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RESEARCH ARTICLE
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SERUM CORTISOL LEVELS IN ASSESSING SEVERITY OF ACUTE STROKE – A CROSS SECTIONAL STUDY IN CHENGALPET MEDICAL COLLEGE & HOSPITAL

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Abstract

Background: In this study we wanted to determine whether the severity of an acute stroke could be correlated with a single measurement of blood cortisol.

Methods: After receiving approval from the institutional ethics committee and signed informed consent from the study participants, a cross-sectional study was carried out on 120 acute stroke patients who presented from Chengalpattu Government Hospital's medical wards and intensive care unit within 24 hours of the stroke beginning. All patient clinical data was concealed from the analysing laboratories. The independent sample t-test was used to calculate the parameter mean values. By using the Chi-Square test, the relationship between blood cortisol levels and stroke scores was evaluated. SPSS, a software programme used for statistical analysis, is used for all statistical analyses. It was determined that a p-value of less than 0.05 was statistically significant.

Results: 50% of the group are male and 50% are female, with an average age range of 50 to 59. The cortisol level was 637 nmol/L on average. Acute ischemic stroke affected 98 out of the 120 patients, while acute hemorrhagic stroke affected 22. The average time was 9.5 hours, and the average SSS score was 20.85. The SSS and serum cortisol correlation coefficient was -0.984, showing a significant link. High serum cortisol levels were associated with lower SSS scores, and the p-value was < 0.001, indicating statistical significance.

Conclusion: Elevations in blood cortisol levels are associated with acute stroke severity. One potential indicator of the severity of a stroke is serum cortisol.

Keywords: Serum Cortisol Levels, Severity of Acute Stroke.

INTRODUCTION

The WHO (World Health Organisation) defines a stroke as a focused disruption of cerebral function caused by a vascular injury that lasts longer than twenty-four hours or results in death. The HPA (Hypothalamo-Pituitary-Adrenal) axis is activated during an acute stroke episode due to the stress response. Increased serum cortisol levels in acute stroke patients have been linked in some studies to larger infarct volumes, more severe strokes, and poorer outcomes, including death. It is unclear if the stress response affects the prognosis on its own or if it is only an epiphenomenon of the severity of the stroke.

Numerous clinical factors, such as the intensity of the symptoms and advanced age, have been found to be possible indicators of prognosis in individuals suffering from acute strokes. However, finding a biomarker to forecast the prognosis of an acute stroke is necessary. Because of the disruption in the HPA axis, the endocrine abnormalities in acute stroke patients are the first detectable changes. Cortisol is a hormone associated with the HPA axis that has a strong circadian rhythm, with levels peaking in the morning and falling later in the day. Equal levels of cortisol were recorded all day long, indicating that during acute stroke, the usual circadian rhythm of cortisol is interrupted.

Increased glucose levels and quick cell mobilisation of lipids and amino acids make all fuel substrates more readily available to different tissues and organs when cortisol is present.[1] However, this reaction has also been linked to ischemia neuronal damage,[2] negative cardiac consequences (such as arrhythmias),[3] and an increase in infections,[4] all of which raise mortality. Thus, a number of studies have connected an increase in cortisol levels to the severity or prognosis of AIS.[5,6]

Research has shown that people who have had an ischemic stroke have altered serum cortisol levels, and that elevated levels of this hormone are independently linked to an increase in the amount of the ischemic lesion. Additionally, it has been noted that ischemic stroke patients' cortisol levels are substantially higher when it comes to mortality.[7,8] Additionally, studies have demonstrated that extended exposure to high cortisol levels is neurotoxic and that the hippocampus volume is less in corticosteroid-using patients.[9] According to certain research, cardiac problems brought on by elevated stress hormone levels may be the cause of the link between high stress hormone levels and less favourable outcomes.[10]

When death occurs within a week after stroke starts and the cause of death is stroke-induced brain injury, there seems to be an independent relationship between S-cortisol and death. Moreover, it has been proposed that glucocorticoids exacerbate neuronal ischemia injury.[11]

Considering this, this study aimed to determine whether the severity of an acute stroke might be predicted from a single blood cortisol sample.

MATERIALS & METHODS

After receiving approval from the institutional ethics committee and signed informed consent from the study participants, a cross-sectional study was carried out on 120 acute stroke patients who presented from Chengalpattu Government Hospital's medical wards and intensive care unit within 24 hours of the stroke beginning. Patients who were pregnant or who had liver impairment were not allowed to participate in the trial. Additionally, individuals under the age of 18 who were taking steroids, rifampicin, ketoconazole, or phenytoin were not allowed. Every patient who arrived at the hospital had their acute stroke severity evaluated using the SSS (Scandinavian Stroke Scale). For all patients, the diagnosis of acute ischemic or hemorrhagic stroke was made using CT imaging. Serum cortisol levels were measured using a competitive immune enzymatic calorimetric method (Dia Metra kit) on blood samples. All patient clinical data was concealed from the analysing laboratories. The independent sample t-test was used to calculate the parameter mean values. By using the Chi-Square Test, the relationship between blood cortisol levels and stroke scores was evaluated. SPSS, a software programme used for statistical analysis, is used for all statistical analyses. It was determined that a p-value of less than 0.05 was statistically significant.

RESULTS

A total of 120 individuals who had CT brain scans performed at the time of admission and were confirmed to have had an acute stroke were included in the study. The patients' ages ranged from 43 to 88 years old, minimum and maximum, respectively. Of the 120 patients, 46% had an acute stroke while they were between the ages of 50 and 59. Additionally, there were roughly 50% men and 50% women. The cortisol level was 637 nmol/L on average. Out of the 120 patients, 42% were not diabetics and 58% were. Of the total, 42% were normotensives and 58% were hypertensives. The mean systolic blood pressure of the 120 cases was 146 mm Hg, while mean diastolic blood pressure was 93 mm Hg. Acute ischemic stroke affected 98 out of the 120 patients, while the acute hemorrhagic stroke affected 22. Of the 98 cases of acute ischemic stroke, 28 had an infarct in the region of the anterior cerebral artery, 57 in the region of the middle cerebral artery, and 13 in the region of the posterior cerebral artery. Of the 22 cases of acute hemorrhagic stroke, 21 involved bleeding in the MCA area and 1 involved bleeding in the ACA region. It is evident that MCA area infarct and haemorrhage were present in the majority of patients. The average time was 9.5 hours, and the average SSS score was 20.85. Out of the 120 patients, 63 showed up in less than eight hours, 49 in between nine and fifteen hours, and six in between sixteen and twenty-four hours. Less than 15 in 20 patients out of 120 had an SSS score. The mean SSS score fell into the severe category at 20, with 89 individuals having scores between 16 and 30 and 11 patients having scores over 30. Serum cortisol levels were less than 500 nmol/L in patients with a score of less than 15 and more than 700 nmol/L in patients with a score of more than 30.

Patient Characteristics (N = 120)	**Percentage (or) Median**	
Age	58.5 (40 – 88)	
Sex (Male)	50%	
H/O Hypertension	58.3%	
H/O Diabetes	58.3%	
Patient Characteristics (N = 120)		
Patient Indicators	**Mean**	**Standard Deviation**
SBP	146.58	25.553
DBP	93.92	13.553
Serum Cortisol	637.15	79.399
SSS	20.85	6.339
Time duration	9.53	3.130
Patient Profile on Admission		
Table 1		

CT Brain	**Frequency**
Hemorrhage	22
Infarct	98
Total	120
Age (in yrs.)	**Frequency**
40 – 49	15
50 – 59	46
60 – 69	39
More than 70	20
Total	120
Gender	**Frequency**
Male	60
Female	60
Total	120
Table 2: CT Brain in Patients	

Duration	**Frequency**
Less than 8 hrs.	63
9 – 15 hrs.	49
16 – 12 hrs.	8
Total	120
SSS	**Frequency**
Less than 15	20
16 – 30	89
More than 30	11
Total	120
SSS	
Table 3	

The cortisol mean values for the infarct and haemorrhage were 665 and 7.99, respectively; the standard deviations were 16.7 and 7.99, with a P value of 0.067. Therefore, it was discovered using an unpaired t-test that there is no significant link between blood cortisol levels and infarction or haemorrhage.

The SSS and serum cortisol correlation coefficient was -0.984, showing a significant link. High serum cortisol levels were associated with lower SSS scores, and the p-value was < 0.001, indicating statistical significance.

Factor	**Correlation Coefficient**	**Significance P-Value**
SBP	0.136	0.140
DBP	0.110	0.233
Serum Cortisol	-0.984	<0.001*
Levels of Correlation with SSS		
Factor	**Correlation Coefficient**	**Significance P-Value**
SBP	-0.121	0.186
DBP	-0.116	0.207
SSS	-0.984	<0.001*
Levels of Correlation with Serum Cortisol		
Table 4		

DISCUSSION

Occurring as a stressor, acute ischemic stroke activates the HPA axis, leading to elevated levels of glucocorticoids. In order to determine whether there is a relationship between serum cortisol levels and the SSS stroke severity score, we measured them in this study.

The study included 120 patients in total who had CT brain scans performed at the time of admission to confirm that they had suffered an acute stroke. The patients' ages ranged from 43 to 88 years old at their youngest. Within the age range of 50 to 59 years, 46% of the 120 patients experienced an acute stroke. Furthermore, there were roughly 50% men and 50% women. It was 637 nmol/L on average for cortisol. Fifty-eight percent of the 120 cases had diabetes, while 42 percent did not. 42% of people had normotensive blood pressure and 58% had hypertension. The mean diastolic blood pressure of the 120 cases was 93 mmhg, while the mean systolic blood pressure was 146 mmhg. Acute hemorrhagic stroke affected 22 instances out of 120, while acute ischemic stroke affected 98. Thirteen of the 98 patients who suffered an acute ischemic stroke had an infarct in the posterior cerebral artery territory, while 57 patients had an infarct in the intermediate cerebral artery territory. The study by Akshat Agarwal et al. found that the mean age in the current series was 72.8 ± 12.54 years.[12] Thirty (46.9%) women and thirty (53.1%) men were there. The prevalence of diabetes mellitus, hypertension, and stroke was noted in 38 (59.4%), 12 (18.8%), and 24 (37.5%) cases,

respectively. These results were consistent with our study.

One acute hemorrhagic stroke patient had bleeding in the ACA region, while the other twenty-one had bleeding in MCA territory. There was a mean time of 9.5 hours and a mean SSS score of 20.85. Of 120 patients, 63 appeared in less than eight hours, 49 in nine to fifteen hours, and six in sixteen to twenty-four hours. Less than 15 in 20 of the 120 patients had an SSS score.

A mean SSS score of 20, which falls into the severe category, was found in 89 patients, with scores ranging from 16 to 30, and 11 patients with scores over 30. At admission, SSS was found to be 36 (21-47) in the study by Akshat Agarwal et al.[12] Serum cortisol levels were less than 500 nmol/L in patients with a score of less than 15 and more than 700 nmol/L in individuals with a score of greater than 30. With a significant association between serum cortisol levels and SSS scores of -0.984, high serum cortisol levels were associated with lower SSS scores. Additionally, a statistically significant p-value of less than 0.001 was found.
These findings are consistent with those of other research that demonstrated a negative correlation between hypercortisolemia and stroke patients' prognoses (longer disability and death), larger ischemic lesions on CT scans, and older age. Strong cortisol levels are predictive of a poor prognosis for stroke, according to a study by H. Christensen et al.[13] Serum cortisol mean: 649 nmol/L (95% CI); P = 0.03; N = 41 In line with the previous research, our investigation also revealed a statistically significant ($P < 0.001$) positive association between blood cortisol levels and the SSS score in predicting the severity of acute stroke.

Significant correlations were seen between the results at 1, 3, 6, and 12 months and serum cortisol, according to Zierath et al.[14] They discovered that, although there was a brief period of time when the correlation between greater cortisol levels and poorer outcomes persisted, the p-values for these intervals were <0.001, <0.001, 0.007, and 0.050 from the study. According to Neidert et al., the severity of the stroke at 90 days and a year after admission was reflected in the cortisol levels on the first day following admission.[15] Stroke in and of itself is a bad sign of prognosis; however, the stress reaction, which includes elevated cortisol as one of its expressions, can exacerbate the situation by causing increased heart rate, blood glucose, and catabolism. The elevated level of cortisol in the serum consequently showed collateral effects, including hippocampal neuronal ischemia injury. Due to the hippocampus's role in the feedback control of the HPA axis, which amplifies both the physiological stress response and the cortisol response, a disruption in hippocampal function may lead to disruptions in the HPA axis. Also linked to unfavourable cardiac outcomes include immunological dysregulation, which raises the risk of infections and raises morbidity and death rates, and arrhythmias or myofibrillar degeneration.[16]

The stress reaction's simultaneous sympathetic activity also has a detrimental cardiac effect. There is no discernible link between cortisol and ischemic stroke, according to certain research.[17] Nevertheless, there may have been some fluctuation in the outcomes because all of these trials only included patients with modest stroke severity[15] or because the patients used sedatives (fentanyl or midazolam) concurrently.
Additionally, Fassbender et al. found a strong correlation between the severity of the disease and an early and persistent activation of the hypothalamic-pituitary-adrenal axis.[18] According to Marklund et al., mortality after 28 days and 1 year were both predicted by greater serum cortisol levels on day 1.[19] The cortisol levels predicted day 90 and one-year mortality, which was also noted in Neidert et al. investigation.[15] The 90th day of the study by Zi et al. The study conducted by Agarwal et al. found a significant correlation between serum cortisol levels and death in individuals who had an acute stroke on day 7.[5]
Neurological decline is linked to high cortisol levels and severe stroke, according to research by Agarwal A. et al.[12] In additional research, similar findings were reported. Research has indicated

that cortisol levels are correlated with stroke-related mortality[20] and lower functional outcome,[21,22] which is consistent with our findings. Additionally, after controlling for stroke severity, research revealed that cortisol was not a reliable indicator of prognosis.[23,24] S-cortisol was only evaluated once, which was one of the study's weaknesses. Adding the element of time into the analysis through serial measurements would have surely helped.

In individuals who have suffered an acute stroke, cortisol is an independent short-term predictor of mortality and functional outcome. It is evident that greater severity is correlated with elevated cortisol following stroke. Significant information can be added to the clinical score by combining a model with other stress hormones such as ACTH, cytokines, and para clinical characteristics. A serum cortisol level measurement can significantly improve the current SSS score by providing predictive information, as therapy options heavily rely on early stroke outcome prediction. The precise pathophysiological mechanism behind this link has to be clarified by additional research, even though blood cortisol has been shown to be an independent indication of stroke severity.

CONCLUSION

Elevations in blood cortisol levels are associated with acute stroke severity. Thus, serum cortisol can be used as a gauge for the severity of a stroke.

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