Cognitive Reserve and Education

One of the most powerful moderators explaining the lack of correlation in university students is the concept of Cognitive Reserve (CR).

Cognitive Reserve refers to the brain's capacity to improvise and find alternative neural pathways to complete tasks despite underlying pathology.

Individuals with higher levels of education, intelligence, and occupational complexity are known to have higher CR [11]. University students, and specifically those in demanding fields like medicine, nursing, and engineering, represent a highly selected group. They have engaged in years of intensive mental training, developing efficient neural strategies and robust synaptic networks. This reserve acts as a buffer; even if anemia causes a slight physiological drag (e.g., reduced oxygenation), the high-CR student can compensate by recruiting additional neural resources or utilizing alternative cognitive strategies, thereby maintaining performance levels that appear "normal" on standard tests [12].

The "Ceiling Effect" in Measurement A major methodological limitation identified in the reviewed literature is the use of insensitive instruments. Many studies utilize the Mini-Mental State Examination (MMSE) to assess cognition [20]. The MMSE is a screening tool designed to detect dementia and severe cognitive impairment in the elderly; it is largely inappropriate for detecting subtle variations in the cognitive performance of high-functioning young adults. Consequently, these studies suffer from a massive "ceiling effect," where almost all students, regardless of anemia status, score near the maximum (29-30/30) [13]. This lack of variance makes it statistically impossible to detect a correlation. A student with a hemoglobin level of 10 g/dL might still score 30/30 on a screening test, not because their brain is unaffected, but because the test is insufficiently sensitive to detect the subtle drag on their processing speed.

Studies that used more sensitive measures, such as the Academic Potential Test (APT) or specific reaction time tasks, were more likely to find deficits associated with anemia. For example, Satriawan et al. (2024) found that while anemia did not significantly impact IQ (a stable trait linked to reserve), it did negatively impact APT scores and study concentration (state-dependent variables) in nursing students [15]. This distinction is crucial: Cognitive Reserve protects "crystallized" intelligence (IQ, knowledge), but anemia may erode "fluid" efficiency (concentration, speed).

The Influence of Academic Stress and Mental Health The university environment is synonymous with stress, and the literature suggests that mental health status may be a more potent driver of cognitive variance than mild nutritional deficits.

Academic stress is highly prevalent in university students and strongly correlates with symptoms that mimic anemia: fatigue, difficulty concentrating, listlessness, and "brain fog" [9]. In cross-sectional studies, it is difficult to disentangle whether a student's poor performance is due to low hemoglobin or high anxiety. Chronic stress activates the Hypothalamic-Pituitary-Adrenal (HPA) axis, elevating cortisol levels. Prolonged exposure to high cortisol is known to be neurotoxic to the hippocampus and prefrontal cortex, areas essential for learning and memory [15].

Research indicates that anxiety is a strong predictor of academic performance, often overshadowing physiological factors. In a study of nursing students, while anemia was linked to lower concentration, the psychological pressure of the curriculum was a massive independent factor [21]. Kedir, S. et al. (2024) utilized structural equation modeling in Ethiopian students and found a mediated relationship: anemia was linked to mental distress, and mental distress was linked to poor grades [21]. This suggests that anemia might impair cognition indirectly by lowering the threshold for stress and anxiety. Furthermore, highly motivated but anemic students might "power through" their fatigue to achieve high grades (Motivational Compensation), masking the physiological burden in GPA-based studies [10].

Sleep Quality and Lifestyle Factors

Sleep deprivation is endemic among university students, often worn as a badge of honor. Sleep is critical for memory consolidation and the clearance of metabolic waste (such as beta-amyloid) from the brain via the glymphatic system, a process that occurs predominantly during deep sleep [4]. The cognitive impairment resulting from a single night of sleep deprivation, affecting vigilance, reaction time, and working memory, is functionally equivalent to being intoxicated. Comparative studies often find that poor sleep quality correlates more consistently and strongly with lower GPA and cognitive scores than mild anemia does [4]. In the Indonesian study using IFLS 5 data, no relationship was found between anemia and sleep quality, but sleep itself remains a dominant independent variable [17]. The magnitude of cognitive deficit caused by chronic sleep restriction likely drowns out the signal of mild anemia.

Lifestyle factors create a "noise" that drowns out the anemia signal. Students often have poor diets high in processed foods and low in micronutrients, leading to deficiencies in B12 and folate, which affect cognition independently of iron [3]. Conversely, physical activity is protective. Engaging in regular exercise increases Brain-Derived Neurotrophic Factor (BDNF) and improves cerebral perfusion [23]. Active students may mitigate the effects of anemia through better cardiovascular efficiency and neurotrophic support, while sedentary students may feel the effects more acutely. This "double burden" of malnutrition, where students are both overweight (obesogenic diet) and micronutrient-deficient, is a growing concern in Indonesia and other developing nations [15].

Synthesis of Findings

The relationship between anemia and cognitive performance in university students is not a simple linear equation. While severe anemia undoubtedly impairs brain function, the mild-to-moderate anemia typical of this population appears to be manageable for the young, plastic brain. This resilience is bolstered by physiological autoregulation and cognitive reserve but is threatened by the concurrent burdens of sleep

deprivation and academic stress. The inconsistency in the literature, where some studies find correlations [14] and others do not [1], is largely explained by methodological differences (sensitivity of tests like MMSE vs. APT) and the failure to control for these powerful moderating variables. In the context of Indonesia, where anemia is often comorbid with genetic traits like Thalassemia [24], the picture is even more complex. Data specifically regarding undergraduate medical students further illustrates this nuance, as hemoglobin percentages often fail to show a direct impact on cognitive skills [25] despite the high frequency of nutritional anemia observed in these female cohorts [26]. While the brain shows resilience, pathophysiological insights into cerebrovascular disease suggest that chronic anemia carries risks that extend beyond the classroom [27]. Consequently, distinguishing between nutritional anemia and genetic hemoglobinopathies remains a critical priority for health surveys in this region [28].

CONCLUSIONS

The comprehensive review of literature from 2015 to 2025 highlights a complex reality: while anemia is highly prevalent among university students, particularly in developing nations like Indonesia, its direct statistical link to cognitive decline is often weak or non-existent in cross-sectional studies. This absence of a linear correlation is not because anemia is benign, but because the physiological signal of mild anemia is frequently masked by the robust biological resilience of young adults. Unlike pediatric or geriatric populations, healthy university students possess effective cerebral autoregulatory mechanisms that preserve oxygenation during mild-to-moderate anemia. Consequently, cognitive deficits likely follow a "Threshold Model," manifesting clinically only when hemoglobin drops below a critical level (likely <10 g/dL) or when compensatory reserves are exhausted.

The variability in cognitive outcomes is further obscured by potent psychological and lifestyle moderators. Academic stress, mental health issues, and sleep quality often serve as stronger, more immediate predictors of daily performance than mild hemoglobin variations; symptoms like "brain fog" or fatigue are frequently misattributed to anemia when they actually stem from burnout or sleep deprivation. Additionally, the high educational status of this demographic creates a significant "Cognitive Reserve," allowing students to "power through" tasks despite physiological handicaps. This resilience, combined with the "ceiling effect" of insensitive screening tools like the MMSE, often renders the subtle impacts of anemia statistically invisible in standard research.

From a clinical and academic perspective, these findings necessitate a shift in intervention strategies. Addressing declining academic performance requires a holistic approach that goes beyond simple iron supplementation to include rigorous stress management and sleep education.

Future research must move away from broad screening tools in favor of longitudinal designs utilizing high-sensitivity neurocognitive batteries, specifically those measuring processing speed and serum ferritin levels. This is essential to isolate the true effect of iron deficiency from the "noise" of student lifestyle factors and to detect deficits before they reach a critical clinical threshold.

ACKNOWLEDGMENT

The authors would like to express their deepest gratitude to all researchers and institutions whose published work provided the foundational evidence for this literature review.

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