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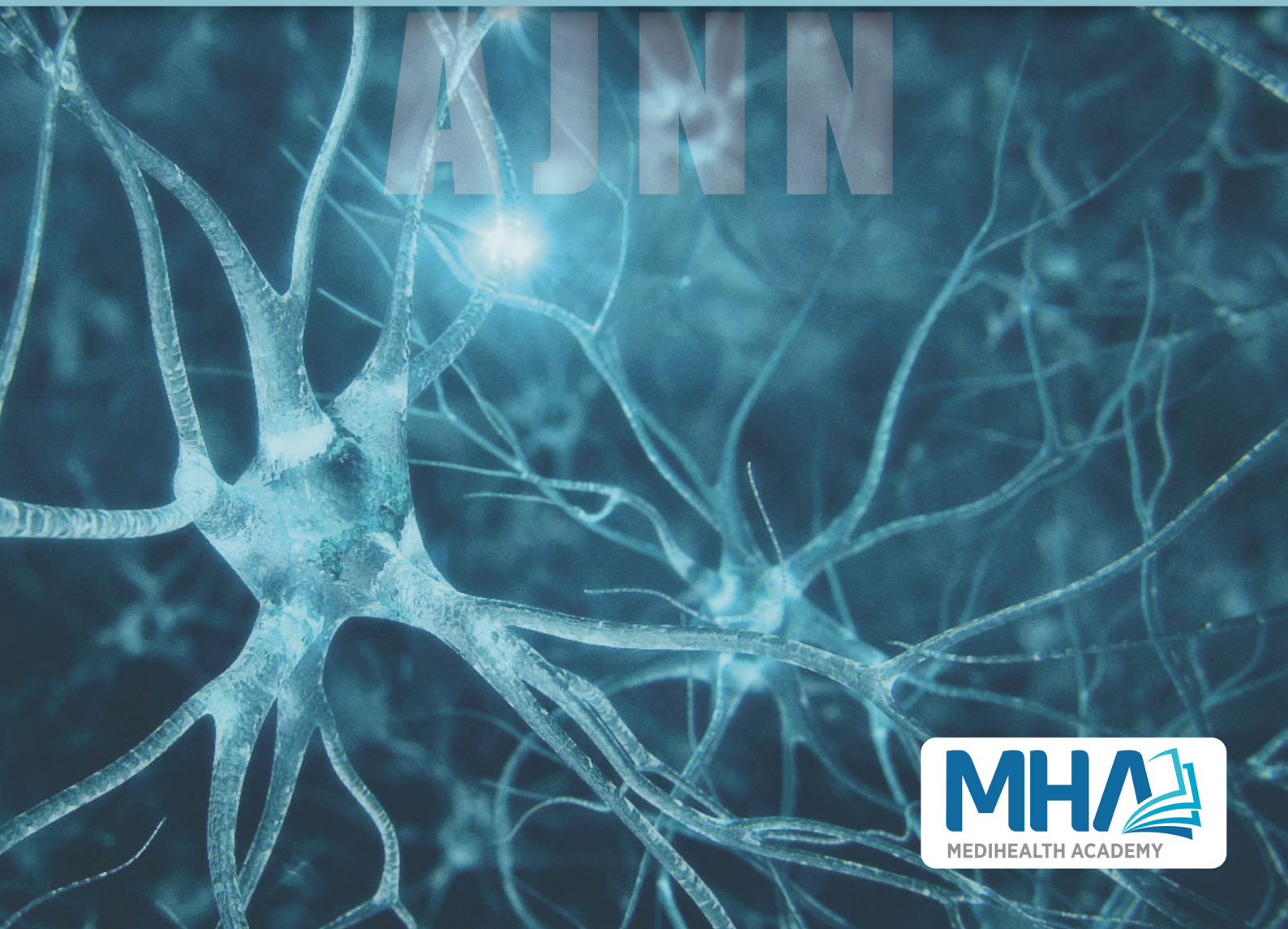

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Academic Journal of Neurology & Neurosurgery

Original Article

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Researching the correlation between clock drawing test outcomes and depression severity in patients with forgetfulness, mild cognitive impairment, and depression

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ABSTRACT

Aims: Depression and mild cognitive impairment (MCI) are syndromes that impair cognitive functions and negatively affect both patients and caregivers. This study aimed to compare Clock Drawing Test (CDT) results in patients with MCI and depression presenting with subjective memory complaints (SMC).

Methods: A total of 96 patients with SMC were retrospectively reviewed. MCI diagnosis was determined using the Standardized Mini-Mental Test (SMMT) administered by a neurologist. Patients with high Beck Depression Inventory (BDI) scores were referred to the psychiatry outpatient clinic and diagnosed with depression. CDT performance was evaluated across diagnostic groups. Statistical analyses were performed to examine differences according to depression status and cognitive assessment scores.

Results: Significant differences were observed between diagnostic groups regarding depression status ($p=0.001$) and SMMT results ($p=0.001$). No significant differences were found in relation to CDT results ($p>0.05$). The findings indicate that depression negatively influences cognitive performance in individuals with SMC, and that SMC is frequently observed in elderly patients.

Conclusion: SMC is common among older adults in tertiary care and should not be overlooked. Depression is associated with both subjective and objective cognitive impairment and represents a risk factor for dementia. Close monitoring of patients with SMC and depression may facilitate early detection of cognitive decline and timely interventions.

Keywords: Dementia, depression, forgetfulness, mild cognitive impairment, clock drawing test, subjective memory complaints

INTRODUCTION

Memory is a cognitive process that defines the perception, organization, encoding, storage, and recall of information. The term "forgetfulness" is a cognitive complaint that describes a perceived subjective impairment.[1] The concept of subjective memory complaints (SMC) is also used instead of the concept of forgetfulness. The memory performance of a person with SMC can be assessed using neuropsychological tests, and the results may indicate that their memory is intact or impaired.[2] SMC is also seen in cognitive disorders such as mild cognitive impairment (MCI) and depression.[3]

MCI is characterized by objectively measurable cognitive deficits on neuropsychological testing, with daily functioning largely preserved or only minimally affected, and it is often accompanied by SMC.[4,5] Nevertheless, the annual conversion rate of MCI cases to dementia has been reported as 6.7%, and the total 5-year conversion rate to dementia as 38.2%.[6]

Similarly, SMC is frequently seen in depression. It is known that cognitive losses secondary to depression, along with SMC, create a dementia-like picture, and this picture is called pseudodementia.[7-9] Recent studies have shown that depression, especially in the elderly, accelerates cognitive decline and doubles the risk of Alzheimer's dementia (AD). It is also thought that the pseudodementia picture that develops may actually be a precursor to a developing dementia picture.[10-12]

Neuropsychological assessment plays an important role in evaluating cognitive functions. The clock drawing test (CDT) is one of the neuropsychological tests used to assess visual-motor functions, planning, sequencing, and abstract thinking skills.[13] During the application of the CDT, cortical areas including the frontal, parietal, and temporal regions are active.[14,15] It is known that cognitive functions such as

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executive function, working memory, episodic memory, attention, and psychomotor processing speed are affected in individuals diagnosed with depression.[16,17]

Both depression and MCI are syndromes that impair cognitive functions and can have significant negative effects on both patients and caregivers. The aim of this study is to present and compare the results of CDT in patients diagnosed with MCI and depression who have SMC.

METHODS

Ethics

This study was conducted with the approval of the Clinical Researches Ethics Committee of Alanya Alaaddin Keykubat University (Date: 20.07.2022, Decision No: 06-06). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Purpose and Type of Study

The purpose of this study is to evaluate depression and MCI diagnoses in patients presenting with SMC, to compare the SMC characteristics of the diagnostic groups, and to examine their CDT performances and the relationship between them.

Study Population and Sample

This study retrospectively examined 96 patients who presented with SMC at the neurology outpatient clinic of a teaching and research hospital between 2020 and 2022. Patients who were literate, presented to the neurology outpatient clinic with complaints of forgetfulness, and had no mental retardation, known neurological disease, psychiatric illness, or medication use were included in the study.

Data Collection and Analysis

This study retrospectively examined the data of patients who presented to a neurology outpatient clinic with SMC. Patients who met the inclusion criteria for the study were included. In the study, patients examined by a neurology specialist were diagnosed with MCI based on the results of the Standardized Mini-Mental Test (SMMT). Patients with high Beck Depression Inventory (BDI) scores were referred to the psychiatry outpatient clinic and diagnosed with depression. The CDT scores of these three groups were evaluated.

Standardized Mini-Mental Test (SMMT)

This is a 30-item measure used to assess various cognitive functions such as orientation, immediate memory, recall, attention, calculation, and language.[18] Low scores indicate cognitive impairment. The validity and reliability study of the Turkish version of the form for educated individuals was conducted by Güngen and colleagues.[19]

Clock Drawing Test (CDT)

This scale is used to assess many different cognitive functions, including executive functions, memory, and attention, primarily visual-spatial functions, and there are many different applications and scoring methods.[20] In a study comparing three different CDT scoring systems, the newly developed algorithm for dementia diagnosis was reported to provide higher specificity and similar or better sensitivity than these three systems, and the scoring method of Shulman and colleagues[13] was described in a meta analysis as one of the most frequently investigated and highly sensitive systems for the CDT. Accordingly, participants are asked to place the numbers and hands of the clock inside a pre-drawn circle to show 10 minutes past 11 o'clock, and scoring is done on a scale of 0 (uncertain) to 5 (perfect clock). The aforementioned application method of the CDT was used in this study.[22]

Beck Depression Inventory (BDI)

Developed by Beck et al.[23] in 1961 to measure the behavioral symptoms of depression in adolescents and adults. Severity is interpreted as follows: 0-9=minimal, 10-16=mild, 17-29=moderate, 30-63=severe. The validity and reliability of the scale have been studied.[24]

Statistical Analysis

The data collected for the study were analyzed using the SPSS (Statistical Program in Social Sciences) 25 program. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to check whether the data collected for the study followed a normal distribution. The significance level (p) for comparison tests was set at 0.05. Since the variables did not follow a normal distribution ($p>0.05$), the analysis was continued using nonparametric test methods. The Mann-Whitney analysis was used for comparisons between independent pairs of groups. Cross-tabulations were created, and Chi-square analysis was applied for the comparison of categorical data. Descriptive values such as mean, standard deviation, median, number, and percentages were used.

RESULTS

In this study, the data of 96 patients who visited a neurology outpatient clinic with SMC were retrospectively examined. The study included 54 patients diagnosed with depression and 42 patients diagnosed with MCI.

No statistically significant differences were observed in the diagnostic groups (depression and MCI) among participants when analyzed by age, gender, and education level ($p>0.05$), (Table 1).

Statistically significant differences were found in diagnostic groups (depression and MCI) according to depression status ($p=0.001$). Statistically significant differences were also found in diagnostic groups (depression and MCI) according to SMMT results ($p=0.001$). However, no statistically significant differences were found in diagnostic groups (depression and MCI) according to clock drawing status ($p>0.05$), (Table 2).

No statistically significant relationship was found between the SMMT and CDT results in either the depression or MCI groups ($p>0.05$). Additionally, since SMMT scores were consistently between 28 and 30 for all participants in the depression group, no differences were observed (Table 3).

DISCUSSION

This study aimed to investigate the prevalence of MCI and depression in patients presenting to the neurology outpatient clinic with SMC, as well as to examine the relationship between these conditions. Tests that can be quickly administered in clinical practice were given to the subjects, and their cognitive performance was assessed objectively.

Table 1. Comparison of demographic variables according to diagnosis groups

		n/%	Groups		Total	χ^2	p
			Depression	MCI			
Gender	Male	n	27	19	46	0.066	0.797
		%	50.0%	45.2%	47.9%		
	Female	n	27	23	50		
		%	50.0%	54.8%	52.1%		
Education	0	n	1	1	2	0.849	0.838
		%	1.9%	2.4%	2.1%		
	1-5	n	10	7	17		
		%	18.5%	16.7%	17.7%		
	6-11	n	29	26	55		
		%	53.7%	61.9%	57.3%		
	≥12	n	14	8	22		
		%	25.9%	19.0%	22.9%		
			Depression	**MCI**	**Mann-Whitney U test**		**p**
Age	Mean±SD		62.46±14.04	67.38±11.18	919.000		0.112
	Median (min-max)		61.5 (27-88)	69 (44-88)			

n: frequency, %, percent, MCI: Mild cognitive impairment, SD: Standard deviation, Min: Minimum, Max: Maximum, *p<0.05; There is a statistically significant difference between the groups

Table 2. Comparison of variables by diagnostic groups

		n/%	Groups		Total	χ^2	p
			Depression	MCI			
Depression	No	n	5	21	26	21.617	0.001*
		%	9.3%	50.0%	27.1%		
	Mild	n	32	16	48		
		%	59.3%	38.1%	50.0%		
	Moderate	n	12	4	16		
		%	22.2%	9.5%	16.7%		
	Severe	n	5	1	6		
		%	9.3%	2.4%	6.3%		
SMMT	28-30	n	54	2	56	114.324	0.000*
		%	100.0%	4.8%	58.3%		
	24-27	n	0	36	36		
		%	0.0%	85.7%	37.5%		
	19-23 mild (demantia)	n	0	4	4		
		%	0.0%	9.5%	4.2%		
CDT	Severe	n	3	4	7	1.077	0.783
		%	5.6%	9.5%	7.3%		
	Moderate	n	10	6	16		
		%	18.5%	14.3%	16.7%		
	Mild	n	8	8	16		
		%	14.8%	19.0%	16.7%		
	Normal	n	33	24	57		
		%	61.1%	57.1%	59.4%		
Variable			**Depression**	**MCI**	**Mann-Whitney U test**		**p**
SMMT	Mean±SD		62.46±14.04	67.38±11.18	903.000		0.001*
	Median (min-max)		61.5 (27-88)	69 (44-88)			

n: frequency, %, percent, MCI: Mild cognitive impairment, SMMT: Standardized Mini-Mental Test, CDT: Clock Drawing Test, SD: Standard deviation, Min: Minimum, Max: Maximum, *p<0.05; There is a statistically significant difference between the groups

Given the limited number of studies evaluating complaints of forgetfulness in the Turkish population, this research is expected to offer helpful information regarding the characteristics of these complaints.[25]

In our study, 96 patients presented to the neurology outpatient clinic with SMC. Among these patients, 42 (43.75%) were diagnosed with MCI, while 54 (56.25%) were diagnosed with depression. Notably, none of these patients had previously sought care from the psychiatry outpatient clinic. This

Table 3. Comparison of SMMT and clock drawing status in groups

Groups			n/%	CDT				Total	χ^2	p
				Severe	Moderate	Mild	Normal			
Depresion	SMMT interval	28-30	n	3	10	8	33	54		
			%	100.0%	100.0%	100.0%	100.0%	100.0%		
		28-30	n	0	0	0	2	2		
			%	0.0%	0.0%	0.0%	8.3%	4.8%		
MCI	SMMT interval	24-27	n	4	6	6	20	36	5.918	0.432
			%	100.0%	100.0%	75.0%	83.3%	85.7%		
		19-23 mild	n	0	0	2	2	4		
			%	0.0%	0.0%	25.0%	8.3%	9.5%		

n: Frequency, %, percent, SMMT: Standardized Mini-Mental Test, MCI: Mild cognitive impairment

finding suggests a need to enhance public awareness about the concepts of forgetfulness, depression, and dementia among these individuals.

SMC can also manifest in psychiatric disorders such as depression in older adults; however, whether SMC should be used as a criterion for diagnosing MCI remains a topic of debate. Among patients diagnosed with MCI, there exists a subgroup that is unaware of their cognitive impairment, exhibiting low insight, and has been shown to progress more rapidly to dementia.[26] Thus, while the necessity of SMC for diagnosing MCI is contentious, it is important to evaluate SMC separately in all elderly individuals, given that MCI is a recognized risk factor for dementia progression.

In our study, the depression levels of patients diagnosed with MCI and depression were examined using the BDI, and a statistically significant difference was found between them (p=0.001). The depression levels of patients diagnosed with depression were found to be higher than those in the MCI group. In a study evaluating MCI, depression diagnosis, and healthy elderly individuals, depression levels were found to be high in the depression group, similar to our study. Unlike our study, this study also included a healthy elderly group, and it was found that the MCI group had statistically higher depression levels than healthy elderly individuals.[27] This finding is consistent with the studies by Hwang and colleagues[28] on the association between depressive symptoms and MCI. It has been determined that depressive symptoms can also be seen in MCI patients, but they are not as severe as in patients diagnosed with depressive disorder.

Studies have shown that there may be a relationship between depression and SMC, and it has also been reported that depression may be one of the early symptoms of dementia.[29-31] Large-scale meta-analyses and longitudinal cohort studies have consistently demonstrated that older adults with depression have a 1.5- to 2.5-fold increased risk of developing dementia. These findings highlight depression not only as a prevalent psychiatric condition in later life, but also as a significant and potentially modifiable risk factor for subsequent cognitive decline.[32,33]

In our study, the CDT was applied to the depression and MCI groups. Our study found no statistically significant difference in the CDT between the depression and MCI groups. In contrast to our study, another study found that the CDT scores of the MCI group were significantly lower than those of the control group of healthy elderly individuals and the depression group (p=0.013 and p=0.012, respectively), while no significant difference was observed between the depression group and the control group (p=0.977) (27). Due to the limited number of studies on this subject and the inconsistency of these data, a general assessment cannot be made. The heterogeneity in studies on the diagnostic accuracy of the CDT is likely due to significant heterogeneity in the underlying study populations (community samples and tertiary care samples). We believe that not evaluating subgroups of patients diagnosed with MCI and depression in our study may also have affected the results.

Limitations

There are limitations that may have affected our study. First, our study did not include a third healthy control group in addition to patients diagnosed with MCI and depression. Second, when evaluating SMC in our patients, their laboratory parameters were not assessed. Patients were given the BDI when evaluating their depression level. Since the patient groups were over 55 years of age, the geriatric depression scale could have been administered to the patients.

CONCLUSION

As a result, SMC is common among elderly individuals receiving tertiary healthcare services. However, the public needs to be made aware of the significance of this complaint. There is also a relationship between SMC and depression, and depression negatively affects individuals' objective performance. Depression is a risk factor for complaints of forgetfulness. Considering that depression is also a risk factor for dementia, it is thought that close monitoring of these individuals may also be beneficial in terms of early diagnosis of dementia.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Clinical Researches Ethics Committee of Alanya Alaaddin Keykubat University (Date: 20.07.2022, Decision No: 06-06).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained. This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and

there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

Concept: ŞÇ, EPZ; Design: ŞÇ, EPZ; Control: EZ, AB; Data Collection and/or Processing: ŞÇ, EPZ; Analysis and/or Interpretation: EPZ; Literature Review: EPZ; Article Writing: EPZ; Critical Review: All Authors.

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Original Article

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Evaluation of anterior pituitary hormonal changes in the acute phase of moderate and severe traumatic brain injury: a Nigerian experience

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ABSTRACT

Aims: Traumatic brain injury (TBI) is associated with acute neuroendocrine alterations involving the hypothalamic-pituitary axis, but the clinical significance of these early hormonal changes remains unclear. The aim of this study was to evaluate the early changes in anterior pituitary hormones following moderate and severe TBI and determine their relationship with injury severity.

Methods: This prospective longitudinal observational study included 42 adult patients with moderate and severe TBI presenting within 24 hours of injury. Serum levels of anterior pituitary hormones [adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), luteinising hormone (LH), and prolactin] were measured at admission, 48 hours, and 7 days post-injury. Data were analysed using SPSS version 20.0.

Results: Acute hormonal alterations were common, with elevated ACTH, LH, and prolactin observed in the majority of patients. No consistent or statistically significant association was found between hormone levels and TBI severity. While mean TSH levels were significantly higher in severe TBI at 7 days (p=0.031), values remained strictly within normal limits. Longitudinal comparisons were notably limited by a high cohort mortality rate.

Conclusion: Acute anterior pituitary hormonal alterations occur almost universally following moderate and severe TBI, reflecting an adaptive, stress-driven neuroendocrine reactivity rather than early pathological hypopituitarism. These isolated acute changes do not correlate with initial injury severity or serve as reliable indicators of primary pituitary failure.

Keywords: Traumatic brain injury, neuroendocrine response, anterior pituitary hormones, acute phase, injury severity

INTRODUCTION

Traumatic brain injury (TBI) is increasingly recognised as a systemic disease with significant neuroendocrine implications involving the hypothalamic-pituitary axis.[1,2] Acute hormonal alterations following TBI are common, particularly in patients with moderate and severe injury; however, their clinical significance and relationship to injury severity remain incompletely understood.[3]

Post-traumatic hypopituitarism (PTHP), once considered rare, is now well documented as a potential long-term complication of TBI, contributing to morbidity and impaired functional recovery.[4,5] However, in the acute phase of injury, hormonal changes may reflect a complex neuroendocrine stress response rather than true pituitary insufficiency.[6,7] Distinguishing between adaptive physiological responses and early pathological dysfunction remains a major challenge in neurotrauma research.

The pituitary gland is anatomically and vascularly vulnerable to traumatic injury. Mechanisms include direct mechanical disruption from basal skull fractures, shearing injury to the hypothalamic-pituitary axis, and secondary insults such as hypoxia, hypotension, and raised intracranial pressure, all of which may compromise pituitary perfusion and function.[6,8] The anterior pituitary, supplied predominantly by the hypophyseal portal system, is particularly susceptible to ischaemic injury and dysfunction.[6]

The anterior pituitary secretes key hormones including adrenocorticotropic hormone, thyroid-stimulating hormone,

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luteinising hormone, follicle-stimulating hormone, growth hormone, and prolactin. Alterations in these hormones have been associated with adverse clinical features such as fatigue, cognitive impairment, and reduced quality of life in TBI survivors.[9] Despite this, routine endocrine evaluation is not commonly performed in the acute management of head-injured patients.[5]

Although several studies have documented neuroendocrine disturbances following TBI, there remains limited data on the pattern and significance of early anterior pituitary hormonal changes in African populations.[8,10]

This study was therefore designed to evaluate changes in anterior pituitary hormone levels during the acute phase of moderate and severe TBI and to determine their relationship with injury severity.

METHODS

This study was conducted with the approval of the Health Research Ethics Committee of the University of Ilorin Teaching Hospital Health Researches Ethics Committee (UITH HREC) (Date: 06.04.2026, Decision No: REC PAN/2026/05/1641). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Written informed consent was obtained from all individual participants prior to their inclusion in the study.

This was a 12-month prospective longitudinal observational study conducted at the Accident and Emergency Unit of the University of Ilorin Teaching Hospital, a Nigerian tertiary institution between June 2015 and June 2016.

Forty-two consenting adult patients presenting within 24 hours of injury with moderate or severe TBI were enrolled. Injury severity was classified using the Glasgow Coma Scale (GCS) score after initial resuscitation, with moderate TBI defined as GCS 9-12 and severe TBI as GCS 3-8.

Demographic data, mechanism and timing of injury, and clinical features were documented. Detailed general and neurological examinations were performed for all patients.

Patients with pre-existing pituitary disorders, severe chronic systemic diseases (such as advanced renal or hepatic failure), those on chronic hormone replacement therapy, pregnant patients, and those with known psychiatric illness were excluded to minimize baseline endocrine confounding. Venous blood samples were obtained at presentation (within 24 hours of injury), and between 08:00 am and 10:00 am at 48 hours and 7 days post-injury to minimize circadian confounding. Serum levels of anterior pituitary hormones (adrenocorticotropic hormone, thyroid-stimulating hormone, luteinising hormone, and prolactin) were measured using a microplate immunoenzymometric assay technique according to manufacturer protocols.

All patients received standard institutional management for TBI, including supportive care, intensive care unit admission for severe cases, and surgical intervention where indicated based on cranial computed tomography findings. No patients received exogenous corticosteroid therapy during the acute study phase.

Statistical Analysis

Data were analysed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean±standard deviation. Data distribution was assessed for normality. Comparisons between groups were performed using appropriate parametric or non-parametric tests. Repeated measures were analysed using repeated measures analysis of variance. Pearson correlation analysis was used to assess relationships between continuous variables, while categorical variables were analysed using the Chi-square test. Statistical significance was set at $p \leq 0.05$.

RESULTS

Socio-Demographic Characteristics of the Study Population

A total of 42 patients were enrolled, comprising 39 males and 3 females (male-to-female ratio 13:1), with a mean age of 40.19±17.34 years (range 18-78 years). Nineteen patients (45.2%) had moderate TBI, while 23 (54.8%) had severe TBI. The majority of patients (57.1%) presented within 6 hours of injury, and road traffic crashes-predominantly motorcycle-related-were the most common mechanism (64.3%).

Management and Outcomes of Patients in the Study

Ten patients (23.8%) required surgical intervention, while 32 (76.2%) were managed conservatively. At discharge, mortality was 45.2%, with the remaining patients distributed across varying levels of neurological recovery.

Anterior Pituitary Hormone Profile of the Study Population

Alterations in anterior pituitary hormone levels were observed across the study population at all-time points. Critically, 100% of the recorded abnormalities for ACTH, LH, and prolactin within the first 24 hours represented absolute clinical elevations above standard reference. Elevated serum adrenocorticotropic hormone (ACTH), luteinising hormone (LH), and prolactin were the most frequently observed abnormalities, occurring in 81.8%, 72.7%, and 57.1% of patients, respectively, within the first 24 hours post-injury. In contrast, follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), and growth hormone (GH) remained within normal reference ranges in the majority of patients.

Comparative analysis between moderate and severe TBI groups demonstrated no consistent or statistically significant differences in mean hormone levels at 24 hours, 48 hours, or 7 days post-injury for most parameters. Although mean ACTH levels were higher in moderate TBI across all time points, these differences were not statistically significant. Similarly, serum LH and prolactin levels showed variable patterns between groups without significant association with injury severity.

Mean serum TSH was significantly higher in patients with severe TBI at 7 days post-injury (2.18±1.61 µIU/ml vs 1.10±0.53 µIU/ml; $p=0.031$); however, values in both groups remained within normal reference ranges.

Serial analysis demonstrated dynamic changes in hormone levels over time, particularly for prolactin and ACTH, though these trends did not correlate with injury severity. It is noteworthy that the number of patients contributing data at later time points decreased due to mortality, which may have influenced longitudinal comparisons.

Overall, no significant correlation was identified between anterior pituitary hormone levels and TBI severity. Detailed hormone profiles and comparisons are presented in Tables 1-4.

DISCUSSION

This study evaluated acute anterior pituitary hormonal changes in patients with moderate and severe TBI and their relationship with injury severity. The findings demonstrate that alterations in anterior pituitary hormone levels are common in the acute phase of TBI, with ACTH, LH, and prolactin being most frequently affected. However, these changes did not show a consistent or statistically significant association with injury severity.

The marked male predominance and the high incidence of road traffic-related injuries observed in this cohort are consistent with previous reports from Nigeria and other regions, reflecting the increased exposure of young males to

Table 4. Anterior pituitary hormone profile in patients with moderate and severe TBI

Hormone	Status	1st 24 hours n=42 (%)	48 hours n=42 (%)	1 week n=42 (%)
FSH	Normal	41 (97.6)	30 (100.0)	21 (100.0)
	Abnormal	1 (2.4)	0 (0.0)	0 (0.0)
LH	Normal	10 (23.8)	15 (51.7)	15 (71.4)
	Abnormal	32 (76.2)	14 (48.3)	6 (28.6)
Prolactin	Normal	18 (42.9)	17 (58.6)	13 (61.9)
	Abnormal	24 (57.1)	12 (41.4)	8 (38.1)
TSH	Normal	42 (100.0)	30 (100.0)	21 (100.0)
	Abnormal	0 (0.0)	0 (0.0)	0 (0.0)
ACTH	Normal	6 (14.3)	5 (16.7)	4 (19.0)
	Abnormal	36 (85.7)	25 (83.3)	17 (81.0)
GH	Normal	39 (92.9)	27 (96.4)	20 (100.0)
	Abnormal	1 (2.4)	1 (3.6)	0 (0.0)
	N/A*	2 (4.8)	14 (33.3)	22 (52.4)

*N/A: Not available-patients who had died at the time of sample collection, TBI: Traumatic brain injury, FSH: Follicle-stimulating hormone, LH: Luteinising hormone, TSH: Thyroid-stimulating hormone, ACTH: Adrenocorticotropic hormone, GH: Growth hormone

Table 1. Comparison of anterior pituitary hormone levels in patients with moderate and severe TBI at 24 hours post-trauma

Time point/variable	Moderate TBI (n=19) mean±SD	Severe TBI (n=23) mean±SD	T	p-value
24 hours				
FSH (mIU/ml)	3.67±1.37	5.41±4.18	-1.950	0.058
LH (mIU/ml)	13.27±8.06	16.91±16.43	-0.956	0.345
Prolactin (ng/ml)	30.00±23.94	25.86±27.35	0.519	0.606
TSH (µIU/ml)	1.24±0.64	1.19±0.74	0.251	0.803
ACTH (pg/ml)	468.16±523.73	270.88±152.81	1.505	0.140
GH (µIU/ml)	14.80±23.20	7.27±5.27	1.233	0.225

*Statistically significant (p ≤ 0.05). TBI: Traumatic brain injury, SD: Standard deviation, FSH: Follicle-stimulating hormone, LH: Luteinising hormone, TSH: Thyroid-stimulating hormone, ACTH: Adrenocorticotropic hormone, GH: Growth hormone

Table 2. Comparison of anterior pituitary hormone levels in patients with moderate and severe TBI at 48 hours post-trauma

Time point/variable	Moderate TBI (n=19) mean±SD	Severe TBI (n=23) mean±SD	t	p-value
48 hours				
FSH (mIU/ml)	2.12±0.74	3.00±1.66	-2.016	0.053
LH (mIU/ml)	8.10±5.05	13.27±11.59	-1.666	0.107
Prolactin (ng/ml)	19.50±10.95	31.45±49.99	-0.987	0.332
TSH (µIU/ml)	1.30±1.14	1.18±0.71	0.317	0.754
ACTH (pg/ml)	414.21±174.75	282.73±213.31	1.832	0.078
GH (µIU/ml)	9.56±14.37	8.20±9.55	0.266	0.792

*Statistically significant (p≤0.05). TBI: Traumatic brain injury, SD: Standard deviation, FSH: Follicle-stimulating hormone, LH: Luteinising hormone, TSH: Thyroid-stimulating hormone, ACTH: Adrenocorticotropic hormone, GH: Growth hormone

Table 3. Comparison of anterior pituitary hormone levels in patients with moderate and severe TBI at 1 week post-trauma

Time point/variable	Moderate TBI (n=19) mean±SD	Severe TBI (n=23) mean±SD	t	p-value
1 week				
FSH (mIU/ml)	3.29±2.15	3.44±1.50	-0.173	0.865
LH (mIU/ml)	6.71±3.07	11.50±8.39	-1.931	0.069
Prolactin (ng/ml)	16.32±10.06	24.21±25.89	-1.017	0.322
TSH (µIU/ml)	1.10±0.53	2.18±1.61	-2.324	0.031*
ACTH (pg/ml)	403.93±292.54	325.71±267.31	0.593	0.560
GH (µIU/ml)	8.18±6.47	11.17±6.05	-0.964	0.348

*Statistically significant (p≤0.05). TBI: Traumatic brain injury, SD: Standard deviation, FSH: Follicle-stimulating hormone, LH: Luteinising hormone, TSH: Thyroid-stimulating hormone, ACTH: Adrenocorticotropic hormone, GH: Growth hormone

high-risk activities.[11,12] The extreme male-to-female ratio (13:1) observed in this study is highly characteristic of neurotrauma demographics in Sub-Saharan Africa. It reflects a profound epidemiological socio-economic reality: young males overwhelmingly dominate high-risk outdoor occupations and commercial motorcycle transport in Nigeria, making them the primary victims of severe road traffic crashes. While this limits the generalizability of our findings to female populations, it accurately portrays the specific high-risk demographic confronting regional emergency units.

A key observation in this study is the predominance of elevated hormone levels, particularly ACTH and prolactin, in the early phase following injury. This pattern is most consistent with activation of the hypothalamo-pituitary axis as part of the systemic stress response to trauma rather than primary pituitary insufficiency.[6,7] Similar findings have been reported in other studies, which suggest that acute neuroendocrine alterations following TBI are often transient and may normalise over time.[13]

When examining immediate clinical trajectories, the cohort's high mortality rate (45.2%) revealed that extreme baseline elevations of ACTH and prolactin were disproportionately concentrated among patients who ultimately succumbed to their injuries. Rather than signaling premature post-traumatic hypopituitarism, these pronounced acute surges serve as profound neuroendocrine markers of maximal, decompensated systemic stress. This aligns with global literature showing that uninhibited HPA axis and prolactin spikes strongly mirror the overall magnitude of structural brain damage and systemic hemodynamic failure, reinforcing their acute prognostic value.

This extreme physiological strain is further evidenced by the ACTH elevation across both moderate and severe TBI groups which likely reflects activation of the hypothalamo-pituitary-adrenal axis in response to physiological stress. Although mean ACTH levels were higher in moderate TBI compared to severe TBI, this difference was not statistically significant and should be interpreted with caution even though similar patterns have been described in previous studies of acute TBI.[13] In addition to the trauma itself, acute intensive care management introduces unavoidable pharmacological confounders. Routine medications administered during neuroresuscitation-such as dopamine infusions, continuous opioid sedation, and anticonvulsants-possess profound modulatory effects on the anterior pituitary. For instance, dopamine strongly suppresses TSH and prolactin secretion, while critical care stress and sedatives can induce transient functional hypopituitarism. Because these therapeutic interventions could not be ethically withheld, their underlying influence remains an inherent factor in acute-phase endocrine profiling.

Consequently, these external clinical influences may explain why alterations in gonadotropins (LH and FSH) were variable. While LH was elevated in a substantial proportion of patients in the early phase, FSH remained largely within normal limits. These findings differ from some reports that describe suppression of the hypothalamo-pituitary-gonadal axis following TBI, highlighting the heterogeneity of endocrine responses in acute brain injury.[14,15]

Parallel to the gonadotropin fluctuations, serum prolactin demonstrated dynamic changes over time, with early elevation followed by gradual normalisation in surviving patients. The lack of a consistent association with injury severity is in keeping with previous studies and underscores the complex regulation of prolactin in the context of acute stress and hypothalamic dysfunction.[8,14] Similarly, although mean serum TSH was significantly higher in severe TBI at one week, values remained within normal reference ranges, limiting the clinical significance of this finding. Similar observations have been reported, where alterations in thyroid function tests in acute TBI did not necessarily reflect true thyroid axis failure.[16]

Overall, the absence of a clear relationship between hormone levels and injury severity suggests that early hormonal changes may not be reliable markers of TBI severity. This finding is consistent with previous reports that emphasise the limited prognostic utility of isolated endocrine measurements in the acute phase of injury.[6]

Limitations

This study has several limitations including sample size constraints, methodological boundaries, and therapeutic confounding. First, the study cohort is relatively small (n=42), which limits the statistical power required to detect subtle subgroups or minor correlations between specific hormone fluxes and injury severity sub-types. However, as one of the very few prospective longitudinal series on the subject matter at hand in this region, it serves as a critical baseline for larger, multicentre neurotrauma registries. Compounding this sample size constraint, serial measurements were affected by mortality, resulting in a reduced number of observations at later time points and potential survivorship bias. From a methodological standpoint, hormonal assays were limited to baseline measurements without dynamic endocrine testing, which restricts definitive assessment of pituitary function. Furthermore, we did not measure downstream target endocrine gland hormones (such as serum cortisol, free thyroxine, or testosterone). The absence of these paired target-gland end points is a limitation that restricts our capacity to map complete feedback-loop integrity or diagnose peripheral glandular exhaustion. Consequently, our findings are strictly indicative of acute anterior pituitary reactivity rather than comprehensive axis function. Finally, complex clinical realities introduced unisolated variables; potential confounding factors such as intensive care supportive management, surgical stress, and routine critical care medications (including sedatives) were not fully isolated, and may have contributed to the acute stress-driven spikes in ACTH and prolactin.

CONCLUSION

This study demonstrates that acute alterations in anterior pituitary hormones-most notably ACTH, LH, and prolactin-are nearly universal following moderate and severe TBI in this Nigerian cohort. Rather than signaling early pathological pituitary failure, these transient hormonal shifts represent a profound, adaptive neuroendocrine stress response to severe systemic and mechanical trauma.

Crucially, the absence of a statistically significant correlation between these early hormone levels and initial GCS scores

suggests that isolated acute endocrine measurements are not reliable predictors of injury severity. While TSH levels showed a statistically significant elevation in severe cases by the seventh day, the values remained well within normal reference ranges, further underscoring the adaptive, homeostatic nature of the acute-phase response.

Given the high mortality rate observed and the dynamic, medication-influenced nature of these acute endocrine profiles, these findings caution clinicians against premature diagnosis of PTHP in the immediate post-injury phase. Management should prioritize standard supportive neuroresuscitation, reserving comprehensive endocrine screening for survivors who display persistent, symptomatic features during long-term recovery. Future regional research utilizing larger, multicentre cohorts and dynamic endocrine testing is warranted to accurately map the longitudinal transition from an adaptive stress response to chronic neuroendocrine dysfunction in African populations.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Health Research Ethics Committee of the University of Ilorin Teaching Hospital Health Researches Ethics Committee (UITH HREC) (Date: 06.04.2026, Decision No: REC PAN/2026/05/1641).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights-including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Conceptualization: NAA; Data Curation: NAA; Formal analysis: NAA; Writing-Original Draft: NAA; Writing-Review & Editing: ASY, OTO, SAB, OOA; Supervision: ASY, OTO, SAB; All authors reviewed the results and approved the final version of the manuscript.

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Original Article

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Comparison of pulmonary and hemodynamic parameters in patients undergoing lumbar disc herniation surgery in prone and sitting-prone positions

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ABSTRACT

Aims: Patient positioning during lumbar spine surgery plays a crucial role in determining both surgical exposure and perioperative physiological stability. This study aimed to compare the effects of prone and sitting-prone (knee-chest) positions on pulmonary and hemodynamic parameters in patients undergoing lumbar disc herniation surgery under general anesthesia.

Methods: This retrospective observational study included 50 patients classified as ASA I–III who underwent lumbar disc herniation surgery between March 2024 and March 2025. Patients were divided into two groups based on intraoperative positioning: prone (n=25) and sitting-prone (n=25). Hemodynamic variables, arterial blood gas parameters, and respiratory mechanics were recorded at three time points: in the supine position, immediately after positioning, and 30 minutes after surgical incision. Statistical analysis was performed using SPSS software, and a p-value <0.05 was considered statistically significant.

Results: Baseline demographic and physiological parameters were comparable between the groups. Following positioning, lower diastolic blood pressure values were observed in the sitting-prone group. At 30 minutes intraoperatively, oxygenation parameters were higher and peak airway pressure values were lower in the sitting-prone group compared to the prone group. These findings indicate improved pulmonary mechanics in the sitting-prone position.

Conclusion: The sitting-prone position appears to provide superior oxygenation and lower airway pressures compared to the prone position, while maintaining acceptable hemodynamic stability. These findings suggest that sitting-prone positioning may be considered a safer and more physiologically advantageous alternative during lumbar spine surgery.

Keywords: Prone position, sitting-prone position, lumbar herniation surgery, pulmonary mechanics, general anesthesia

INTRODUCTION

Low back pain represents one of the leading causes of disability worldwide and affects approximately 80% of individuals at some point in their lives.[1] Among its etiologies, lumbar disc herniation (LDH) is a predominant condition characterized by the displacement of intervertebral disc material, resulting in nerve root compression and radicular symptoms.[2] While conservative management remains the first-line treatment, surgical intervention is indicated in cases of progressive neurological deficits, severe pain, or failure of non-operative therapy.[2]

Lumbar spine surgeries are commonly performed under general anesthesia, where patient positioning becomes a critical factor influencing both surgical access and physiological responses. The prone position is the most frequently utilized approach, allowing optimal visualization of posterior spinal structures. However, it is associated with significant physiological alterations, including increased intra-abdominal pressure, decreased venous return, reduced cardiac output, and impaired pulmonary function.[3,4]

The increase in intra-abdominal pressure in the prone position leads to cephalad displacement of the diaphragm, resulting in decreased functional residual capacity and lung compliance.[5] Consequently, airway pressures increase, and ventilation-perfusion mismatch may occur, potentially leading to hypoxemia and postoperative pulmonary complications.[6]

The sitting-prone (knee-chest) position, in which the hips and knees are flexed while the chest is supported and the

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abdomen remains free from compression, has been proposed as an alternative technique designed to reduce abdominal compression and improve surgical exposure (Figure).

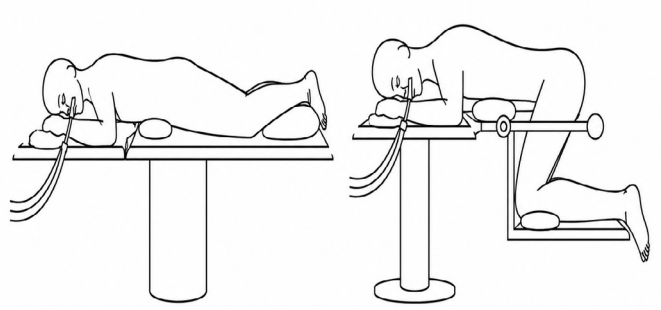

Figure. Prone and sitting prone position

METHODS

This study was conducted with the approval of the Non-interventional Researches Ethics Committee at Kırıkkale University (Date: 28.05.2025, Decision No: 2025.05.03). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Ethical approval was obtained retrospectively for the review of archived anesthesia and patient records. The medical records of patients who underwent lumbar disc herniation surgery between March 2024 and March 2025 were retrospectively reviewed.

A total of 50 patients aged 18 years and older, classified as ASA I-III, were included in the study. Patients were divided into two groups according to surgical positioning: the prone group (n=25) and the sitting-prone group (n=25). Exclusion criteria included ASA IV-V classification, incomplete clinical data, and the use of regional anesthesia.

All patients underwent a standardized anesthesia protocol. Following routine monitoring, anesthesia was induced with propofol, fentanyl, and rocuronium. Endotracheal intubation was performed, and mechanical ventilation was initiated in volume-controlled mode. Ventilator settings included a tidal volume of 6-8 ml/kg, a respiratory rate of 12-15 breaths per minute, and a PEEP of 5-8 cmH_2O. End-tidal CO_2 was maintained within the range of 30-40 mmHg. Anesthesia maintenance was achieved using sevoflurane and remifentanil infusion.

Hemodynamic parameters, including heart rate, systolic and diastolic blood pressure, and oxygen saturation, were recorded at three time points: in the supine position, immediately after positioning, and 30 minutes after the initiation of surgery. Arterial blood gas analysis was performed concurrently, measuring pH, PaO_2, $PaCO_2$, and SaO_2. Respiratory mechanics were evaluated by measuring peak airway pressure (Ppeak).

Statistical Analysis

The data was performed using SPSS version 25.0. Continuous variables were expressed as mean±standard deviation. Intergroup comparisons were conducted using appropriate parametric or non-parametric tests based on data distribution. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study population consisted of 50 patients, with 25 patients in each group. There were no statistically significant differences between the groups in terms of demographic characteristics, including age, sex, body weight, height, and ASA classification (p>0.05) (Table 1).

Table 1. Demographic and baseline characteristics of the patients

Parameter	Prone group (n=25)	Sitting-prone group (n=25)	p-value
Age (years)	45.2±12.1	46.8±11.5	>0.05
Gender (M/F)	14/11	13/12	>0.05
Weight (kg)	78.4±10.2	76.9±9.8	>0.05
Height (cm)	168.3±7.1	169.1±6.5	>0.05
ASA (I/II/III)	10/11/4	9/12/4	>0.05

M: Male, F: Female, ASA I: Healthy patient, ASA II: Patient with mild systemic disease, ASA III: Patient with severe systemic disease

In the supine position, no significant differences were observed between the groups in terms of hemodynamic parameters or arterial blood gas values, confirming comparable baseline physiological conditions. Hemodynamic parameters measured at different time points are presented in Table 2. Following positioning, diastolic blood pressure was significantly lower in the sitting-prone group (p<0.05). At 30 minutes intraoperatively, heart rate was significantly lower in the prone group compared to the sitting-prone group (p<0.05).

Table 2. Hemodynamic parameters at different time points

Parameter	Time	Prone group	Sitting-prone group	p-value
HR (bpm)	Supine	78±10	80±9	>0.05
	Position	82±11	85±10	>0.05
	30 min	76±9	84±10	<0.05
SBP (mmHg)	Supine	125±15	128±14	>0.05
	Position	120±13	118±12	>0.05
	30 min	118±12	115±11	>0.05
DBP (mmHg)	Supine	78±9	80±8	>0.05
	Position	76±8	70± 7	<0.05
	30 min	75±7	72±6	>0.05

HR: Heart rate, bpm: Beats per minute, Min: Minute, SBP: Systolic blood pressure, mmHg: Millimeters of mercury, DBP: Diastolic blood pressure

Following positioning, diastolic blood pressure was found to be significantly lower in the sitting-prone group compared to the prone group (p<0.05). However, no significant differences were observed in systolic blood pressure, heart rate, or oxygen saturation at this stage.

At 30 minutes after the initiation of surgery, significant differences emerged between the groups. The sitting-prone group demonstrated significantly higher PaO_2 and SaO_2 values compared to the prone group (p<0.05), indicating improved oxygenation. Conversely, peak airway pressure was significantly higher in the prone group (p<0.05) (Table 3).

Table 3. Respiratory and arterial blood gas parameters

Parameter	Time	Prone group	Sitting-prone group	p-value
PaO_2 (mmHg)	Supine	92±8	93±7	>0.05
	Position	95±9	100±8	>0.05
	30 min	90±7	102±9	<0.05
SaO_2 (%)	Supine	97±1	97±1	>0.05
	Position	97±1	98±1	>0.05
	30 min	96±1	99±1	<0.05
$PaCO_2$ (mmHg)	Supine	38±3	37±3	>0.05
	Position	39±3	38±3	>0.05
	30 min	40±4	38±3	>0.05
Ppeak (cmH_2O)	Supine	18±3	17±2	>0.05
	Position	22±4	19±3	<0.05
	30 min	24±4	20±3	<0.05

PaO_2: Partial pressure of arterial oxygen, Min: Minute, SaO_2: Arterial oxygen saturation, Ppeak: Peak airway pressure, cmH_2O: Centimeters of water

DISCUSSION

The present study demonstrates that patient positioning during lumbar spine surgery significantly influences both pulmonary and hemodynamic parameters. Our findings suggest that the sitting-prone position provides superior oxygenation and lower airway pressures compared to the conventional prone position, while maintaining overall hemodynamic stability.

The prone position has long been considered the standard approach in lumbar spine surgery due to its ability to provide optimal surgical exposure. However, it is well established that this position is associated with increased intra-abdominal pressure, which leads to cephalad displacement of the diaphragm and a subsequent reduction in functional residual capacity and lung compliance.[3,9] These physiological alterations result in increased airway pressures and may impair gas exchange. The significantly higher peak airway pressures observed in the prone group in our study are consistent with these previously reported findings.

In contrast, the sitting-prone position appears to mitigate many of these adverse respiratory effects. By allowing the abdomen to remain free and reducing intra-abdominal pressure, this position facilitates diaphragmatic excursion and improves lung compliance. This likely explains the significantly higher PaO_2 and SaO_2 values observed in the sitting-prone group at 30 minutes intraoperatively. Improved oxygenation in this position may be attributed to better ventilation-perfusion matching, as has been suggested in previous studies evaluating positional effects on pulmonary physiology.[10]

Another important finding of this study is the difference in airway pressures between the two groups. Elevated peak airway pressure is clinically relevant, as it is associated with an increased risk of barotrauma and ventilator-induced lung injury. The lower Ppeak values observed in the sitting-prone group suggest that this position may offer a protective advantage for the lungs, particularly in patients with pre-existing pulmonary compromise.

The hemodynamic effects of patient positioning must also be carefully considered. In our study, diastolic blood pressure was significantly lower in the sitting-prone group immediately after positioning. This finding may be explained by reduced venous return due to gravitational effects and decreased preload, which are known consequences of elevated positioning.[8,11] Although this reduction in blood pressure did not appear to result in clinically significant instability in our cohort, it underscores the importance of vigilant hemodynamic monitoring and appropriate fluid management when using the sitting-prone position.

Interestingly, heart rate was found to be lower in the prone group at 30 minutes intraoperatively. While the clinical significance of this finding is uncertain, it may reflect compensatory autonomic responses to differences in preload and vascular resistance between the two positions. Further studies incorporating advanced hemodynamic monitoring techniques could provide more insight into these mechanisms.

When interpreting our findings, it is important to consider the broader clinical implications. Improved oxygenation and reduced airway pressures are particularly advantageous in patients with limited pulmonary reserve, obesity, or chronic respiratory disease. In such populations, even modest improvements in respiratory mechanics may translate into reduced perioperative morbidity. Therefore, the sitting-prone position may be especially beneficial in selected high-risk patient groups.

Our findings are generally consistent with the existing literature, which suggests that minimizing abdominal compression during prone positioning improves respiratory outcomes. However, direct comparisons between prone and sitting-prone positions remain limited, and our study contributes to this relatively underexplored area. By providing comparative data, this study helps to clarify the physiological advantages of the sitting-prone position.

Limitations

Despite these strengths, several limitations should be acknowledged. First, the retrospective design of the study introduces the possibility of selection bias and limits the ability to establish causal relationships. Second, the relatively small sample size may reduce the statistical power to detect subtle differences between groups. Third, we did not evaluate postoperative outcomes such as pulmonary complications, length of hospital stay, or patient recovery, which would provide a more comprehensive assessment of the clinical impact of positioning.

CONCLUSION

The sitting-prone position appears to offer meaningful advantages in terms of pulmonary function by improving oxygenation and reducing airway pressures. While careful attention must be paid to potential hemodynamic changes, these effects are generally manageable in clinical practice. Taken together, our findings support the consideration of sitting-prone positioning as a viable and potentially superior alternative to the traditional prone position in lumbar spine surgery. Future prospective, randomized controlled studies with larger sample sizes are needed to validate these findings and further explore the long-term outcomes associated with

different surgical positions. Additionally, incorporating advanced monitoring techniques, such as dynamic lung compliance measurements and cardiac output monitoring, may provide deeper insights into the physiological mechanisms underlying the observed differences.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Non-interventional Researches Ethics Committee at Kırıkkale University (Date: 28.05.2025, Decision No: 2025.05.03).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained. This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Conceptualization: IG; Methodology: IG, SD; Data Collection: SD; Statistical Analysis: SD; Writing-Original Draft: SD, IG; Writing-Review & Editing: IG, MÖ.

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Case Report

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Cerebral infarction following snake bite: observation of a case at the Sourô Sanou University Hospital in Bobo-Dioulasso

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ABSTRACT

Snake bites are a public health problem in developing countries. Neurovascular complications are rare. We report a case of cerebral infarction at the Sourô Sanou University Hospital Center in Bobo-Dioulasso complicating a snake bite. The patient was a 44-year-old left-handed man with no cardiovascular risk factors, presenting with left hemiplegia and expressive aphasia two days after a snake bite (reported to be a viper). Cerebral computed tomography revealed a well-systematized right temporo-parietal cortico-subcortical hypodensity in the deep and superficial territory of the right middle cerebral artery (MCA). He received polyvalent antivenom from Vins Bioproducts Ltd and symptomatic treatment from the first day. The outcome was unfavorable, and the patient died on the eighth day after the bite. Cerebral infarction is a rare complication of snake bite envenomation. However, it is responsible for high morbidity and mortality in our context.

Keywords: Cerebral infarction, envenomation, ophidian, Bobo-Dioulasso, Burkina Faso

INTRODUCTION

Snake bite envenomation remains a major public health challenge in tropical areas, particularly in West Africa. According to the WHO, approximately 5.4 million bites occur worldwide each year, of which 1.8 to 2.7 million result in clinical envenomation, causing between 81.410 and 137.880 deaths annually, as well as permanent disability in many cases.[1,2]

In Burkina Faso, this burden is particularly heavy, especially in rural areas. A recent study in the Cascades region (2016-2021) showed that 42% of patients hospitalized for envenomation had complications, and that delayed access to care, lack of antivenom, and harmful traditional practices (tourniquets, incisions) were strongly associated with these complications.[3] However, access to antivenom has improved recently. In 2023, the government subsidized antivenom serums, reducing their cost to 2.000 CFA francs, a major step forward for the rural population.[4] At the same time, traditional medicine continues to play a central role. An ethnobotanical study conducted in 2025 documents the use of plants by traditional practitioners to neutralize venom. More than 60% of them report effective remedies, and nearly half refer patients to hospitals when their treatment alone is not sufficient.[5]

Despite this progress, serious neurological complications such as strokes remain poorly documented. At the Sourô Sanou University Hospital in Bobo-Dioulasso, two recently reported cases of cerebral hemorrhage following envenomation demonstrate the lethal and disabling potential of these rare forms.[6]

In this context, it is essential to raise awareness of atypical neurovascular forms (ischemic or hemorrhagic) and the need to improve care (diagnosis, antivenom, intensive care), especially in an under-resourced health system. We present here a case of cerebral infarction following a viper bite at the Sourô Sanou University Hospital Center, illustrating one of the most severe and little-known complications in Burkina Faso.

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CASE

The patient is a 44-year-old male farmer, independent, left-handed, residing in a rural area (Seguéré, Bama department, Houet province, Guiriko region); with no particular medical history or cardiovascular risk factors, who was bitten by a snake on his right thumb on November 2, 2025, at around 6 p.m. while working in the fields. The snake was described as a viper (killed after the bite and not available for identification). The bite immediately caused local swelling at the site. At the local health facility, he received one ampoule of Vins Bioproducts Ltd's Africa polyvalent antivenom upon arrival, approximately 8 hours after the bite, symptomatic treatment with hydrocortisone 200mg/6 hours, paracetamol 1g/8h, vascular filling with isotonic saline solution 500ml/24h, probabilistic dual antibiotic therapy consisting of ceftriaxone 2g/24h and metronidazole 500mg/8h, and nursing care.

The following day, his condition deteriorated rapidly with the onset of motor deficit in the left side of his body and loss of speech. He was referred to the medical center with a surgical unit in Dandé. There, he received a second dose of polyvalent antivenom from Vins Bioproducts Ltd, the same symptomatic treatment, and was evacuated to the emergency department of the Souro Sanou University Hospital. He was transferred to the neurology department 24 hours after his admission to the emergency department.

The clinical examination carried out three days after the onset of symptoms found that he was in WHO stage III general condition, with normal consciousness and correct hemodynamic parameters: blood pressure of 120/70 mmHg, temperature of 37.5 degrees Celsius, pulse of 70 beats/min, respiratory rate of 20 cycles/min, and peripheral oxygen saturation of 96% in ambient air. The locoregional examination revealed inflammatory swelling of the right thumb with traces of hooks. The neurological examination noted proportional flaccid left hemiplegia affecting the face with motor strength rated at 0/5 in the limbs, abolished osteotendinous reflexes on the left side of the body but present and normal on the right, an indifferent plantar reflex on the left and a flexed reflex on the right, expressive aphasia, left hemineglect, and left lateral homonymous hemianopia, resulting in a National Institutes of Health Stroke Scale (NIHSS) score of 18.

Laboratory tests showed hyperleukocytosis with 12.370 cells/mm³, predominantly neutrophils (73.3%), hemoglobin level of 13.6 g/dl, and platelets at 158.000 cells/mm³. Blood ionogram, urea, and creatinine levels were normal. CRP was not performed; TP/TCA-INR, D-dimers, fibrinogen, and creatine kinase were not performed (blood was uncoagulable after several attempts at blood sampling without a tourniquet).

In the absence of magnetic resonance imaging, which was unavailable in our setting, a cerebral computed tomography performed 24 hours after the onset of the deficit revealed heterogeneous cortico-subcortical hypodensity in the right fronto-parieto-temporal region, well systematized in the superficial and deep territory of the right middle cerebral artery (MCA), with hemorrhagic transformation, a mass effect on neighboring structures, and subfalcial involvement. Figure shows cerebral computed tomography images of the patient's cerebral parenchymal lesions.

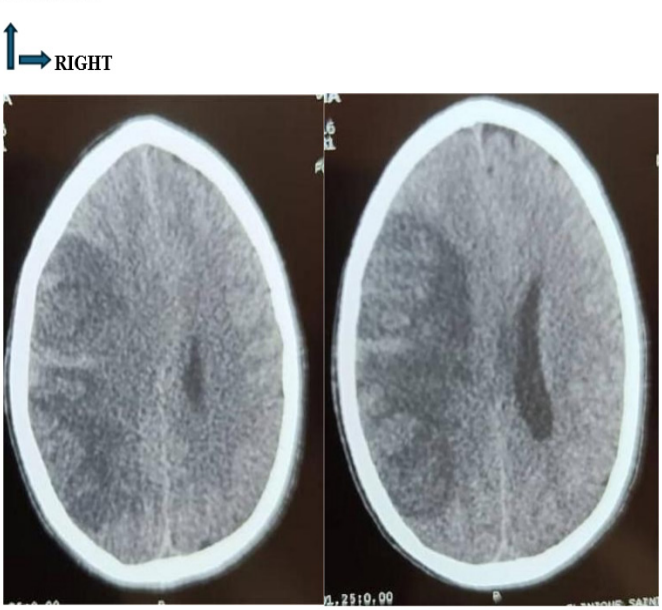

Figure. Cerebral computed tomography images of the patient's lesions
Heterogeneous cortico-subcortical hypodensity in the right fronto-parieto-temporal region, well localized in the superficial and deep territory of the right middle cerebral artery, with hemorrhagic transformation, mass effect on neighboring structures, and subfalcine involvement

In the neurology department, he received an antiplatelet agent based on acetylsalicylic acid 100mg/day, enoxaparin 0.4 ml SC/24 hours, continuation of probabilistic dual antibiotic therapy, paracetamol 1 g/8 hours, isotonic saline solution 500/24 hours, and mannitol 20% 100 ml/8 hours for 48 hours.

The outcome was marked on day 8 after the bite by the patient's death from cardiorespiratory arrest.

DISCUSSION

Cerebral infarction secondary to snake bite envenomation remains a rare but potentially fatal complication. Our patient, a 44-year-old man with no history of cardiovascular disease, fits the profile described in several series in which victims of post-venom stroke are generally young, healthy adults, mainly exposed for agricultural reasons.[7,8] In these studies, male predominance and rural context are regularly reported as exposure factors.

Our patient's profile is consistent with observations from cases published in Asia and Africa, where post-viper bites infarcts occur in young subjects, often without comorbidities.[7,9] This similarity reinforces the hypothesis of a direct causal link between the venom and the neurovascular event, rather than a stroke linked to classic risk factors.

Although the species has not been formally identified by a professional, those around the patient describe it as a viper. The species most commonly found in the geographical context of Burkina Faso is a viper of the genus Echis or Bitis. Viperids are known for their hemotoxic venoms, rich in metalloproteinases and snaclecs responsible for platelet activation and a paradoxical prothrombotic state.[10,11] These mechanisms are well documented in the literature as being capable of inducing cerebral arterial thrombosis, even in the presence of consumptive coagulopathy.[10,11] The cases of ischemic stroke after viper bites described by Vasconez-Gonzalez et al.[7] clearly illustrate this process.

The 48-hour delay between the bite and the onset of neurological deficit is comparable to that reported in series of post-viperid strokes, where strokes usually occur between 24 and 72 hours after envenomation.[7,10] This delay corresponds to the time required for the activation of coagulation cascades, the formation of microthrombi, and their migration to the cerebral territory, particularly to the branches of the MCA.

Our patient had severe coagulopathy ("uncoagulable blood"), a classic marker of severe viper venom envenomation.[10,11] However, the progression to ischemic infarction despite this apparent incoagulability confirms the well-described pathophysiological paradox: local platelet activation with systemic consumption, creating an environment conducive to arterial thrombosis.[10,11] Several authors have reported sylvian infarcts in patients with similar coagulopathy.[11]

Viper venoms contain several bioactive components such as metalloproteinases, serine proteases, and C-type lectin-like proteins (snaclecs), which play a central role in venom-induced coagulopathy. These toxins can activate platelets and coagulation factors, triggering a prothrombotic cascade that promotes the formation of microthrombi in the arterial circulation. Paradoxically, this occurs in the context of systemic consumption of coagulation factors and fibrinogen depletion, a condition often referred to as venom-induced consumptive coagulopathy. This dual mechanism explains why arterial thrombosis, including cerebral infarction, may occur despite apparent incoagulability of blood samples.

In addition to coagulation disturbances, viper venoms can directly damage the vascular endothelium. Metalloproteinases are known to induce endothelial injury, disruption of the vascular basement membrane, and inflammatory responses. This endothelial dysfunction promotes platelet aggregation and localized thrombus formation, creating conditions similar to a vasculitic process within cerebral vessels.

Secondary systemic factors may further contribute to cerebral ischemia after envenomation. Hypotension, dehydration, systemic inflammatory response, or microvascular dysfunction can aggravate cerebral hypoperfusion. In patients with extensive MCA territory involvement, these factors may accelerate infarct progression and worsen neurological outcomes.

The cerebral computed tomography scan showing an infarction in the territory of the right MCA is consistent with the most frequent descriptions in the literature, where post-envenomation infarcts often affect the sylvian territories, sometimes in the form of multiple infarcts.[7,9,11] The lack of MRI is a common limitation in African settings, as highlighted in African venom series where advanced imaging is rarely available.[3,15,16] Nevertheless, the clinical and cerebral computed tomography findings allow a reasonable diagnosis to be made.

Treatment is based on the early administration of antivenom, ideally within the first 6 hours according to WHO recommendations.[16] In our case, a prolonged delay between the bite and the first dose of antivenom was noted, a situation that is common in rural areas and described as a factor for poor prognosis.[15,16] Studies show that even with antivenom, some patients develop strokes or die, particularly in the absence of adequate biological monitoring or imaging.[7,15,16] Our patient's situation illustrates the structural limitations encountered in West Africa: unavailability of hemostasis testing, lack of MRI, inability to consider thrombolysis or neurointensive monitoring; all factors that may have contributed to the unfavorable outcome.

The administration of antiplatelet therapy and prophylactic anticoagulation in this patient despite the presence of coagulopathy may appear paradoxical. However, several reports of viper envenomation describe thrombotic complications resulting from platelet activation and microvascular thrombosis. In this context, low-dose acetylsalicylic acid and prophylactic enoxaparin were introduced to limit further thrombotic extension, particularly given the large territorial infarction. This therapeutic approach remains controversial but has been described in similar cases where the thrombotic component of venom-induced coagulopathy is suspected.

The fatal outcome observed is consistent with the trend reported in several cases of post-viperid stroke, where mortality remains high, often exceeding 30-40% depending on the series.[7,13,15] Systemic complications, uncontrolled coagulopathy, delays in treatment, and the lack of specialized intensive care are the major determinants of mortality.[7,15,16]

Contribution of This Case

This case contributes several important elements to African and international literature:

- Confirmation that ischemic infarction following viper envenomation can occur in West Africa, a region where publications on neurological complications are rare.
- Illustration of the "consumptive coagulopathy+arterial thrombosis" paradox, a mechanism that is increasingly recognized but still under-documented in tropical countries.
- Highlighting of diagnostic and therapeutic challenges in resource-limited areas.
- Importance of strengthening policies to combat envenomation (rapid access to antivenom, imaging, staff training).

CONCLUSION

Cerebral infarction is a rare but severe complication of viper envenomation. Early recognition of neurovascular complications and rapid access to antivenom and specialized care are essential to improve outcomes, particularly in resource-limited settings.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

This case report did not receive any financial support.

Author Contributions

Study Design: ZA; Data Collection: ZA; Manuscript Writing and Editing: ZA; Data Collection: SAA; Clinical Follow-up: SAA; Therapeutic Monitoring: SAA; Manuscript Review: OPV, LDL, NC, MA; Editing and Validation: OPV, LDL, NC, MA.

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Letter to the Editor

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Intranasal esketamine use in treatment-resistant depression: mechanism of action, clinical adverse effects, contraindications, safe administration protocol, and treatment process

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Dear Editor,

The U.S. Food and Drug Administration (FDA) has increasingly focused on breakthrough molecular mechanisms, rapidly acting medications, and expanded therapeutic indications in the treatment of depression. During this period, psychiatric interventions targeting N-methyl-D-aspartate (NMDA) receptors and intracellular signaling pathways have gained prominence, moving beyond the traditional monoamine (serotonin/norepinephrine) hypothesis. This article reviews the mechanism of action, clinical adverse effects, contraindications, safe administration protocols, and treatment process associated with esketamine, one of these novel therapeutic approaches.

Esketamine monotherapy approval: Previously approved only for use in combination with an oral antidepressant, this rapidly acting NMDA receptor modulator administered as a nasal spray has now received approval for use as monotherapy in adults with treatment-resistant depression. Whereas conventional selective serotonin reuptake inhibitors (SSRIs) typically require 6-8 weeks to achieve a clinically meaningful therapeutic response, newly approved NMDA-targeting therapies may produce rapid symptom relief within days.[1]

Esketamine is a paradigm-shifting molecule in psychiatry that exerts its effects through cellular pathways fundamentally distinct from those of conventional antidepressants. While traditional antidepressants such as SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) primarily aim to increase synaptic concentrations of serotonin, norepinephrine, or dopamine, esketamine directly targets the glutamatergic system, the brain's principal excitatory neurotransmitter network.[2]

Esketamine is the (S)-enantiomer of racemic ketamine and exhibits substantially higher affinity for NMDA receptors. At the cellular level, its therapeutic effects are mediated through the following sequence of events: Esketamine selectively and reversibly antagonizes NMDA (N-methyl-D-aspartate) receptors located on inhibitory gamma-aminobutyric acid (GABA)-ergic interneurons. This blockade reduces inhibitory neuronal activity, resulting in a process known as disinhibition. Consequently, a rapid and robust release of glutamate occurs from pyramidal neurons within the prefrontal cortex. The released glutamate subsequently binds to α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors on neighboring neurons. Activation of AMPA receptors increases intracellular sodium influx, leading to neuronal excitation. This AMPA-mediated signaling stimulates the synthesis and release of brain-derived neurotrophic factor (BDNF). BDNF then activates downstream signaling pathways, including the mammalian target of rapamycin (mTOR) pathway.[3]

In brains affected by chronic stress and depression, where synaptic connections have become weakened or diminished, activation of the mTOR pathway promotes the rapid formation of new synaptic connections and dendritic spines within hours. In summary, whereas conventional antidepressants primarily seek to alter neurochemical concentrations in the brain, esketamine appears to facilitate rapid restoration of neural architecture through enhancement of synaptic plasticity.

Despite its rapid antidepressant effects, esketamine requires close clinical monitoring because of its acute central nervous

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system effects.[4] Adverse effects generally begin within 10-15 minutes after administration, peak at approximately 40 minutes, and typically resolve completely within 1.5-2 hours. According to clinical studies, the most commonly reported acute adverse effects include dissociation (the most frequently reported adverse effect), sedation and dizziness, transient increases in blood pressure (typically a temporary rise of approximately 10-20 mmHg in systolic blood pressure and 5-10 mmHg in diastolic blood pressure following administration), cognitive disturbances, and nausea and vomiting. Although ulcerative cystitis has been associated with chronic ketamine misuse, the risk appears to be very low at therapeutic doses; nevertheless, vigilance is warranted during long-term treatment. Esketamine is classified as a controlled substance, and caution should be exercised in individuals with a history of substance use disorders due to its potential to activate reward pathways. Clinicians should remain aware of its potential for misuse and dependence.

Esketamine represents a novel therapeutic approach for the management of treatment-resistant depression (TRD) and patients presenting with acute suicidal ideation. In contrast to conventional antidepressants, which typically exhibit a therapeutic lag of several weeks, esketamine exerts a rapid-onset action within hours of administration. This swift response is mediated by the promotion of neuroplasticity and the accelerated repair of synaptic connectivity, thereby playing a critical role in the immediate suppression of suicidal thoughts.[5] TRD is clinically defined by an inadequate response to at least two distinct lines of traditional antidepressant therapies, such as SSRIs or SNRIs, administered at adequate dosages and durations; in this refractory cohort, esketamine significantly enhances the probability of clinical remission and sustained recovery.[5] Given the profound risk of mortality associated with major depressive disorder, the fast-acting property of esketamine is potentially life-saving. Clinical data indicate that a reduction in suicidal tendencies can be observed as early as 2 to 4 hours post-initial administration.[6] Consequently, supervised clinical or inpatient administration of esketamine serves as a crucial intervention for crisis stabilization and immediate symptomatic relief in severe psychiatric emergencies.[6] However, due to the transient physiological and psychological changes induced by the medication, its use is absolutely contraindicated in certain patient populations. Esketamine is contraindicated in patients for whom transient increases in blood pressure or intracranial pressure could pose a significant or life-threatening risk. Table summarizes conditions in which esketamine use is absolutely contraindicated, as well as other medical conditions that require extreme caution or avoidance during treatment.

Table. Medical conditions in which esketamine use is absolutely contraindicated and conditions requiring extreme caution

Absolute contraindications	Conditions requiring particular caution
Aneurysmal vascular diseases	Uncontrolled hypertension and cardiovascular disorders
Arteriovenous malformations	Patients presenting with active psychotic symptoms
History of intracerebral hemorrhage	A history of manic episodes
Hypersensitivity	A history of hypomanic episodes

(Adapted from McIntyre et al.[11])

Safe administration protocol: Due to its adverse-effect profile, esketamine nasal spray cannot be purchased from a pharmacy and self-administered at home. The safety protocol includes the following steps: The patient self-administers the medication intranasally under the supervision of a psychiatrist or trained nurse in a certified healthcare facility. Following administration, blood pressure is monitored, and the patient remains under observation in the clinic for a minimum of 120 minutes until any dissociative and/or sedative effects have fully resolved. Patients are strictly prohibited from driving motor vehicles or operating heavy machinery requiring sustained attention on the day of treatment. Normal daily activities may generally be resumed the following day. One of the most commonly reported adverse effects of esketamine is nausea and vomiting. To minimize this risk, patients should abstain from consuming solid food for at least 2 hours prior to the start of the treatment session. In addition, the intake of liquids, including water, should be discontinued at least 30 minutes before administration to reduce the likelihood of vomiting and to optimize treatment tolerability. If the patient uses other intranasal medications (e.g., allergy nasal sprays), these should be administered at least 1 hour before esketamine to avoid interference with its absorption through the nasal mucosa. Immediately before treatment, the patient's blood pressure should be assessed. If baseline blood pressure is considered dangerously elevated (e.g., ≥140/90 mmHg), the treatment session should be postponed until adequate blood pressure control has been achieved.[4]

The treatment course consists of two main phases: the Induction (Initiation) Phase and the Maintenance Phase. Each esketamine nasal spray device contains 28 mg of esketamine. Depending on the patient's clinical needs, two devices (56 mg) or three devices (84 mg) are administered per treatment session. The induction phase encompasses Weeks 1-4 and involves treatment twice weekly. Treatment is initiated with 56 mg on the first day. During subsequent sessions, the dose may be maintained at 56 mg or increased to 84 mg, depending on the patient's tolerability and the treating physician's clinical judgment. The primary objective of this phase is to rapidly promote the restoration of synaptic connectivity in the brain and achieve an acute reduction in depressive symptoms.[4] The Optimization and Maintenance Phase encompasses Week 5 onward. Once depressive symptoms have been adequately controlled, the frequency of treatment sessions is gradually reduced: Once weekly (56 mg or 84 mg) on Weeks 5-8, and typically once every two weeks (or once weekly, depending on the patient's clinical status) on Week 9 onward. The duration of maintenance therapy varies according to the patient's clinical response and sustained remission and may continue for several months.

When more than one device is used during a treatment session (56 mg or 84 mg total dose), a 5-minute interval should be observed between administrations of each device. This interval facilitates optimal absorption of the medication through the nasal mucosa. Following administration, the patient is transferred to a comfortable, quiet room with subdued lighting. To facilitate tolerance of transient dissociative experiences, patients may be encouraged to listen

to music or use an eye mask during the observation period. Approximately 2 hours after administration, the patient may be discharged if blood pressure has returned to an acceptable range and all clinically significant sedative and dissociative effects have resolved. Patients are required to arrange for a responsible accompanying person to escort them home following each treatment session.

Esketamine is a pharmaceutical product that has been approved and licensed by the Turkish health authorities, specifically the Turkish Medicines and Medical Devices Agency (TİTCK).[7] However, the current approved indication in Turkiye continues to specify the use of esketamine in combination with an oral antidepressant.[7] Although the U.S. FDA expanded approval in January 2025 to permit the use of esketamine as a standalone (monotherapy) treatment for treatment-resistant depression, this indication expansion has not yet been fully incorporated into Turkish regulatory guidance and prescribing information.[8]

Because esketamine is a specialized ketamine derivative with recognized abuse and misuse potential, it is subject to the red prescription (controlled substance) system in Turkiye. Consequently, patients are not permitted to purchase the medication from a pharmacy for home use or self-administration. Administration of esketamine is restricted to authorized healthcare settings and must be conducted under direct medical supervision. Treatment may be provided only in appropriately equipped psychiatric centers, university hospitals, and selected private hospitals that have received authorization from the Ministry of Health. Concurrently, esketamine nasal spray represents a high-cost biopharmaceutical intervention. Within the framework of the Turkish healthcare system, whether the Social Security Institution (SGK) will incorporate this agent into its comprehensive reimbursement scheme-and under what stringent regulatory criteria, such as a formal medical board consensus report-remains a pivotal subject of debate regarding equitable access to treatment.

In Turkiye, the clinical stabilization of acutely depressed patients presenting to emergency departments with suicidal ideation typically necessitates prolonged hospitalization extending over several weeks. Consequently, the potential of esketamine to mitigate suicidal thoughts within a 2-to-4-hour window post-administration could substantially alleviate the acute clinical burden imposed on emergency departments and psychiatric inpatient units.[9] Furthermore, approximately 30% to 40% of patients diagnosed with major depressive disorder in Turkiye exhibit resistance to conventional pharmacotherapies, specifically SSRIs and SNRIs. Historically, therapeutic options for this treatment-resistant cohort were largely restricted to electroconvulsive therapy (ECT) or the off-label utilization of intravenous ketamine infusions.[10] In this context, esketamine introduces a regulatory-approved and standardized therapeutic alternative formally sanctioned by the Turkish Ministry of Health.

The ongoing clinical and academic debate surrounding esketamine utilization in Turkiye-interpreted through the lens of national major depressive disorder epidemiology, TRD dynamics, and acute suicidal crisis management-underscores the necessity for a meticulous evaluation of this agent's therapeutic potential and clinical risk-benefit profile. In the context of Turkish neuropsychiatry, esketamine emerges as a transformative intervention, particularly for acute crisis stabilization. However, maximizing its clinical efficacy and translational utility is strictly contingent upon several critical parameters: the standardization of clinical infrastructure within medical institutions, stringent patient selection criteria implemented by psychiatric clinicians, and, pivotally, the establishment of sustainable fiscal frameworks and healthcare reimbursement policies designed to mitigate socioeconomic disparities in treatment accessibility.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient for the publication of this correspondence and any related clinical details.

Peer Review Process

This letter was externally peer-reviewed.

Conflict of Interest

The authors declare no conflicts of interest.

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