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ORIGINAL ARTICLE

Serum Cortisol Level as a Biomarker in Predicting the Severity of Stroke

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Abstract

Background: A number of clinical and radiological indicators can reliably detect the prognosis of a stroke. Improved biomarkers for predicting prognosis in acute ischemic and hemorrhagic stroke are still elusive. **Aims and Objective:** The present study was aimed to observe whether serum cortisol acts a biomarker in predicting the severity of stroke. **Materials and Methods:** A prospective study performed among 50 patients with ischemic in Group A and 50 patients with hemorrhagic stroke in Group B. The random serum cortisol of these patients was compared with the NIHHS score. **Results:** Incidence of hypertension was significantly higher in group Bthan group A (72% vs. 38%; P<0.0001). Both systolic and diastolic BP were significantly higher in group B in comparison to group A (P<0.001). Severity of stroke was significantly higher in group B in comparison to group A (P<0.001). Mean cortisol levels were significantly more in group B in comparison to group A (P<0.001). Also, a statistically significant correlation with raised serum cortisol levels and the severity of stroke irrespective of type of stroke was observed. **Conclusion:** The study revealed that serum cortisol can be used as a biomarker for the prediction of severity of stroke.

Keywords

Stroke, Diabetes, Hypertension, Coronary Artery Disease, Hemorrhagic Stroke

Introduction

According to American Stroke Association, stroke occurs when vascular events cause immediate focal damage to brain, retina or spinal cord. Stroke is a leading cause of death and disability throughout the world[1]. Stroke is defined by the rapid onset of focal neurological dysfunction, which is of vascular origin. The commencement of a stroke is defined as the time when the patient was last known to be healthy[2]. Rendering to data from the 2016 Global Burden of Disease, which was released in 2019, one in every four persons will suffer a stroke throughout their lifetime[3]. As perWHO [World Health Organization], the annual number of ischemic and hemorrhagic (which includes intracerebral and subarachnoid hemorrhage) strokes is estimated at 9.6 million and 4.1 million respectively. The treatment of ischemic stroke in the hyper-acute and early acute phase has made significant progress in the last five years. At present the diagnosis of stroke is done clinically and

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confirmed radiologically. An ideal stroke biomarker should be able to differentiate between the type of stroke, its severity and help in prognosis. The test should be cheap and easy to perform. Markers of brain injury includes cellular fibronect in (c-FN), glial fibrillary acidic protein (GFAP), matrix metalloproteinase (MMP-9), neuron specific enolase (NSE) and S100 calcium binding protein â (S100â). However, improved biomarkers for predicting prognosis in acute stroke still remain elusive. The timing of biomarker measurement, particularly during window period when decision making is most important, requires urgent and systematic study[4].

Stroke has been linked to increases in stress indicators like cortisol, according to several recent researches[5]. An increase in cortisol levels might be expected when the HPA axis is activated during an acute or severe sickness like stroke. The diurnal variation of serum cortisol levels is lost in these patients. When cortisol is released, it affects the metabolism of glucose, protein, and lipids through the hypothalamic–pituitary–adrenal system (HPA).[6] Cardiac output is also increased in these patients. Some studiesshowed correlation amid cortisol and inflammatory markers and the possible effects of cortisol on prognosis is more initiated from inflammatory responses than stress.[7] Ischemic stroke patients have shown a change in their blood levels of this hormone. Studies show that individuals with ischemic stroke who have high cortisol levels are more likely to die.[8, 9] However, there are very less studies regarding estimation of serum cortisol level in estimating severity hemorrhagic stroke. Hence, the present study was aimed to observe whether serum cortisol acts a biomarker in predicting the severity of stroke.

Material and Methods

Study details: This was a prospective analytical study stratified over severity scales (NIHSS Scale) carried out in the Department of Medicine, IMS & SUM Hospital, Bhubaneswar, a tertiary care hospital catering patient of eastern India. Each of the 100 patients participated in the study were admitted to IMS & SUM Hospital met the inclusion criteria and supplied in their written/informed consent. All patients were above 18 years of age. All cases of stroke satisfying the inclusion and exclusion criteria admitted within 72 hrs of onset of neurological event were included in the study. The Ethical Committee of IMS & SUM Hospital approved the study, and informed/written consent was obtained from the patients and/or their family members after thoroughly explaining the process.

Methodology: In this prospective analytical study detailed history and thorough clinical examination were done. The data of each patient collected in the specific proforma which includes, patient name, age, sex, demographic details, presenting complaints, risk factors, past history, drug history, general examination, vital signs, system examination, severity assessment by using National Institute of Health Sciences Scale (NIHSS) at the time of admission, Random serum cortisol levels, CT Brain plain/MRI brain/carotid doppler, and serum cortisol levels are compared with NIHSS score.

Statistical Analysis

The data collected was analysed using SPSS software version 20. The descriptive statistics/measures (mean with standard deviation, median, and range for continuous variables and numbers and percentage for categorical variables) used to analyse the data, chi square test was used to see association of qualitative variables and parametric and non-parametric test as appropriate was used for quantitative variables.

Results

The present study was aimed to evaluate correlation between serum cortisol and type and severity of stroke. A total of 100 subjects were included in this study over the period of 18 months. Results of the study showed that 50 patients had ischemic(Group A), and 50 patients had hemorrhagic stroke(Group B) (*Fig. 1*).

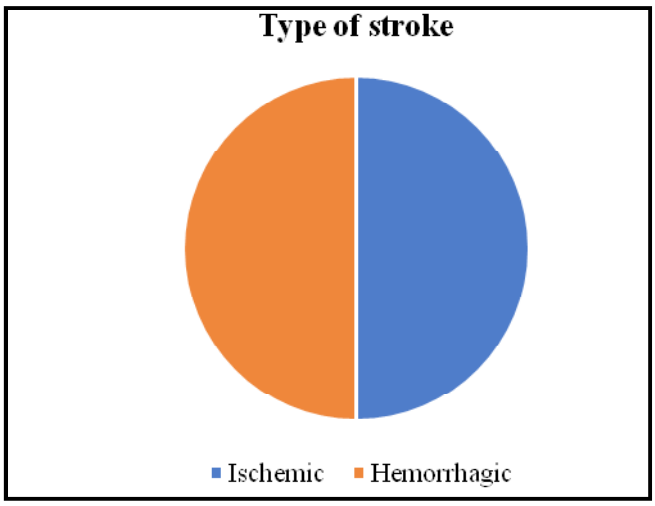

Figure 1: Type of Stroke

Comparison of clinical parameters: In this study, most of the patients were [in group A (60%) and group B (46%)] above 60 years. There was no age-based difference between both groups (P=0.289). Results showed that 58% patients in group A and 70% in group

B were males. There was no significant sex-based difference between both groups (P=0.211). The incidence of hypertension was significantly higher in group in comparison to group A (72% vs. 38%; P<0.0001). The incidence of diabetes was not significantly different in group in comparison to group A (26% vs. 44%; P = 0.059). Similarly, the incidence of coronary artery disease was not significantly different in group in comparison to group A (24% vs. 26%; P = 0.817). Both systolic and diastolic BP were statistically significantly higher in group B in comparison to group A (P<0.001). Also, the severity of stroke was significantly higher in group B in comparison to group A (P<0.001). Mean NIHSS score was significantly higher in group B in comparison to group A (P<0.001). The clinical parameters were presented in the *table1*.

Table 1:Clinical parameters

Clinical parameters	Group A (N=50)	Group B (N=50)	P-value
Age group (Years)			
31-40	5	3	0.289
41-50	5	10	
51-60	10	14	
>60	30	23	
Sex			
Male	29	35	0.211
Female	21	15	
Hypertension			
Yes	19	36	<0.001*
No	31	14	
Diabetes			
Yes	13	22	0.059*
No	37	28	
Coronary artery disease			
Yes	12	13	0.817
No	38	37	
Blood pressure			
Systolic BP	143.20±21.33	181.0±14.74	<0.001*
Diastolic BP	88.0±13.09	102.20±9.54	
NIHSS score on admission			
Minor stroke	6	3	<0.001*
Moderate stroke	38	19	
Moderate to severe stroke	5	19	
Severe stroke	1	9	
Mean NIHSS Score	8.92±5.37	16.40±5.55	<0.001*

*Pvalue <0.05 is considered as statistically significant

Serum cortisol levels: Serum cortisol levels and NIHSS score were depicted in *table 2*. Serum cortisol levels were significantly higher in group B in comparison to group A (P=0.021). The mean serum cortisol levels were increased in both the groups, in both ischemic and hemorrhagic stroke the serum cortisol levels were high and statistical difference was observed (P=0.046). Also, serum cortisol levels rise with the severity of the stroke and not the type of the stroke as reflected with the P values. Comparing group-A and group-B there is no difference however there is a statistically significant increase down the column as the severity of stroke increases.

Discussion

Stroke is the 2nd utmost reason of death universally and a chief cause of disability, with acumulative prevalence in emerging nations. Ischaemic stroke caused by arterial occlusion is accountable for the mainstream of strokes. Serum cortisol, serum ACTH, and catecholamine levels rise in the first few days following an acute stroke because of a stress reaction. In both cerebral infarction and intracerebral haemorrhage, the serum cortisol and serum ACTH response has been found. The presence of high s-cortisol and s-ACTH levels has been linked to a bad prognosis. According to some studies, the link between high levels of stress hormones and a poor outcome may be due to cardiac abnormalities caused by the stress hormones. To what extent stress response contributes to stroke prognosis has yet to be established. There were 53 patients aged more than 60 in our research. The frequency of strokes increases every decade beyond the age of 45,for individuals 65 and older, more than 70 percent of all strokes occur.[10] The mean age of the patients studied by other recent reports was 72.2 years.[11] As a result, our findings are in line with above study.

We found that 64% of the participants in our research were males. The total lifetime stroke risk in men was estimated to be 1 in 6 for men and 1 in 5 for women, with men having greater rates in their early years and women in their later years.[12] Every year, 55,000 more women than males have a stroke as a result of their higher life expectancy.[13, 14] In our study, 55% of the stroke victims

Table 2: Serum cortisol levels and NIHSS score

Parameters	Group-A (n=50)	Group-B (n=50)	P-value
Serum cortisol(nmol/ml)			
Normal	23	12	0.021*
High	27	38	
Serum cortisol(nmol/ml)	638.94±129.53	691.58±131.01	0.046*
NIHSS score	**Serum Cortisol**	**Serum Cortisol**	
Minor stroke (1-4)	414.9±133.4	424.1±128.5	0.726
Moderate stroke (5-15)	453.3±151.24	461.2±131.6	0.784
Moderate - severe stroke (16-20)	718.5±161.8	712.3±153.2	0.818
Severe stroke (21-42)	791.1±171.92	887.2±153.19	0.004*
P-value	P<0.01	P<0.01	

*Pvalue<0.05 is considered as statistically significant

had high blood pressure. As we become older, our chance of developing hypertension, the most common and controllable risk factor for stroke, rises by 90%.[15] Blood pressure is strongly linked to both fatal and non-fatal stroke in men and women of all ages, according to a number of long-term studies. Blood pressure raises the relative risk of stroke in men and women by 1.7 and 1.9 folds, respectively, starting in middle age.[12] In another study, 59% of the patients had high blood pressure[11]. A total of 58 (57%) of the participants in Fatima and Khan's research had been diagnosed with hypertension. When it came to people who hadn't previously been diagnosed with hypertension, 10 new cases were discovered. It was found that 68 individuals had elevated blood pressure.[16] In our study diabetes was found to be present in the blood of nearly 50% of the participants. Uncontrolled hyperglycaemia, intensifies the threat of ischemic and haemorrhagic strokes in patients. In those with diabetes, ischemic stroke has a unique clinical pattern. For example, diabetics are more prone than non-diabetics to show indications of lacunar cerebral infarction such as limb weakness and dysarthria. The frequency of subcortical infarction in individuals with diabetes was greater in 1983 than in 2002, according to the Lausanne Stroke Registry; whereas the prevalence of intracerebral haemorrhage was lower (ICH).[17] Compared to nondiabetics, individuals with ischemic stroke and diabetes had a greater prevalence of lacunar infarcts and hypertension.[18]

Participants with coronary artery disease (CAD) were found in 25% of the patients in this investigation. The Bhatia et al research had a total of 300 participants. There were 41 previously identified cases of definite CAD among the patients.[19] The cortisol levels of 65 percent of the participants in this research were elevated. When it comes to stroke, higher levels of cortisol were shown to be associated with the severity of the illness. Good-outcome cortisol was 258.10±77.91 nmol/l and poor-outcome cortisol was 585.77±113.34 nmol/l, according to Fatima and Khan[16] and their colleagues. According to the results, the two groups had risen in serum cortisol levels with increasing functional severity but not the type of stroke (p0.05).[20] A higher cortisol response was found in patients who had insular involvement in a less severe stroke in this investigation. In our investigation, we found a correlation between severe stroke and elevated cortisol levels. Cortisol has been demonstrated to be a risk factor for death following a stroke, as well as a risk factor for a poorer functional result. Cortisol levels and the SSS score (Siriraj Stroke score) were shown to have a statistically significant connection.[7] Serum cortisol levels were increased in seven cases reported by other study[21]. A NIHSS score of 6 or above was found in all individuals with a blood cortisol level of greater than 690nmol/L. Nearly all patients with increased cortisol levels had an NIHSS score of 6 or above, which indicates a moderate to severe stroke.

Conclusion

Serum cortisol level was found to have a significant positive correlation with worsening of stroke and it can be concluded that serum cortisol can be used as

prognostic indicator of severity of stroke. This test can be carried out easily which makes it conveniently to use serum cortisol as biomarker for stroke severity prediction.

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Conflicts of Interest

There are no conflicts of interest.

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