Serum C-Reactive Protein as a Prognostic Biomarker in Acute Ischemic Stroke

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Abstract- Background and Objectives: Stroke is a serious neurological disease which is a major cause of death and disability throughout the world. CRP an inflammatory marker increases in response to stroke, so can be used as a predictor for functional outcome in acute ischemic stroke. In this study, role of serum CRP in assessing the disease severity and short-term functional outcome in an acute ischemic stroke is evaluated. Method: Prospective observational study. Results: Maximum number of cases were between 51-60 years, with a mean age of 62.3 years. Study shows 16% had minor stroke, 58% had moderate stroke, 22% had moderate to severe stroke and 4% had severe stroke. 34 cases got negative and 16 had positive CRP results. CRP and stroke severity by NIHSS score is significantly related in this study (Chi- square value 23.46, p value-0.001). Hypertension (p value 0.047), dyslipidaemia (p value 0.036), smoking (p value 0.031) is positively correlated with the short-term functional outcome after AIS. At the time of discharge 4% cases were independent, 28% with mild, 34% with moderate, 20% with severe and 14% with total dependency. Conclusion: CRP levels in the very early phase of acute ischemic stroke can beused as an independent prognostic factor for short term outcome and for assessing the severity of stroke.

Key words: Acute Ischemic Stroke, CRP, Barthel Index

INTRODUCTION

Stroke is one of the leading causes of death and the *main causes of disability worldwide. As per WHO, 15 million people suffer from stroke every year.[1] Worldwide, 70% of strokes and 87% of both stroke-related deaths and disability-adjusted life years occur in low and middle-income countries. Stroke mainly affect individuals at the peak of their productive life. Even though it has got high impact on socio- economic development, this growing crisis has received very little attention till date.[2]*

WHO defines stroke as" rapidly developing clinical symptoms/signs of focal or global loss of brain function, with symptoms lasting more than 24 hrs or leading to death, with no apparent cause other than that of vascular origin".[3] New definition of stroke has been proposed by the American Stroke Association "CNS infarction is defined as the brain, spinal cord, or retinal cell death attributable to ischemia based on pathological, imaging, or other objective evidence of cerebral, spinal cord or retinal focal ischemic injury in a defined vascular distribution or clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury based on symptoms persisting ≥24 hours or until death, and other etiologies excluded. Ischemic stroke is an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction".[4] When blood flow is quickly restored brain tissue can recover fully and the patient's symptoms are only transient is called Transient Ischemic Attack (TIA).[5]

Studies shows that C-reactive protein, a peripheral marker of inflammation, can also be used as a marker of generalized atherosclerosis.[6] Acute stroke may trigger an inflammatory response that leads to increased levels of CRP. CRP has the potential to serve as both a prognostic indicator following vascular events as well as a potential predictor of future vascular events due to the association between inflammation and atherosclerosis. CRP is an acute phase reactant produced not only by the liver but also in vascular smooth muscle cells and adiposities.(7-10)

MATERIAL AND METHODS

Study design:
The clinical study was performed at tertiary care hospital of the Guntur district, Andhra Pradesh, India from Jan 2024 to June 2024. Laboratory data were collected.

CRITERIA FOR PATIENT SELECTION:

INCLUSION CRITERIA:

1. Symptom onset within 24 hours of admission
2. Age more than 18 years
3. Patients with focal neurological deficits and MRI Brain confirmed acute ischemic stroke
4. Patients with new onset stroke with past history /newly detected hypertension, diabetes mellitus and dyslipidaemia are included
5. Patients with habits of alcohol intake, smoking and OCPs are included

EXCLUSION CRITERIA:

1. MRI brain confirmed hemorrhagic stroke
2. Symptom onset >24 hours
3. Patients with recent ACS, Cerebrovascular events or any infections that affect CRP value

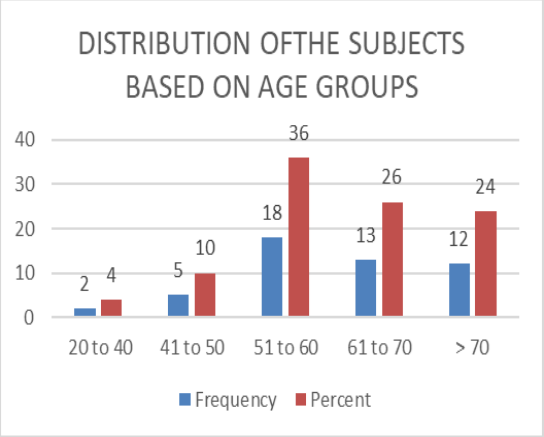
STUDY DESIGN: Prospective observational study
DURATION OF STUDY:6 months from the approval of ethical committee
SAMPLING METHODS: Nonprobability purposive sampling
SAMPLE SIZE: 50 patients who met all the inclusion criteria during the study period

RESULTS AND ANALYSIS

Total 50 cases with cerebrovascular accident due to ischemia between age of 23 to 85 years were studied.

TABLE 1: DISTRIBUTION OFTHE SUBJECTS BASED ON AGE GROUPS

Age groups (Years)	Frequency	Percent
20 to 40	2	4.0
41 to 50	5	10.0
51 to 60	18	36.0
61 to 70	13	26.0
> 70	12	24.0
Total	50	100.0



In this study youngest of the population was 23 years and oldest was 85 years. Maximum number of cases were in between 51-60 years with a mean age of 62.3 years

TABLE 2: RISK FACTORS OF AIS

RISK FACTORS	SEX		
	F	M	TOTAL
Hypertension	11	28	39
Dm	9	27	36
Dyslipidemia	4	11	15
Heart Diseases	3	7	10
Smoking	0	18	18
Alcohol	0	11	11
Ocps	0	0	0

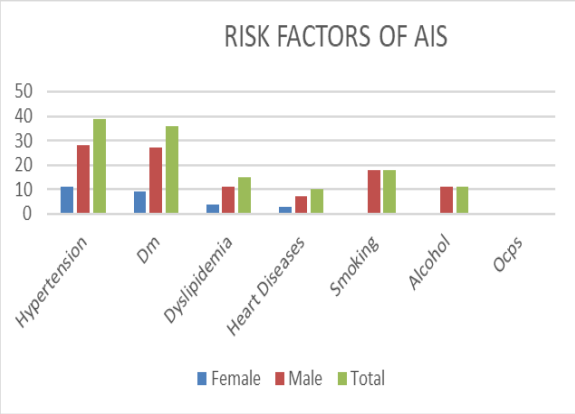


TABLE 3: DISTRIBUTION OF THE SUBJECTS BASED ON CLINICAL FEATURES

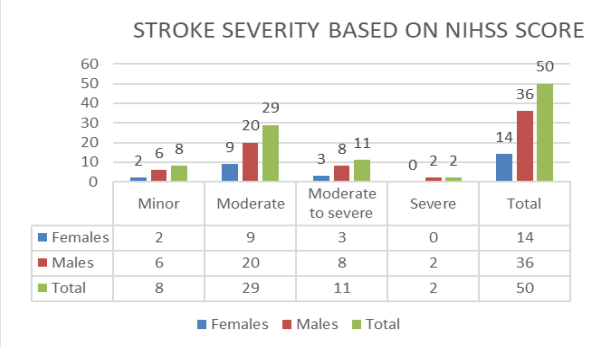
Clinical features		Frequency
Level of consciousness	Alert	29
	Verbal response	10
	Pain response	9
	Unresponsive	2
Speech disturbances	-	9

	+	41
Motor involvement	-	7
	+	43
Sensory involvement	-	43
	+	7
Cranial Nerve palsy	-	15
	+	35
Bowel and bladder involvement	-	45
	+	5
Cerebellar signs	-	43
	+	7
Handedness	L	3
	R	47

In this study 58% cases were alert,20%were responding to verbal commands, 18%were pain responsive and 4% were unresponsive.86% of the patients had weakness of limbs and 70% had cranial nerve involvement. Cerebellar ischemia was seen in 14% cases.

TABLE 4: STROKE SEVERITY BASED ON NIHSS SCORE

NIHSS	SEX		Total
	Females	Males	
Minor	2	6	8
Moderate	9	20	29
Moderate to severe	3	8	11
Severe	0	2	2
Total	14	36	50



When stroke severity classified according to NIHSS, study shows 16% had minor stroke, 58% had moderate stroke, 22% had moderate to severe stroke and 4% had severe stroke. Among these females were more affected with moderate stroke and in other severity classifications males were more affected than females.

TABLE 5: CRP WITH AGE GROUPS

Age groups (years)	CRP CATEGORY	
	NEG	POS
20 - 40	1	1
41-50	3	2
51 -60	13	5
61 -70	7	6
> 70	10	2
Total	34	16

In the study total of 34 cases got negative CRP results and 16 had positive CRP results. The age group 51-60 years had maximum number of cases and negative CRP levels.The age group 61-70 years had maximum number of cases with positive CRP levels.

TABLE 6: NIHSS WITH CRP

NIHSS	CRP		Total
	NEGATIVE	POSITIVE	
Minor	8	0	8
	23.5%	0.0%	16.0%
Moderate	24	5	29
	70.6%	31.2%	58.0%
Moderate to severe	2	9	11
	5.9%	56.2%	22.0%
Severe	0	2	2
	0.0%	12.5%	4.0%
Total	34	16	50
	100.0%	100.0%	100.0%

CRP and stroke severity by NIHS score was significantly related in this study (Chi- square value 23.46, p value=0.001). When CRP is less than 6mg/L, maximum number of cases comes under minor to moderate stroke. When CRP values more than 6mg/L, cases had moderate- severe to severe stroke. This indicates that, the increase in CRP levels were directly proportional to stroke severity.

TABLE 7: DEPENDENCY AT DISCHARGE BY BARTHEL INDEX

Dependency at discharge (Functional outcome)	Age groups(years)					Total
	20 to 40	41 to 50	51 to 60	61 to 70	> 70	
IND	0	0	1	0	1	2
	0.0%	0.0%	5.6%	0.0%	8.3%	4.0%
MILD	0	0	5	2	7	14
	0.0%	0.0%	27.8%	15.4%	58.3%	28.0%
MD	1	3	6	5	2	17
	50.0%	60.0%	33.3%	38.5%	16.7%	34.0%
SD	0	2	3	4	1	10
	0.0%	40.0%	16.7%	30.8%	8.3%	20.0%
TD	1	0	3	2	1	7
	50.0%	0.0%	16.7%	15.4%	8.3%	14.0%

Dependency of the patients at discharge evaluated by Barthel index. Out of total 50 cases 4% cases were independent at the time of discharge, 28% had mild dependency, 34% had moderate dependency, 20% had severe dependency and 14% were totally depended. In elderly age group most of the patients had moderate to severe dependency.

In this study 2 cases had mild dependency at admission, and both improved to independent on discharge. Out of 24 cases who were moderately dependent at the time of admission, 54.2% got improved to mild dependency and rest have same outcome at the time of discharge. In severely dependent group there were 16 cases, 50% cases had no change in dependency on discharge, 37.5 % improved to moderate and 6.3% become totally dependent. Out of 8 cases with total dependency at admission 25% got slight improvement and rest remained the same. Most of the mild and moderate dependent cases on admission had good short- term functional outcomes. Those who were severely dependent on admission had made no significant improvements in short-term functional outcomes.

TABLE 8: DEPENDENCY OF PATIENTS AT ADMISSION AND AFTER 7 DAYS

Dependency at admission	Dependency after 7 days					Total
	IND	MILD	MD	SD	TD	
MILD	2	0	0	0	0	2
	100.0%	0.0%	0.0%	0.0%	0.0%	100.0%
MD	0	13	11	0	0	24
	0.0%	54.2%	45.8%	0.0%	0.0%	100.0%
SD	0	1	6	8	1	16
	0.0%	6.3%	37.5%	50.0%	6.3%	100.0%
TD	0	0	0	2	6	8
	0.0%	0.0%	0.0%	25.0%	75.0%	100.0%
Total	2	14	17	10	7	50
	4.0%	28.0%	34.0%	20.0%	14.0%	100.0%

TABLE 9: RELATION OF DEPENDENCY WITH RISK FACTORS

Risk Factors		DEPENDENCY AT DISCHARGE						Chi-square value	p value
		IND	MILD	MD	SD	TD	Total		
HTN	-	2	4	3	2	0	11	9.62	0.047*
	+	0	10	14	8	7	39		
DM	-	2	5	4	1	2	14	7.33	0.12
	+	0	9	13	9	5	36		
DYSLIPIDEMIA	-	2	13	11	7	2	35	10.28	0.036*
	+	0	1	6	3	5	15		
HD	-	2	12	16	5	5	40	8.85	0.065
	+	0	2	1	5	2	10		
	-	2	12	12	4	2	32		

SMOKING	+	0	2	5	6	5	18	10.62	0.031*
ALCOHOL	-	2	11	16	5	5	39	7.88	0.096
	+	0	3	1	5	2	11		
OCPs	-	2	14	17	10	7	50	-	-
	+	0	0	0	0	0	0		

CRP and stroke severity by NIHS score was significantly related in this study (Chi- square value 23.46, p value=0.001). When CRP is less than 6mg/L, maximum number of cases comes under minor to moderate stroke. When CRP values more than 6mg/L, cases had moderate- severe to severe stroke. This indicates that, the increase in CRP levels were directly proportional to stroke severity.

According to the findings, hypertension, dyslipidaemia, and smoking are all associated with dependency after an acute ischemic stroke. Higher grades of dependency were seen in those who had any of these risk factors. Since the sample size is small, further studies with a bigger sample size are needed to assess the relationship between other risk factors and dependency.

TABLE 10: RELATION BETWEEN SEVERITY OF STROKE AND DEPENDENCY

NIHSS	DEPENDENCY AT DISCHARGE					Total
	IND	MILD	MD	SD	TD	
Minor	1	5	2	0	0	8
	50.0%	35.7%	11.8%	0.0%	0.0%	16.0%
Moderate	1	9	14	4	1	29
	50.0%	64.3%	82.4%	40.0%	14.3%	58.0%
Moderate to severe	0	0	1	6	4	11
	0.0%	0.0%	5.9%	60.0%	57.1%	22.0%
Severe	0	0	0	0	2	2
	0.0%	0.0%	0.0%	0.0%	28.6%	4.0%
Total	2	14	17	10	7	50
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Chi-square value- 40.78						
p value-0.001*						

In this study, when serum CRP levels were compared with short-term functional outcome, they showed a positive correlation. That is, when CRP levels are less than 6 mg/L, functional outcomes are better, with the majority of patients having mild, moderate, or independent status; when CRP levels are greater than 6 mg/L, functional outcomes are poor, with the majority of patients having severe or total dependency (chi-square value 46.06 and p value 0.001).

In this study group, only 19 patients underwent thrombolysis according to ASA criteria, of whom the maximum number of patients had a better outcome. One of the thrombolysed patients was independent; eight each had mild or moderate dependency; and two were severely dependent. Among non-thrombolysed patients, 10 had severe dependency,5 had total dependency, and 9 had moderate dependency. It concludes that with thrombolysis, outcomes can be improved.

CONCLUSION

In this study, functional outcomes were better when CRP levels were below the normal range (6 mg/L), while they were worse when CRP levels were above the normal range. CRP levels in the very early phase of acute ischemic stroke can be used as an independent prognostic factor for short term outcome and for assessing the severity of stroke.

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