

Executive Functions as Predictors of Anxiety and Depression in Patients with Hemolytic Uremic Syndrome

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Abstract:

This study aimed to examine the predictive role of executive functions in anxiety and depression among children and adolescents diagnosed with Hemolytic Uremic Syndrome (HUS). A descriptive correlational design was employed. The study sample consisted of 40 patients with HUS, aged between 5 and 18 years, recruited from pediatric nephrology departments in specialized hospitals. The study instruments included the Executive Functions Scale, the Spielberger Anxiety Scale, and the Beck Depression Inventory, in addition to a demographic and clinical data form. Data were analyzed using non-parametric tests, correlation coefficients, and multiple regression analysis. Results revealed significant positive correlations between executive function deficits and levels of anxiety and depression. Impairments in working memory, inhibition, planning, and monitoring were significantly associated with higher anxiety and depressive symptoms. Regression analysis indicated that working memory and inhibition were significant predictors of both anxiety and depression, explaining 65% of the variance in anxiety and 66% of the variance in depression. Gender differences were not significant in most executive function dimensions or depression; however, females exhibited higher anxiety levels compared to males. These findings underscore the critical role of executive functions in emotional regulation among pediatric patients with HUS. The study highlights the importance of integrating psychological assessment and targeted interventions focusing on executive function deficits into routine medical care to reduce emotional distress and enhance psychological well-being.

Keywords: Executive Functions, Anxiety, Depression, Hemolytic Uremic Syndrome.

An introduction:

In recent years, scientific interest in the Kingdom of Saudi Arabia has increased in alignment with the objectives of Vision 2030, particularly in studying the complex interactions between chronic physical illnesses and mental health. This interest is especially evident among patients suffering from conditions that affect the central nervous system. Hemolytic Uremic Syndrome (HUS) is considered one of the most prominent rare and life-threatening medical conditions, as it affects the kidneys and microvasculature and is often accompanied by neurological complications that impair patients' cognitive and psychological functioning. This syndrome has been identified as the most common cause of acute renal failure in children and predominantly affects younger age groups; however, it can also occur in adults, particularly following certain types of bacterial infections (Krishna, 2024; Kuter, 2023).

The present study aims to explore the impact of Hemolytic Uremic Syndrome on executive functions and its relationship with anxiety and depression. HUS, first identified more than 45 years ago, It is characterized by a triad of hemolytic anemia, thrombocytopenia, and acute renal failure. The syndrome primarily affects children under the age of four and remains the leading cause of acute kidney failure in this age group. The most common form, diarrhea-associated HUS (D-HUS), occurs in previously healthy children aged between six months and five years and is often preceded by watery diarrhea that may progress to hemorrhagic colitis. HUS represents a complex medical condition in which immunological, hematological, and neurological factors intersect, creating a fertile ground for the emergence of psychological and behavioral symptoms among affected individuals (Gehad et al., 2023).

In the context of these acute physical and neurological changes, patients with Hemolytic Uremic Syndrome frequently exhibit a range of psychological disorders, most notably anxiety and depression, either as natural or pathological responses to sudden health changes, associated functional impairments, fear of complications, and lifestyle alterations. Recent studies have demonstrated that chronic organic disorders may negatively affect higher cognitive processes, particularly what are known as *executive functions*. These functions include organization, planning, emotional regulation, attention, and cognitive flexibility—skills that are essential for healthy psychological and behavioral adjustment (Shuweikh, 2022; Ajilchi & Nejati, 2017).

Despite the abundance of studies addressing the relationship between psychological disorders and executive functions in patients with chronic diseases, the psychological literature lacks focused research on patients with Hemolytic Uremic Syndrome in particular, especially within the Arab context. This highlights a significant knowledge gap that the present study seeks to address by examining the relationship between executive functions and both anxiety and depression among patients with HUS. The study aspires to contribute

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scientific recommendations that support the development of psychological support programs and cognitive-based interventions tailored to this population, thereby improving their quality of life and psychological and social adjustment.

Scientific research has also targeted the reciprocal relationship between executive functions and mood states such as anxiety and anger. Some studies emphasize that experiencing negative emotional states leads to impairments in executive functioning, while others suggest that deficits in executive functions negatively influence mood regulation and contribute to lowered emotional well-being (Shields, Moons, Tewell, & Yonelinas, 2016).

Problem of the study

Hemolytic Uremic Syndrome (HUS) is a rare and serious disease that affects kidney function and the central nervous system and poses a genuine threat to life, particularly among young children and the elderly (Unified Medical Dictionary, 2017; Krishna, 2024). Although medical advances have improved its diagnosis and treatment, the psychological and cognitive dimensions associated with HUS remain largely neglected, especially within Arab research contexts.

The first major issue lies in the scarcity of Arab scientific research addressing the psychological effects of Hemolytic Uremic Syndrome, particularly anxiety and depression as common manifestations among patients. These symptoms may arise as a result of health-related trauma, repeated hospitalizations, or disease complications that disrupt individuals' lifestyles and autonomy. The second issue concerns the limited number of Arab studies that have examined executive functions among patients with HUS, despite the fact that these functions constitute the cornerstone of daily cognitive performance and include essential skills such as planning, organization, emotional regulation, problem-solving, and cognitive flexibility (Bradshaw & Mattingley, 2001).

International literature indicates a strong association between anxiety and depression and impairments in executive functions among individuals with chronic illnesses or acute neurological conditions (Ajilchi & Nejati, 2017). Some studies further suggest that executive dysfunction in these patients may not be solely organic in origin but may also result from cumulative psychological and behavioral interactions.

Previous research has reported reduced prefrontal cortex activity following chemotherapy in cancer patients, along with significant declines in executive functions compared to healthy individuals (Kesler, Kent, & O'Hara, 2011). Other studies have confirmed that childhood cancer survivors are at increased risk of deficits in executive functions (EF) and working memory (WM) (Pererson & Jacobson, 2022). In a study of 61 children with brain tumors, most executive functions were found to be significantly impaired compared to healthy controls, with no differences observed within the patient group based on tumor type or treatment modality (Harman et al., 2019). Similarly, an examination of 166 children with brain and blood cancers aged between 6 and 23 years revealed no differences in executive functions among patients with different cancer types;

however, significant deficits were observed when compared with healthy peers, favoring the control group (Sharkey, Hardy, Gioia, Weisman, & Walsh, 2022).

Executive dysfunction affects various aspects of life. In terms of mental health, it is associated with addiction, depression, obsessive-compulsive disorder, anxiety, attention-deficit/hyperactivity disorder, communication disorders, and schizophrenia. Regarding physical health, executive dysfunction has been linked to obesity, overeating behaviors, and non-adherence to medical advice (Dang, 2014; Insel, Morrow, Brewer & Figuered, 2006).

Nevertheless, this relationship remains insufficiently explored within the Arab environment, particularly among patients with Hemolytic Uremic Syndrome, who represent a psychologically and biologically vulnerable group experiencing symptoms that intertwine neurological, psychological, and cognitive dimensions. This underscores the urgent need for a comprehensive psychological-cognitive study that examines these patients from a holistic perspective, integrating executive functions, anxiety, and depression, with the aim of establishing a scientific framework that may contribute to improving their psychological and cognitive care.

Accordingly, the research problem is defined by the following main questions:

1. Are there statistically significant differences between male and female patients with Hemolytic Uremic Syndrome in executive functions, anxiety, and depression?
2. Is there a correlational relationship between executive functions, anxiety, and depression among patients with Hemolytic Uremic Syndrome?
3. Do Executive Functions Predict Anxiety and Depression in Patients with Hemolytic Uremic Syndrome (HUS)?

Objectives of the Study

The present study seeks to achieve the following objectives:

1. To determine the prevalence and severity of depression and anxiety among patients diagnosed with Hemolytic Uremic Syndrome (HUS).
2. To identify the need for designing psychological therapeutic interventions that assist patients with Hemolytic Uremic Syndrome in adapting to the nature of the disease and enhancing their responsiveness to medical and psychological treatment plans.
3. To provide a cognitive framework for understanding executive functions among patients with Hemolytic Uremic Syndrome.
4. To enrich the scientific literature with a contemporary empirical study examining executive functions and their relationship with anxiety and depression in patients with Hemolytic Uremic Syndrome, in light of the scarcity of research addressing the interaction among these variables.

Significance of the Study

The significance of this study stems from its focus on a relatively rare clinical population—patients with Hemolytic Uremic Syndrome—who have received limited attention in psychological research, particularly within the Arab context. Moreover, the

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study underscores the importance of understanding the interplay between psychological and cognitive dimensions by examining the relationship between executive functions on the one hand and anxiety and depression on the other. This integrative approach facilitates the development of more effective, evidence-based psychological interventions grounded in sound scientific principles.

1. This study contributes to bridging the knowledge gap related to the psychological aspects of patients with Hemolytic Uremic Syndrome, a rare population that has been insufficiently explored in Arab psychological literature.

2. It enriches the field of cognitive psychology by investigating the relationship between executive functions and psychological disorders—specifically anxiety and depression—among a population affected by a chronic medical condition, thereby supporting future research endeavors.

3. The study employs multiple theoretical frameworks (cognitive, executive, and biopsychosocial models), which enhances a comprehensive understanding of the impact of the disease on psychological and cognitive functioning.

4. It opens new research avenues for examining the relationship between organic diseases and cognitive and psychological disorders from a multidisciplinary perspective.

5. The findings provide physicians and mental health professionals with evidence-based insights that may assist in designing specialized psychological support and rehabilitation programs for patients with Hemolytic Uremic Syndrome.

6. The study contributes to the development of early diagnostic and screening programs aimed at detecting symptoms of anxiety, depression, and executive dysfunction, enabling timely and effective therapeutic intervention.

7. It supports multidisciplinary medical and psychological care teams in developing strategies to enhance psychological adjustment and improve quality of life for patients throughout different stages of treatment.

8. The study offers a reliable database that can be utilized in the design of individual or group-based psychological counseling programs tailored to the specific characteristics and needs of this patient population.

Concept of the study and Theoretical Farmwork

Given the multiplicity and overlap of concepts related to the topic of the present study, it was necessary to define both the theoretical and operational definitions of its core terms in order to ensure conceptual clarity and methodological precision. These concepts include *executive functions* as higher-order cognitive processes that regulate behavior and thinking, *anxiety* and *depression* as the most prominent psychological disorders associated with organic diseases, and *Hemolytic Uremic Syndrome* as the clinical framework around which the study revolves.

(1) Executive Functions

Executive functions represent the highest levels of cognitive performance associated with the prefrontal cortex of the brain. They encompass a set of higher-order cognitive processes responsible for the self-regulation of behavior. These processes include planning, cognitive flexibility, organization, inhibition of automatic responses, attentional control, and working memory.

Executive functions have been defined as the mental capacities that enable individuals to set goals, maintain them in active memory, monitor performance during execution, and inhibit distraction caused by goal-irrelevant stimuli (Shuweikh, 2022). These functions are essential for academic and social success, adaptation to life stressors, and effective decision-making in complex and dynamic situations. Executive functioning may be negatively affected in the presence of psychological disorders or chronic organic illnesses—such as Hemolytic Uremic Syndrome—thereby impairing an individual’s ability to interact adaptively with their environment.

(2) Anxiety

Anxiety is defined as a negative emotional state characterized by feelings of tension and persistent anticipation of potential threats or adverse events. It is typically accompanied by physiological changes such as increased heart rate, muscle tension, and rapid breathing, as well as cognitive arousal manifested in difficulty concentrating and preoccupation with negative thoughts (Beck, 2005, p. 8).

Anxiety is among the most prevalent psychological disorders, particularly among patients with chronic organic diseases. Threats to health, lifestyle changes, and continuous exposure to pain or medical treatment all contribute to heightened anxiety and apprehension in affected individuals. The literature indicates that chronic anxiety adversely affects executive performance by weakening attention, disrupting thinking processes, and reducing the ability to regulate behavior and make sound decisions (Ajilchi & Nejati, 2017).

(3) Depression

Depression is a complex mood disorder characterized by persistent sadness, diminished motivation, and a marked loss of interest or pleasure in daily activities. It is also associated with significant changes in sleep patterns, appetite, concentration, and social and occupational functioning (American Psychiatric Association, 2013).

Depression tends to develop cumulatively among individuals facing chronic health conditions such as Hemolytic Uremic Syndrome, as patients live under the burden of future uncertainty, fear of relapse, and feelings of helplessness or loss of control. Ibrahim (1998) described depression as “an unbearable effort, in which one feels that energy has been depleted even for performing simple routine tasks,” a description that reflects the profound psychological exhaustion experienced by affected individuals. From a cognitive perspective, depression is associated with reduced executive efficiency, manifested in slowed cognitive processing, impaired decision-making, and diminished cognitive flexibility and attention (Beck, 2005).

(4) Hemolytic Uremic Syndrome

Hemolytic Uremic Syndrome is a rare and potentially life-threatening disorder that typically affects children under the age of five, although it may also occur in adults, particularly in cases of severe bacterial infection or as a result of drug-related or immune-mediated complications. The syndrome results from damage to small blood vessels, leading to hemolysis (destruction of red blood cells), thrombocytopenia (reduced platelet count), and acute kidney injury.

Escherichia coli is a Gram-negative bacterium that normally inhabits the intestines of humans and animals. While most strains are harmless and even beneficial—such as those involved in vitamin K production—certain strains, including *E. coli* O157:H7, are pathogenic and can cause severe illnesses such as bloody diarrhea, kidney failure, and Hemolytic Uremic Syndrome, particularly among children and older adults. Transmission typically occurs through contaminated food or water or through direct contact with infected individuals or animals (Centers for Disease Control and Prevention, 2018).

The most common cause of Hemolytic Uremic Syndrome is infection with *Escherichia coli*, which damages the endothelial lining of blood vessels and leads to the formation of microthrombi that obstruct capillaries in vital organs such as the kidneys, brain, and heart (Trachtman et al., 2012).

Clinical manifestations include marked pallor, cutaneous or internal bleeding, reduced urine output, and neurological disturbances such as irritability, seizures, or coma in advanced cases. Without prompt medical intervention, the condition may progress to permanent kidney failure or life-threatening cardiac and neurological complications (Kuter, 2023; Karpman, Loos, Tati, & Arvidsson, 2016).

Due to the complexity and multidimensional nature of this syndrome, recent research has emphasized the importance of investigating its associated psychological and neurological consequences—particularly anxiety, depression, and executive function impairments—which may persist even after physical recovery.

Theoretical Models Explaining the Study Concepts

First: Bradshaw's Executive Function Model

Bradshaw's Executive Function Model (Bradshaw & Mattingley, 2001) is a neurocognitive framework that emphasizes the role of the frontal lobes as the central hub of executive functions. According to this model, executive functions operate as a “supervisory control system” that regulates behavior through a set of higher-order cognitive tasks.

Higher cognitive functions refer to complex mental abilities employed when individuals engage in situations requiring thinking, planning, decision-making, or problem-solving. These functions act as a “conductor of an orchestra,” organizing and coordinating all other cognitive skills.

Bradshaw and Mattingley (2001) conceptualized executive functions as a set of complex neural processes localized in the frontal lobes, including: (1) planning and

organization, (2) decision-making, (3) emotional regulation, (4) perseverance, (5) flexible attention, and (6) inhibition of automatic responses. These functions are closely linked to psychological and cognitive adaptation and are sensitive to emotional stressors such as anxiety and depression. Emotional disorders place excessive demands on the executive system, thereby impairing individuals' capacity for self-regulation and control (Anderson, 2008).

Bradshaw further noted that brain injury or severe stress—such as that associated with chronic illnesses—can disrupt executive functioning. This observation is particularly relevant to patients with Hemolytic Uremic Syndrome, who experience concurrent organic and psychological stressors.

Second: The Cognitive Model of Anxiety and Depression

The cognitive model developed by Aaron Beck and his colleagues posits that automatic thoughts and negative cognitive schemas about the self, the world, and the future play a central role in the onset and maintenance of anxiety and depression. According to this model, individuals with anxiety tend to exaggerate potential threats and focus disproportionately on negative aspects of experience, whereas individuals with depression adopt pessimistic cognitive patterns centered on worthlessness, helplessness, and hopelessness.

In anxiety, individuals overestimate potential threats and become distressed by minor risks, resulting in excessive consumption of cognitive and emotional resources and a persistent state of anticipation and fear. In depression, cognitive distortions manifest as hopelessness, diminished self-worth, and loss of motivation. These maladaptive cognitive patterns impair executive functioning by negatively affecting planning, organization, and emotional regulation (Beck, 2005).

This model partially explains how psychological symptoms associated with chronic organic diseases—such as anxiety and depression—can contribute to executive function decline. Negative cognitive schemas interfere with individuals' capacity for effective planning, decision-making, and emotional control, thereby linking cognitive theory with executive functioning (Beck, 2005).

Third: The Biopsychosocial Model of Chronic Illness

The biopsychosocial model is one of the most comprehensive and influential frameworks in understanding illness. It was introduced by the American psychiatrist George Engel in 1977 as a response to the limitations of the traditional biomedical model, which focuses exclusively on biological factors. Engel emphasized that illness cannot be fully understood without considering psychological and social dimensions alongside biological processes (Engel, 1977).

According to this model, individuals are not merely biological organisms but active agents who continuously interact with their psychological and social environments. Consequently, health-related suffering—particularly in chronic diseases—is the result of the

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interaction among these three dimensions. This makes the model especially suitable for explaining the psychological and cognitive changes observed in patients with Hemolytic Uremic Syndrome.

Components of the Model and Its Application to Patients with HUS

1. **Biological Factors:** These include the physical manifestations of the disease, such as hemolysis, thrombocytopenia, and acute kidney injury. Neurological complications resulting from microvascular obstruction may also affect the brain—particularly the frontal lobes—leading to executive dysfunction (Kuter, 2023).

2. **Psychological Factors:** These involve emotional and cognitive responses to the illness, such as anxiety, depression, feelings of helplessness, and fear of relapse. While such responses are natural, they become problematic when they develop into chronic disorders that impair quality of life and daily functioning (Trachtman et al., 2012).

3. **Social Factors:** These include family and social support, quality of healthcare services, socioeconomic status, and illness-related stigma. Patients who lack adequate social support or perceive themselves as a social burden are more vulnerable to psychological disorders, which in turn affect their ability to regulate behavior and emotions.

This model explains the dynamic interaction among biological, psychological, and social factors and demonstrates how dysfunction in one domain may amplify the effects of the others. It provides a comprehensive explanation for the deterioration of executive functions and the escalation of anxiety and depression symptoms among patients with Hemolytic Uremic Syndrome. Furthermore, it supports the development of integrated therapeutic and rehabilitation strategies that address all three dimensions rather than focusing solely on medical treatment.

Previous research has consistently established a strong relationship between executive functions and emotional disorders, particularly anxiety and depression, across a wide range of clinical and non-clinical populations. Numerous studies have demonstrated that deficits in executive functions—such as working memory, cognitive flexibility, planning, and inhibitory control—are significantly associated with higher levels of anxiety and depressive symptoms. These findings support the view that executive functions play a central role in emotional regulation and psychological adjustment in various clinical conditions (Ajilchi & Nejati, 2017; Ibrahim, 1998).

Despite this well-documented relationship, there is a noticeable lack of empirical studies that directly examine the association between executive functions, anxiety, and depression among patients with Hemolytic Uremic Syndrome (HUS). To date, most research on HUS has primarily focused on its medical, renal, and neurological outcomes, with limited attention given to its psychological and cognitive consequences.

However, available studies investigating the neurological and psychological sequelae of HUS indicate that patients often experience long-term emotional distress, including symptoms of anxiety and depression, along with cognitive complaints related to attention

and executive functioning. These findings suggest that HUS may adversely affect cognitive–emotional regulation processes, thereby indirectly implicating executive functions in the psychological adjustment of these patients (Tonković et al., 2025; Long-term health-related quality of life..., 2016).

Accordingly, the current study is grounded in existing theoretical and empirical evidence while addressing a clear research gap. By examining executive functions as predictors of anxiety and depression among patients with Hemolytic Uremic Syndrome, this study extends prior research into a rare clinical population and contributes a novel and specialized perspective to the literature.

In recent years, clinical psychology has shown increasing interest in examining the complex interactions between **executive functions** and psychological disorders such as **anxiety and depression**, given the vital role of executive functions in psychological and behavioral adjustment. Several studies have also highlighted the impact of chronic organic diseases—such as renal failure and **hemolytic uremic syndrome (HUS)**—on patients’ psychological and cognitive functioning. Accordingly, previous studies were organized into two main axes relevant to the current research, followed by a critical commentary.

Previous research consistently emphasizes that executive functions constitute a core component of cognitive and behavioral regulation and are sensitive to psychological and health-related factors. However, most studies have focused on non-clinical or common clinical populations, which highlights the need to extend research to rare clinical groups such as patients with hemolytic uremic syndrome. While existing studies confirm the negative impact of anxiety and depression on daily functioning and quality of life, few have examined their relationship with executive functions within this specific clinical context. Accordingly, the current study seeks to address this gap by linking executive functions with anxiety and depression among patients with HUS, thereby contributing a novel and specialized perspective.

Hypotheses

1. There are significant gender differences in executive functions, anxiety, and depression in patients with hemolytic uremic syndrome.
2. There are significant correlations between executive functions, anxiety, and depression in patients with hemolytic uremic syndrome.
3. Executive functions predict anxiety and depression in patients with hemolytic uremic syndrome.

Study Methodology and Procedures

1. Study Design

The study employed a descriptive design, incorporating both correlational and comparative approaches. This design was chosen for its ability to analyze relationships between psychological variables and to interpret differences between groups based on specific factors. It was deemed suitable for the study objectives, which aimed to examine

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the nature of the relationship between executive functions and anxiety and depression, as well as to compare the levels of these variables according to demographic factors such as age, gender, and disease duration.

2. Study Sample

The initial sample consisted of approximately 50 patients clinically diagnosed with Hemolytic Uremic Syndrome (HUS), recruited in collaboration with the Pediatrics and Nephrology Departments of the hospitals where the patients receive ongoing medical care. aged 5 to 18 years ($M = 12.87$, $SD = 3.34$).

Table (1)
Demographic Characteristics of the
Standardization Sample (n = 40)

Variable	Categories	Frequency
Gender	Male	22
	Female	18
Education Level	Primary	3
	Below Average	12
	Secondary	18
	University	7
Family Monthly Income	Low	5
	Medium	28
	High	7
Disease Duration	<1 year	3
	1–3 years	7
	>3 years	30
Treatment Type	Dialysis	20
	Eculizumab	15
	Ravulizumab	5
Mother's Education	Primary	4
	Below Average	10
	Secondary	20
	University	6
Father's Education	Primary	8
	Below Average	4
	Secondary	20

Variable	Categories	Frequency
	University	8
Receiving Psychological Support	Yes	5
	No	35

3. Study Instruments

A set of standardized and age-appropriate psychological instruments was used, including:

1. **Executive Functions Scale (Ghada Abdel Ghaffar, 2015):** This tool measures the core components of higher cognitive processes, such as planning, persistence, cognitive flexibility, organization, and emotional regulation. It is specifically designed for children and adolescents, with confirmed validity and reliability in Arab populations.

2. **Spielberger Anxiety Scale (Abdel-Raqeeb Al-Bahiri, 2005):** This scale consists of items designed to assess anxiety symptoms in children and adolescents, including tension, rapid heartbeat, shortness of breath, and trembling. It was selected for its suitability for clinical pediatric samples.

3. **Beck Depression Inventory (Beck, 2005):** This inventory assesses depressive symptoms such as sadness, loss of motivation, sleep or appetite disturbances. It was chosen for its appropriateness for the study's age group and availability in a standardized Arabic version.

4. **Demographic and Medical Data Form:** A standardized form developed by the researcher to collect preliminary information about participants, including age, gender, disease duration, date of diagnosis, type of treatment received, medical history, and family/social support.

The standardization sample consisted of 15 patients diagnosed with Hemolytic Uremic Syndrome (HUS), aged 5 to 18 years ($M = 11.27$, $SD = 4.96$). The sample included both genders and diverse educational backgrounds, family income levels, disease durations, treatment types, and parental education levels. A small proportion of the sample received psychological support, while most participants did not. This sample was used to examine the reliability and validity of the instruments employed in the study, including the Executive Functions Scale, the Anxiety Scale, and the Depression Scale.

Construct validity was evaluated using two complementary approaches: internal consistency and discriminant validity. Internal consistency was assessed by calculating the correlation of each item with its respective subscale and total score. For the Executive Functions Scale, all item-total correlations were statistically significant, indicating high internal consistency. Correlations between each subdimension and the total score were also significant: planning ($r = 0.896$), working memory ($r = 0.762$), monitoring ($r = 0.857$), inhibition ($r = 0.878$), and organization ($r = 0.781$). Similarly, the Anxiety Scale and the

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Depression Scale demonstrated strong item-total correlations (ranging from 0.461 to 0.921), supporting the internal reliability of these measures. No items were removed, resulting in final scale compositions of 40 items for executive functions, 6 items for anxiety, and 5 items for depression.

Discriminant validity was examined using the extreme groups method. Participants were divided into high- and low-score groups based on quartile cutoffs for each measure. For executive functions, the low group scored below 77 and the high group above 106; for anxiety, the low group scored below 6 and the high group above 11; and for depression, the low group scored below 11 and the high group above 15. The Mann–Whitney U test revealed significant differences between these groups across all scales ($p \leq 0.02$ – 0.01), confirming the scales' ability to distinguish between different levels of functioning and symptomatology.

Reliability was further evaluated using Cronbach's alpha and the split-half method with Spearman–Brown correction. For the Executive Functions Scale, Cronbach's alpha ranged from 0.818 to 0.925 across subdimensions and reached 0.951 for the total score, while split-half reliability ranged from 0.715 to 0.894 for subdimensions and 0.886 for the total score. The Anxiety Scale demonstrated Cronbach's alpha of 0.881 and split-half reliability of 0.806, and the Depression Scale showed Cronbach's alpha of 0.876 and split-half reliability of 0.850. These results indicate a high level of internal consistency and stability for all instruments, supporting their appropriateness for use in the current study.

Overall, the psychometric evaluation confirmed that the instruments are reliable, valid, and suitable for assessing executive functions, anxiety, and depression among children and adolescents with HUS, providing a solid methodological foundation for the study.

Results

(1) There are significant gender differences in executive functions, anxiety, and depression among patients with Hemolytic Uremic Syndrome (HUS).

To test this hypothesis, the researchers calculated the mean ranks for executive functions, anxiety, and depression according to gender (male vs. female), and assessed the significance of differences using the Mann–Whitney U test. The results are presented in Table 2.

Table (2)
Mann–Whitney U Test Results for Gender Differences in Executive Functions, Anxiety, and Depression (n = 40)

Variables	Mean Rank – Males (n = 22)	Mean Rank – Females (n = 18)	Z	Sig
Executive Function Dimensions				
Planning	20.14	21.10	-0.253	ns
Working Memory	19.52	22.13	-0.689	ns

Variables	Mean Rank –	Mean Rank –	Z	Sig
Monitoring	23.62	15.30	2.198	0.01
Inhibition	22.34	17.43	1.297	ns
Organization	20.74	20.10	0.171	ns
Total Executive Function	21.52	18.80	0.715	ns
Anxiety	16.82	26.63	-2.602	0.01
Depression	20.08	21.20	-0.299	ns

The results in Table 2 indicate no significant gender differences in most executive function dimensions, including planning, working memory, inhibition, organization, and the total executive function score, as well as in depression. In contrast, females showed significantly lower performance in monitoring ($Z = 2.198$, $p = 0.01$) and reported higher levels of anxiety ($Z = -2.602$, $p = 0.01$) compared to males. These findings suggest that while most aspects of executive functioning and depression are comparable across genders, females with HUS may experience greater difficulties in monitoring and higher anxiety levels than their male counterparts.

The results of the first hypothesis indicate that there are no significant gender differences in most executive function dimensions (planning, working memory, inhibition, organization) and depression among children and adolescents with Hemolytic Uremic Syndrome (HUS). However, females demonstrated significantly lower performance in monitoring and higher levels of anxiety compared to males. These findings suggest that gender may selectively affect specific executive processes and emotional responses in pediatric patients with HUS.

These results are partially consistent with previous research on executive functions and psychological outcomes in clinical populations. Studies have highlighted that executive functions are generally vulnerable to chronic illness and stress, regardless of gender, which could explain the non-significant differences observed in most executive dimensions and depression (Shuweikh, 2022; Abdel-Wahab, El-Bahiri, & Raslan, 2016). Similarly, Khuraisi (2017) found that executive deficits can occur across both male and female adolescents, particularly in high-stress or chronic conditions, supporting the lack of significant gender differences in planning, working memory, and organizational abilities.

On the other hand, the higher anxiety levels among females align with broader literature indicating that females are more prone to anxiety symptoms in both clinical and non-clinical populations (Hanan & Awda, 2020; Lotfy, 2016). This gender-related vulnerability could be explained by biological, hormonal, and psychosocial factors, including differences in stress reactivity, coping strategies, and emotional regulation (Barkley, 2012). In the context of HUS, where the disease and treatment processes are highly stressful, females may experience heightened anxiety, which in turn could affect their

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monitoring abilities, as monitoring requires sustained attention, error detection, and self-regulation (Diamond, 2013).

The current findings extend previous studies by demonstrating that, even in a rare clinical condition such as HUS, gender differences may manifest selectively in certain executive functions and emotional domains, rather than uniformly across all cognitive and affective variables. This highlights the importance of tailored psychological interventions, especially for female patients, to support emotional regulation and monitoring skills alongside medical treatment.

(2) There are significant correlations between executive functions, anxiety, and depression in patients with Hemolytic Uremic Syndrome:

To test this hypothesis, Pearson's correlation coefficient was calculated between the scores of the study sample on executive functions and anxiety and depression. The results are presented in Table 3.

Table (3)
Pearson's Correlation Coefficients Between Executive Functions
and Anxiety and Depression in Patients with HUS (n = 40)

Executive Function Dimensions	Anxiety	Depression
Planning	0.578**	0.429**
Working Memory	0.789**	0.736**
Monitoring	0.431**	0.316*
Inhibition	0.268	0.015
Organization	0.155	0.097
Total Executive Function	0.518**	0.329*

- * $p < 0.05$, ** $p < 0.01$

As shown in Table 3, the total scores of anxiety and depression were positively and significantly correlated with the executive function dimensions of planning, working memory, monitoring, and the total executive function score. This indicates that higher levels of anxiety and depression are associated with greater impairments in planning, working memory, monitoring, and overall executive functioning in patients with HUS.

Conversely, no significant correlations were observed between anxiety and depression and the executive function dimensions of organization and inhibition, suggesting that these aspects of executive functioning may be less affected by emotional disturbances in this patient population.

The results of the current study indicate that anxiety and depression are significantly positively correlated with several dimensions of executive functions, including planning, working memory, monitoring, and the overall executive function score, among patients with Hemolytic Uremic Syndrome (HUS). This suggests that higher levels of psychological

distress are associated with greater deficits in these cognitive control processes. These findings are consistent with the theoretical framework that positions executive functions as critical regulators of emotional and behavioral adaptation (Miyake et al., 2000; Diamond, 2013). Impairments in these functions, particularly in working memory and planning, can reduce individuals' ability to organize, regulate, and execute goal-directed behavior, which in turn may exacerbate the experience of anxiety and depressive symptoms.

Previous research has documented similar relationships in other clinical and non-clinical populations. For instance, Hanan and Awda (2020) found that elevated depression levels in elderly participants were associated with deficits in working memory and attention. Similarly, Latif Al-Sharbini (2016) reported that anxiety and depression among patients with chronic physical illnesses significantly affected cognitive control, including monitoring and planning abilities, ultimately reducing quality of life. Moreover, Asmaa Al-Sers, Walaa Hassan, and Mohamed El-Bahiri (2015) demonstrated significant negative correlations between executive function components (working memory, cognitive flexibility, inhibition) and anxiety scores, highlighting that impaired executive processes often co-occur with emotional dysregulation.

The present study extends these findings to a rare clinical population, patients with HUS, for whom research on the interplay between executive functioning and emotional disorders is scarce. While executive functions such as organization and inhibition were not significantly correlated with anxiety or depression in this sample, the observed relationships with planning, working memory, and monitoring align with neuropsychological studies indicating that these dimensions are particularly vulnerable to the effects of stress and mood disturbances (Miyake et al., 2000; Diamond, 2013). This selective vulnerability may reflect the specific cognitive demands required by these functions and the impact of emotional dysregulation on goal-directed behavior.

In sum, the current findings support the hypothesis that executive functions are closely linked with anxiety and depression and provide empirical evidence for the theoretical framework positing a bidirectional relationship between cognitive control and emotional well-being. Importantly, these results fill a gap in the literature by documenting these associations in children and adolescents with HUS, suggesting the need for integrated psychological and cognitive interventions to improve both emotional and executive functioning in this population.

Executive functions predict anxiety and depression in patients with Hemolytic Uremic Syndrome (HUS):

To examine the validity of this hypothesis, multiple regression analysis was employed to determine the extent to which executive function dimensions predict anxiety and depression among patients with Hemolytic Uremic Syndrome. Prior to conducting the regression analysis, the assumptions required for its application were examined. First, the assumption of normality was tested by inspecting skewness coefficients for the independent

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variables. The results indicated that skewness values for all executive function dimensions fell within acceptable limits, suggesting the absence of significant deviation from normality. Second, the assumption of no multicollinearity among the independent variables was verified. Multicollinearity occurs when high linear correlations exist among predictor variables, typically when correlation coefficients exceed ± 0.80 . Examination of the intercorrelation matrix revealed that none of the correlations among executive function dimensions exceeded this threshold, indicating that the predictors were sufficiently independent. Accordingly, multiple regression analysis was considered appropriate. The results are presented in Tables (4) and (5).

Table (4)

Results of Multiple Regression Analysis

Predictor Variables: Executive Function Dimensions

Dependent Variable: Total Anxiety Score in Patients with HUS

Predictor Variables	B	β	t	Sig.
Constant	12.672	—	6.740	0.01
Planning	0.068	0.106	0.159	n.s.
Working Memory	0.705	0.756	4.742	0.01
Monitoring	0.095	0.090	0.523	n.s.
Inhibition	0.828	0.654	3.301	0.01
Organization	0.180	0.198	1.270	n.s.

$F = 12.67$, $p < 0.01$, $R^2 = 0.65$

Table (5)

Results of Multiple Regression Analysis

Predictor Variables: Executive Function Dimensions

Dependent Variable: Total Depression Score in Patients with HUS

Predictor Variables	B	β	t	Sig.
Constant	5.175	—	3.124	0.01
Planning	0.051	0.102	0.498	n.s.
Working Memory	0.688	0.936	5.919	0.01
Monitoring	0.048	0.046	0.271	n.s.
Inhibition	0.168	0.408	2.273	0.05
Organization	0.053	0.073	0.474	n.s.

$F = 12.981$, $p < 0.01$, $R^2 = 0.66$

The findings of the multiple regression analyses presented in Tables (4) and (5) indicate that working memory and inhibition are significant predictors of both anxiety and depression in patients with Hemolytic Uremic Syndrome. Working memory emerged as the strongest predictor, demonstrating a highly significant effect on anxiety and depression at

the 0.01 level. Inhibition also showed a significant predictive contribution, reaching statistical significance at the 0.01 level for anxiety and at the 0.05 level for depression.

In contrast, the executive function dimensions of planning, monitoring, and organization did not exhibit significant predictive effects on either anxiety or depression. This suggests that emotional disturbances in patients with HUS are more closely related to core executive processes responsible for cognitive control and emotional regulation rather than higher-order organizational or planning abilities. Furthermore, the overall regression models were statistically significant, as indicated by the F-values. The executive function dimensions collectively explained 65% of the variance in anxiety and 66% of the variance in depression, reflecting a strong explanatory power. These findings highlight the substantial role of executive dysfunction in emotional outcomes among patients with HUS. From a theoretical standpoint, impairments in working memory may limit patients' capacity to regulate intrusive negative thoughts and illness-related worries, thereby increasing susceptibility to anxiety and depressive symptoms. Similarly, deficits in inhibitory control may hinder the ability to suppress maladaptive emotional responses and rumination, further exacerbating psychological distress. Therefore, deficits in these executive function components appear to represent key cognitive mechanisms underlying anxiety and depression in patients with Hemolytic Uremic Syndrome.

From a theoretical perspective, executive functions are conceptualized as higher-order cognitive processes responsible for goal-directed behavior, emotional regulation, and adaptive coping (Miyake et al., 2000; Diamond, 2013). Among these functions, working memory and inhibition are considered core executive processes that play a central role in controlling attention, regulating emotions, and managing intrusive thoughts (Baddeley, 2012). Impairments in working memory may reduce individuals' capacity to hold and manipulate information effectively, thereby limiting their ability to reappraise stressful experiences or regulate illness-related worries. This cognitive vulnerability may, in turn, increase susceptibility to anxiety and depressive symptoms.

Similarly, deficits in inhibitory control may impair the ability to suppress negative emotional responses, ruminative thinking, and maladaptive coping strategies. According to cognitive models of anxiety and depression, difficulties in inhibiting irrelevant or distressing thoughts contribute significantly to emotional dysregulation and the persistence of negative affect (Joormann & Gotlib, 2010; Beck, 2008). Thus, the present findings align with theoretical assumptions that core executive deficits constitute key cognitive mechanisms underlying emotional disorders.

The current results are also consistent with numerous empirical studies conducted in various clinical and non-clinical populations. Previous research has demonstrated strong associations between impairments in working memory and elevated levels of anxiety and depression in patients with chronic medical conditions, neurological disorders, and psychiatric populations (Snyder, Miyake, & Hankin, 2015; Rock et al., 2014). Similarly,

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inhibitory dysfunction has been repeatedly linked to increased emotional distress, particularly anxiety-related symptoms characterized by heightened arousal and intrusive thoughts (Eysenck et al., 2007).

Although direct studies examining executive functions as predictors of anxiety and depression in patients with HUS remain scarce, research addressing the neuropsychological and psychological consequences of HUS suggests that the condition may be associated with cognitive and emotional vulnerabilities. Previous studies have reported long-term neurological, cognitive, and emotional sequelae among pediatric and adolescent patients with HUS, including attention difficulties, executive dysfunction, and emotional problems (Trachtman et al., 2012; Garg et al., 2003). These findings provide indirect support for the present results and underscore the plausibility of executive dysfunction as a contributing factor to emotional disturbances in this patient population.

In contrast, the non-significant predictive role of planning, monitoring, and organization may suggest that higher-order executive skills are less directly involved in emotional symptomatology compared to core regulatory processes. This interpretation is supported by prior literature indicating that emotional disorders are more strongly associated with deficits in basic executive control mechanisms than with complex planning or organizational abilities (Snyder et al., 2015). Such findings reinforce the distinction between “core” and “higher-order” executive functions and their differential relevance to emotional regulation.

Overall, the substantial proportion of variance explained by executive function dimensions—65% for anxiety and 66% for depression—highlights the central role of executive dysfunction in shaping emotional outcomes among patients with Hemolytic Uremic Syndrome. These findings contribute to the existing literature by extending evidence from other clinical conditions to a relatively under-researched population, thereby addressing an important research gap. Clinically, the results emphasize the importance of incorporating cognitive and executive function assessments into psychological evaluation and intervention programs for patients with HUS, with particular attention to working memory and inhibitory control deficits.

The study examined gender differences and the relationship between executive functions, anxiety, and depression in children and adolescents with Hemolytic Uremic Syndrome (HUS). Findings indicated no significant gender differences in most executive function dimensions or depression, suggesting that HUS-related cognitive and emotional burdens affect both genders similarly. However, females showed lower monitoring performance and higher anxiety, highlighting selective gender-related vulnerabilities likely influenced by biological, hormonal, and psychosocial factors.

Correlation analyses revealed significant positive associations between anxiety, depression, and executive functions, particularly planning, working memory, and monitoring. Regression analyses further identified working memory and inhibition as key

predictors of both anxiety and depression, explaining 65–66% of the variance. These results underscore that core executive processes are crucial for emotional regulation, while higher-order functions like planning and organization have a less direct impact on emotional outcomes.

Overall, the study extends existing literature by demonstrating that executive dysfunction contributes significantly to emotional difficulties in HUS patients, emphasizing the need for integrated cognitive and psychological interventions, with special attention to female patients.

Recommendations

- **Comprehensive Assessment:** Include evaluation of working memory, inhibition, anxiety, and depression in routine psychological assessments of HUS patients.
- **Integrated Interventions:** Develop programs targeting both executive function deficits and emotional symptoms.
- **Gender-Sensitive Support:** Provide tailored interventions for females, focusing on anxiety management and monitoring skills.
- **Early Screening:** Identify executive dysfunction and emotional distress early to prevent worsening of psychological outcomes.
- **Future Research:** Conduct longitudinal and neuropsychological studies to clarify causal relationships between executive functions and emotional disorders in HUS.
- **Multidisciplinary Care:** Encourage collaboration among pediatricians, psychologists, and neuropsychologists to address both medical and psychological needs.

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