Original Article

A Prospective Study of Serum Cortisol Level as a Prognostic Factor in Acute Ischemic Stroke

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Abstract

Background: Acute ischemic stroke (AIS) is a leading cause of mortality and long-term disability worldwide. Identifying reliable biomarkers for early prognostication can aid in risk stratification and management. Serum cortisol, a stress hormone, has been proposed as a potential indicator of disease severity and outcome in AIS. This study aimed to evaluate the relationship between serum cortisol levels, stroke severity, and short-term functional outcomes in patients with acute ischemic stroke. **Material and Methods:** This prospective cross-sectional study was conducted in the Department of General Medicine at Meenakshi Medical College, Hospital, and Research Institute. Fifty patients aged 18 years or older, admitted within 72 hours of the onset of an acute ischemic event, were included. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) at admission, and functional outcomes were reassessed after 15 days using the Modified Rankin Scale (mRS). Serum cortisol levels were measured by enzyme immunoassay, and values greater than 690 nmol/L were considered elevated. Statistical analysis was performed using SPSS 2020, with $p < 0.05$ considered significant. **Results:** The majority of patients were between 61 and 70 years of age, with a male predominance. Hypertension was the most common comorbidity, followed by diabetes mellitus and coronary artery disease. Elevated serum cortisol levels (>690 nmol/L) were significantly associated with higher NIHSS scores (>6) at admission and poorer functional outcomes, reflected by higher mRS scores (>3) during follow-up. Patients with lower cortisol levels (≤690 nmol/L) demonstrated milder stroke severity and better recovery. **Conclusion:** Serum cortisol levels show a positive correlation with stroke severity and adverse functional outcomes in acute ischemic stroke. Early cortisol estimation may serve as a useful prognostic biomarker for patient stratification and management.

Keywords: Acute ischemic stroke, Serum cortisol, NIHSS, Modified Rankin Scale, Prognostic marker.

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Introduction

Acute ischemic stroke (AIS) remains a leading cause of death and long-term disability worldwide, with substantial individual and societal burden despite advances in acute reperfusion therapies and supportive care. Early and accurate prognostication is essential for triage, informed decision-making, and the allocation of resources; however, clinical scores alone (for example, the NIH Stroke Scale) do not fully capture the heterogeneity of biological responses to cerebral ischemia.[1]

Activation of the hypothalamic–pituitary–adrenal (HPA) axis is a consistent component of the systemic stress response to acute brain injury, and cortisol — the end product of this axis — increases in the early phase after stroke.[2] A large systematic review of studies measuring cortisol after stroke reported that cortisol is frequently elevated in the first week following the event and that higher cortisol concentrations have been associated with greater dependency, delirium, depression, and increased mortality in many cohorts. However, some relationships were not independent of initial stroke severity.[3]

Early primary research and prospective observational studies have also shown positive correlations between admission cortisol levels and markers of neurological injury, including clinical severity scores, infarct volume, and short-term mortality, supporting the hypothesis that hypercortisolemia reflects the magnitude of cerebral insult and the systemic response to it.[2,3] Experimental and translational work suggests several mechanisms by which glucocorticoid excess could influence post-stroke outcomes, including effects on glucose metabolism, immune and inflammatory pathways, blood–brain barrier integrity, and hippocampal neuroplasticity, all of which may exacerbate neuronal injury and impair recovery.[4] Taken together, these data suggest that a single, early measurement of serum cortisol may have utility as a prognostic biomarker in AIS; however, the findings are heterogeneous and require validation in different settings and populations.[1,4,6]

In this context, the present prospective cross-sectional study was undertaken to examine the relationship between serum cortisol measured on the morning after admission and clinical measures

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of stroke severity (NIHSS at admission) and short-term functional outcome (modified Rankin Scale at 15 days) among patients with acute ischemic stroke admitted within 72 hours of symptom onset.

Materials and Methods

This prospective cross-sectional study was conducted in the Department of General Medicine at Meenakshi Medical College, Hospital, and Research Institute. A total of 50 patients with a diagnosis of acute ischemic stroke were enrolled in the study. All patients were admitted within 72 hours of the onset of neurological symptoms and fulfilled the predefined inclusion and exclusion criteria. The study population consisted of individuals aged above 18 years, with the diagnosis of acute ischemic stroke confirmed by non-contrast computed tomography (CT) of the brain. Patients below 18 years of age, pregnant women, individuals with liver disease, malignancy, or hemorrhagic stroke, those with acute febrile illness, or who had undergone major surgery within the preceding three weeks were excluded. Additionally, patients receiving immunosuppressants, corticosteroids, rifampicin, or phenytoin were also excluded from the study to avoid confounding effects on serum cortisol levels.

Data for each participant were systematically collected using a structured proforma that recorded demographic details, presenting complaints, past medical and drug history, and risk factors such as hypertension, diabetes, and coronary artery disease. Each patient underwent a detailed general and systemic examination. Stroke severity was assessed at admission using the National Institutes of Health Stroke Scale (NIHSS), and functional outcome was reassessed 15 days after admission using the Modified Rankin Scale (mRS). Serum cortisol estimation was performed on the morning following admission, and values greater than 690 nmol/L were considered elevated. The association between serum cortisol levels, NIHSS score (categorized as ≤6 and >6), and mRS score (≤3 and >3) was evaluated to determine the prognostic relevance of cortisol levels in acute ischemic stroke.

For biochemical analysis, 5 mL of venous blood was collected from each patient on the morning after admission. After clotting, samples were centrifuged, and the separated serum was used for cortisol estimation. Quantitative measurement of serum cortisol was performed using an enzyme immunoassay (EIA) based on a competitive binding principle. In this method, unlabelled cortisol from the patient's sample competes with enzyme-labelled cortisol for a limited number of antibody binding sites on a microplate coated with polyclonal antibodies. After incubation and washing to remove unbound substances, a substrate solution containing tetramethylbenzidine (TMB) was added. The enzymatic reaction was stopped with a stop solution, and absorbance was measured at 450 nm using a microplate reader. The colour intensity was inversely proportional to the cortisol concentration. Cortisol values were determined from a standard calibration curve generated using known standards.

Statistical analysis was carried out using SPSS software (version 2020). Continuous variables were expressed as mean ± standard deviation and compared using the independent samples t-test. Categorical variables and correlations between serum cortisol levels and stroke severity scales (NIHSS and mRS) were analyzed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

Results

The present prospective study included a total of 50 patients diagnosed with acute ischemic stroke. The age distribution of participants is shown in Table 1. The majority of patients belonged to the 61–70-year age group, indicating a higher prevalence of ischemic stroke among elderly individuals. Patients below 50 years constituted a smaller proportion of the study population, suggesting that stroke occurrence was comparatively uncommon in younger adults.

The gender distribution is presented in Table 2, revealing a male predominance in the study population. This observation suggests that males were more frequently affected by acute ischemic stroke than females in the present cohort.

The comorbidity profile of patients, depicted in Table 3, demonstrates that hypertension was the most prevalent comorbid condition, followed by diabetes mellitus and coronary artery disease. The presence of these vascular risk factors highlights their contributory role in the pathogenesis of ischemic stroke.

The correlation between serum cortisol levels and the National Institutes of Health Stroke Scale (NIHSS) score at admission is illustrated in Table 4. A higher NIHSS score, indicative of greater stroke severity, was predominantly associated with elevated serum cortisol levels (>690 nmol/L). Conversely, patients with lower NIHSS scores tended to have serum cortisol levels ≤690 nmol/L, suggesting a positive correlation between cortisol concentration and stroke severity.

Similarly, Table 5 shows the relationship between serum cortisol levels and the Modified Rankin Scale (mRS), which reflects functional outcomes following stroke. Patients with higher cortisol levels were more likely to exhibit poor functional recovery (mRS > 3), whereas those with lower cortisol concentrations had better functional outcomes (mRS ≤ 3). This finding indicates that elevated serum cortisol at admission may serve as a potential predictor of adverse neurological outcomes in acute ischemic stroke.

Table 1: Age-wise Distribution of Patients

Age Group (Years)	n	%
31–40	3	6
41–50	4	8
51–60	9	18
61–70	19	38
71–80	11	22
81–90	4	8
Total	50	100

Table 2: Gender-wise Distribution of Patients

Gender	n	%
Male	29	58
Female	21	42
Total	50	100

Table 3: Distribution of Comorbidities among Patients

Comorbidity Type	n	%
Diabetes Mellitus	13	26
Hypertension	20	40
Coronary Artery Disease (CAD)	13	26

Table 4: Correlation between Serum Cortisol Levels and NIHSS Score at Admission

NIHSS Score on Admission	Serum Cortisol ≤690 nmol/L		Serum Cortisol >690 nmol/L	
	n	%	n	%
≤6	15	65.2	0	0.0
>6	8	34.8	27	100.0
Total	23	100	27	100

Table 5: Correlation between Serum Cortisol Levels and Modified Rankin Scale (mRS)

mRS Score	Serum Cortisol ≤690 nmol/L		Serum Cortisol >690 nmol/L	
	n	%	n	%
≤3	18	78.3	1	3.7
>3	5	21.7	26	96.3
Total	23	100	27	100

Discussion

In this prospective cohort of fifty patients with acute ischemic stroke, elevated morning serum cortisol measured on the day after admission was strongly associated with markers of greater neurological impairment and poorer short-term functional outcome. Patients with cortisol levels greater than 690 nmol/L were concentrated in the group with higher NIHSS scores at admission and worse mRS scores at 15 days. This pattern is consistent with multiple prior observations that activation of the HPA axis and resulting hypercortisolaemia mirror the intensity of the acute stress response to cerebral ischemia and relate to adverse clinical trajectories. Longitudinal hormonal profiling after stroke has shown time-phased increases in HPA and sympathetic markers that align with clinical severity and prognosis, supporting the biological plausibility of the associations observed in our sample.[7]

Several clinical studies have reported similar prognostic links between higher admission cortisol and worse functional outcomes or increased mortality, and our results corroborate these findings in a hospital-based Indian cohort. Hospital cohorts and observational series have repeatedly found that greater cortisol elevations are more frequent among patients with more severe strokes and that cortisol may add prognostic information beyond routine clinical measures in some settings. Our observations align with the findings of previous hospital-based studies, which identified cortisol as a predictor of short-term functional outcome and a marker that correlates with stroke severity scales.[8,9]

The relationship between cortisol and early outcome is biologically plausible through several intersecting mechanisms. Excess glucocorticoids influence glucose homeostasis, immune and inflammatory responses, and blood–brain barrier integrity, and they have documented effects on hippocampal and cortical neurons that may impede neuroplasticity and recovery. These mechanistic pathways have been discussed in translational and clinical syntheses, offering a credible explanation for why substantial HPA activation after stroke can predict poorer early recovery. Recent scoping and systematic reviews that examined cognitive, emotional, and functional sequelae after stroke emphasized that elevated cortisol in the acute phase is linked to later cognitive decline, depression, and functional impairment, reinforcing the clinical relevance of early cortisol measurement as a stress-responsive biomarker.[7,10]

Notably, earlier work has also highlighted complexity in the cortisol–outcome relationship: both markedly low and markedly high cortisol concentrations have been associated with adverse outcomes in some cohorts, implying a non-linear association and suggesting that inadequate HPA activation may be detrimental in certain patients. In contrast, excessive activation may be harmful in others. This nuance—reported in long-standing observational studies—suggests that a single absolute threshold may not apply across all populations and that cortisol's prognostic value could depend on timing, comorbidity profile, and stroke subtype. Such heterogeneity may partly explain inconsistencies between studies and underlines the need for cautious interpretation of single-timepoint cortisol measurements.[11]

The present study has limitations that should be acknowledged. The sample size was modest and drawn from a single tertiary centre, so estimates of association may be imprecise and not fully generalizable. Cortisol was measured once (the morning after admission), which captures an early snapshot but does not characterize temporal dynamics; several prior studies used serial measurements to define prognostic trajectories more accurately. We assessed short-term outcome at 15 days; longer follow-up would be required to establish whether the observed associations persist for 3-month or later endpoints commonly used in stroke research. Finally, unmeasured confounders—such as pre-existing psychiatric disease, circadian disruption before sampling, or concurrent acute medical complications—may have influenced cortisol levels and outcomes, despite our exclusion criteria and prospective data collection. These limitations mirror those noted in previous literature and argue for larger multicentre prospective studies with serial hormonal profiling and extended follow-up to refine threshold values and adjust for potential confounders.[12,13]

Clinically, our results add to the accumulating evidence that early serum cortisol measurement may help identify patients at higher risk of severe early neurological deficit and poor short-term recovery. If validated in larger and more diverse cohorts, cortisol could be tested as part of multimodal prognostic models that combine clinical scores (for example, the NIHSS), imaging markers, and blood biomarkers to improve early risk stratification and tailor monitoring and rehabilitation intensity. Future research should prioritize standardized sampling times, prospective assessment of serial changes, exploration of non-linear risk relationships, and evaluation of whether interventions that modify stress responses (pharmacological or rehabilitative) can alter outcomes in patients with pronounced HPA activation.[14,15]

Conclusion

The findings of this study demonstrate that elevated serum cortisol levels are significantly associated with greater neurological impairment and poorer functional outcomes in patients with acute ischemic stroke. Higher cortisol concentrations correlated positively with increased NIHSS scores at admission and higher mRS scores during follow-up, suggesting that serum cortisol may serve as a reliable biochemical marker of stroke severity and prognosis. Therefore, early measurement of serum cortisol could aid in identifying high-risk patients and assist clinicians in predicting disease outcomes, enabling the development of timely and appropriate management strategies.

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Conflicts of interest

There are no conflicts of interest.

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