Original Research Paper

Volume-8 | Issue-12 | December-2018 | PRINT ISSN No 2249-555X

General Medicine

A STUDY TO EVALUATE CRP AS A PROGNOSTIC MARKER IN ACUTE ISCHAEMIC STROKE

G. Yashwanath Reddy — Senior Resident, Department of General Medicine, Government Medical College/GGH, Mahabubnagar, Telangana

Nishanth T* — Associate professor of medicine, Department of General Medicine, Government Medical College/GGH, Mahabubnagar, Telangana *Corresponding Author

ABSTRACT

INTRODUCTION: Stroke remains a major cause of human mortality and morbidity. In spite of our increasing understanding of the pathophysiology and epidemiology of cardiovascular diseases and stroke and continuing advances in prevention and treatment, the burden of above said diseases is high.

AIMS OF THE STUDY: To observe plasma CRP levels in acute ischemic stroke. To evaluate the role of CRP(C-Reactive protein) as a prognostic and diagnostic aid in acute ischaemic stroke. To evaluate CRP levels as a risk factor in acute ischemic stroke.

METHODOLOG: The present study was a hospital based, prospective, case control study conducted on 60 patients and 60 age and sex matched controls admitted with clinically first attack of stroke to medicine intensive care unit or acute medical ward of SVS medical college & Hospital, Mahabubnagar between september 2015 to august 2017.

RESULTS: Of the total 60 patients 37 were males and 23 were females with male to female ratio of 1.6:1. The maximum thrombotic stroke patients were in the age group of 61 – 70 constituting 30% of the study population. 82% of patients had sudden onset of symptoms while 11% developed the symptoms gradually. (33.3%) had infarction in the parietal lobe, followed by frontal and fronto-parietal areas which had 13.4% each. Diabetes was the most important risk factor for acute ischaemic stroke affecting 33.4% of the cases. Smoking was the most common non-modifiable risk factor(26.6%).There was statistically significant rise in systolic and diastolic blood pressure in case compared to controls. Elevation of CRP and lipid profile parameters in patients were statistically significant compared to controls.

CONCLUSION: Stroke incidence increases with advancing age and is more in males when compared to females. C-reactive protein is an independent risk predictor for ischemic stroke. C-reactive protein level increases as age advances and has no significant gender predilection. C-Reactive level cannot differentiate the subtypes (cortical and sub cortical) of cerebral infarct at the time of early diagnosis. C-Reactive protein is a sensitive parameter to predict future stroke.

KEYWORDS : Stroke, CRP, ischemic stroke

INTRODUCTION

Stroke is a devastating and disabling disease with significant amount of residual deficits leading to socio and economic loss. It is defined as an abrupt onset of a neurological deficit that is attributable to a focal vascular cause[1]. It is the second leading cause of death worldwide[1]. It is estimated to account for 7 to 8 million deaths yearly throughout the world and represents 13% of all causes of death[2]. Some of the recent studies have demonstrated the stroke pattern to a considerable extent in our country with prevalence rate of 471/100000 population[3]. Recent studies identified that 7% of medical and 45% of neurological admissions were due to stroke with the mortality rate of 9% at the time of discharge and 20% at one month[4]. They caused significant physical, emotional and cognitive disabilities among survivors accounting for 2 3.6% of total disability associated life years (DALY). Several modifiable factors are known to increase the liability to stroke. The most important are hypertension (HTN), Type 2 diabetes mellitus 2 (T2DM), atrial fibrillation (AF), Dyslipidemia and cigarette smoking. Ischemic stroke accounts for 50% to 85% of strokes worldwide[5]. Hemorrhagic strokes are due to subarachnoid hemorrhage (SAH) or intra cerebral hemorrhage (ICH) accounting for 1 to 7% and 7 to 25% 5 of strokes respectively. In India it comprises of 4% of medical admissions in major hospitals and 20% of diseases of central nervous system (CNS)[6]. The global burden of diseases studies projects that the total deaths from stroke in India will surpass established market prevalence by the year 2020[7]. At the turn of 20th century, Sir Williams Osler (1908) and Ophulus (1921) proposed that infection could be a casual factor in pathogenesis of atherosclerosis. Infact research of more than a century has implicated various microorganisms as potential link between inflammation and the pathogenesis of atherosclerosis. Indeed atherosclerosis is now accepted as an inflammatory disease, possible infections include chlamydia, H-pylori, Herpes and CMV. Researchers found a protein in their several years study in first attack of myocardial infarction or stroke and this is C- reactive protein[8,9].

Apparently measuring C-reactive protein might provide novel method to detect worrisome level of atherosclerosis in otherwise healthy persons. This new finding assumed importance to researchers as they raised the possibility that atherosclerosis may be at least partly and inflammatory process disease. Antimicrobial and antiviral therapy may some day become the part and parcel of therapies to prevent heart attack and stroke. Limited works have been published on CRP changes in stroke in India despite high incidence of CVA in India.

AIMS AND OBJECTIVES:

The present study was undertaken with the following aims and objectives.

1. To observe plasma CRP levels in acute ischemic stroke.
2. To evaluate the role of CRP as a prognostic and diagnostic aid in acute ischaemic stroke.
3. To evaluate CRP levels as a risk factor in acute ischemic stroke.

METHODOLOGY

The present study was a hospital based, prospective, case control study conducted on 60 patients and 60 age and sex matched controls admitted with clinically first attack of stroke to medicine intensive care unit or acute medical ward of SVS medical college & Hospital, Mahabubnagar between september 2015 to august 2017.

Inclusion criteria:

1. Age group 20-80 years
2. Patients with either or both type 2 diabetes mellitus and hypertension
3. Ischemia proved by CT scan brain, in all cases of the study

Exclusion Criteria:

1. Age > 80 and < 20 years.
2. Patients with history of heart disease- any valvular heart disease, infective endocardittis, myocardial infarction.
3. Patients with previous history of stroke or TIA.
4. Patients collagen vascular diseases,active tuberculosis, arteritis.
5. Patients with hemorrhagic stroke, tumor, subarachnoid hemorrhage.
6. Patients with head injury within past 3 months.
7. CT negative stroke.
8. Patients with meningitis, brain abscess or any chronic infection that affect CRP value.

Detailed clinical history was taken from either the patient or his/ her

relatives or attender and detailed examination details were noted down. NIH stroke scale was assessed in all patients to assess the neurological disability and its prognosis. Detailed neurological examination was done based on proforma. All other systems like cardiovascular system, gastrointestinal system, and respiratory system were examined in detail. Detailed investigations including blood hemoglobin, TLC, DLC, urine routine, FBS, lipid profile, ECG, chest X-ray, 2D-ECHO were done CT scan after 24 hours after onset of symptoms and C-reactive protein estimation was done anytime between 12-72 hours of symptom onset.

CT Scanning.
Data were presented as mean±SD values were called significant (if $p<0.005$).The chi square test was used in most cases to compare frequency distribution.

RESULTS

There were 250 cases of first episode stroke in SVS medical college and Hospital during the period of september 2015 to august 2017. Of those 200 cases were CT proved ischaemic stroke. Of those 60 cases were studied after excluding the patients using the exclusion criteria. 60 age and sex matched controls were studied as the control group.

Of the total 60 patients with first episode of stroke 37 (61.6%) were males and 23(38.4%) were females with male to female ratio of 1.6:1..

Table 1 : Age and Sex Distribution in Study Group (N = 60)

Age in years	No. of patients				Total	Percentage
	Male	Percentage	Female	Percentage		
21 – 30	0	0	0	0	0	0
31 – 40	4	10.8	0	0	4	6.6
41 – 50	6	16.2	6	28.1	12	20.0
51 – 60	8	21.6	4	17.4	12	20.0
61 – 70	10	27.0	8	37.8	18	30.0
71 – 80	9	24.4	5	21.7	14	23.4

Table 1 shows maximum thrombotic stroke patients were in the age group of 61 – 70 constituting 30% of the study population. Young stroke (age <40 years) were found only in 6.6% (Ratio of 1:15) of cases all of whom were males. Women < 50 years accounted only for 6 cases i.e. 10% of the total cases.

Table 2 : Age and Sex Distribution of Control Group (N = 60)

Age in years	No. of patients				Total	Percentage
	Male	Percentage	Female	Percentage		
21 – 30	0	0	0	0	0	0
31 – 40	4	10.8	0	0	4	6.6
41 – 50	6	16.2	6	28.1	12	20.0
51 – 60	8	21.6	4	17.4	12	20.0
61 – 70	10	27.0	8	37.8	18	30.0
71 – 80	9	24.4	5	21.7	14	23.4

Table 2 shows that similar age and sex matched controls were taken for the study as CRP increases with age.

Table-3: Clinical Picture (N=60)

	No. of cases	Percentage
Mode of onset		
Sudden (within minutes)	49	82.0
Gradual (within hours)	11	18
Level of consciousness		
Alert	36	60.0
Drowsy	16	26.6
Comatose	8	13.4
Convulsions		
Present	10	16.6
Absent	50	83.4
Headache / vomiting		
Present	14	23.3
Absent	46	76.7
Facial weakness		
Present	20	33.3%
Absent	40	66.7%
Dysarthria		
Present	18	30%
Absent	42	70%

Table 3 shows the clinical presentation, 82% of patients had sudden onset of symptoms while 11% developed the symptoms gradually. 60% were alert at the time of presentation while 26.6% were drowsy and 13.4% were comatosed. Convulsions were present in 16.6% and head ache / vomiting in 23.3% of the cases. 33.3% had facial weakness while 30% of the patients had dysarthria at admission.

Table 4 : Localization of Lesions on CT Scan (N=60)

	No. of cases	Percentage
Cortical		
Frontal	8	13.4
Parietal	20	33.3
Temporal	2	3.3
Parietotemporal	6	10.0
Frontoparietal	8	13.4
Sub cortical		
Basal ganglia, Thalamus	12	20.0
Internal capsule	4	6.6

Cortical infarction constituted 73.4% of cases in which maximum cases (33.3%) had infarction in the parietal lobe, followed by frontal and fronto-parietal areas which had 13.4% each. Sub cortical infarction constituted 26.6% with basal ganglia and / or thalamus involved in 20% cases.

Table 5: NIH Stroke Scale (N-60)

NIH Scale	No. of patients		Total	Percentage
	Male	Female		
Minor Stroke (1-4)	8	2	10	16.6
Moderate Stroke (5-15)	18	15	33	55
Moderate - Severe Stroke (16-20)	10	4	14	23.4
Severe Stroke (> 20)	1	2	3	5

Minor stroke accounted for 16.6% cases, while most patients (both male and female) 55% had moderate stroke, only 5% cases had severe stroke, whilst 23.4 percentage of patients had moderate to severe stroke.Diabetes was the most important risk factor for acute ischaemic stroke affecting 33.4% of the cases of which 14 were males and 6 females, in which 12 males and 2 females were known diabetics, where as 2 males and 4 females were newly detected diabetics. Hypertension accounted for 26.6% of the cases, in which 12, 6 males, 6 females were known cases, whereas 4 cases i.e. 2 males and 2 females were newly diagnosed as hypertensives. Combination of diabetes and hypertension as risk factors of acute ischamic stroke was seen in 23.4% of the cases of which 12 were known cases and only 2 were newly detected.

16.6% of the cases in the study had no risk factors of either diabetes or hypertension or both.

Among the nonmodifiable risk factors 26.6% were smokes only while 20% were both smokers and consumed alcohol, whilst 6.7% had all 3 risk factors of smoking, consuming alcohol and eating tobacco.Total number of deaths in the study were 14 (10 males, 4 females). Diabetic deaths constituted for 35.7% of the cases of them 3 were males and 2 females with 1 male and 1 female being newly detected while 2 males and 1 female were known cases. Hypertensive group saw 21.4% (3) deaths in total and mortality was seen only in known cases of which 2 were males and one female. In Diabetic and hypertensive group (28.6%) they were 4 deaths in total and all were males of which 2 were newly detected and 2 were known cases. 2 more deaths occurred of whom neither had diabetes nor hypertension. Of them one was male and one female.

Of the 60 cases under study 76.6% improved, 23.4% expired. Of the 20 diabetics 15 improved and 5 expired where as of the 16 hypertensives 13 improved and 3 expired. Of the 14 patients who were both diabetic and hypertensive 10 patients improved whereas 8 out of 10 patients improved in non hypertensive, non diabetic group.

The total number of deaths were 14, of which 71.4% were males and 28.6% were females. All females deaths occurred in the age group of 61 –70. Whereas most deaths in males were in the age group of 71– 80 constituting 28.6% of the cases. Total incidence of mortality (42.9%) was highest in age group of 61 – 70.

Table 6 : Blood pressure in study and control group

	Mean systolic BP in mm hg	Mean diastolic BP in mm Hg	P value
Study group (N=60)	160.2+26.12	94.52+13.96	>0.01
Control group (N=60)	122.1+5.47	77.76+5.9	>0.01

The average systollic blood pressure was 160.2 + 26.12 in the study group. Whereas in the control group it was 122.1 + 5.47 with the p value of >0.01 which shows that systollic blood pressure significantly raised in the study group and was statistically highly significant. The mean diastollic blood pressure was 94.52 + 13.96 in the study group while in the control group it was 77.76 + 5.9 with a p value of >0.01 which shows that diastollic blood pressure was significantly raised in the study group.

Table 7 : Biochemical parameters in study and control group

Biochemical parameters	Study group (N=60)	Control group (N=60)	p value
Means serum urea (mg/dl)	32.54+29.80	20.72+2.80	<0.01
Mean Serum creatinine (mg/dl)	1.04+0.36	0.77+0.20	<0.01
Mean fasting blood sugar (mg/dl)	144.4+58.2	85.58+7.2	<0.01

Mean serum urea was 32.54 + 29.80 in the study group and 20.72 + 2.80 in the control group it shows that serum urea levels were significantly raised in the study group and with p value of <0.01 shows it was statistically significant. Mean serum creatinine was 1.04+0.36 in the study group and 0.77+0.20 in the control group, which shows that serum creatinine, were significantly raised in the study group and with p value <0.01 shows that it was statistically highly significant. Mean FBS was 144.4+58.2 in the study group and 85.58+7.2 in the control group which shows again that FBS levels were significantly raised in the study group with p value of <0.01.

Table 8 : Lipid profile in study and control group

Biochemical parameters (in Mg/dl)	Study group (N=60)	Control group (N=60)	P value
Means serum Cholesterol	190.8+35.3	159.6+21.8	<0.01
Mean Serum HDL	41.2+7.64	44.5+9.79	<0.05
Mean serum LDL	118.78+33.9	90.10+17.69	<0.01
Mean serum Triglycerides	192.5+78.4	141.36+41.3	<0.01

Table 8 shows serum cholesterol, LDL, TG, was <0.01 and p value of HDL was <0.05 implying that the lipid profile was altered in the study group and was statistically highly significant.

Table 9 : C-reactive protein level in CT proved ischaemic stroke patients

	C – reactive protein Levels			
	< 6mg / dl	Percentage	> 6mg/dl	Percentage
Study group (N=60)	6	10	54	90
Control (N=60)	53	88	7	12

X2 = 73.65, p < 0.001

Table 9 shows CRP values of CT evaluated ischemic stroke patients after admission, > 12 hours < 72 hours after the symptoms onset 54 of the 60 thrombotic stroke patients had CRP >6 mg/dl only 6 patients had CRP<6mg/dl (P <0.001). Chi- square test value was 73.65, which is statistically very significant. Only 7 patients in the control group had CRP>6mg/dl

Table 10 : CRP levels in relation to age (N = 60)

Age in Years	CRP Values		Total
	> 6mg/dl	< 6mg/dl	
21 – 30	0	0	0
31 – 40	2	2	4
41 – 50	11	1	12
51 – 60	11	1	12
61 – 70	16	2	18
71 – 80	12	2	14

Table 10 shows the relation of CRP values with age, i.e. CRP level is more between the age group of 61 – 70 and is less in young adults (< 40 years of age

ISCUSSION

Strokes kill 5 million people each year. Cerebrovascular disease is the second cause of death world wide[10,11].

Kristensen B[12] et al documented young ischemic strokes occuring in patients younger than 45 years old was rare and less than 5 percent of all cerebral infarctions. A recent stroke registry study by T.Song – Hai Lee[13] et al revealed that the incidence of young stroke was 6.8% of all strokes.

In our study young ischemic stroke less than 40 years of age constitutes 6.6% of all strokes and highest incidence in males was noticed after the age of 61-70 years i.e.27% and in females also the incidence was highest in the age group of 61-70years i.e.37.8%.

The greater prevalence of stroke in men is well known, but recent issues emphasize the importance of stroke in women[14]. Over the entire life time,16% of women but only 8% of men will die of stroke[15]. Knowledge of sex differences might be of interest in improving preventive strategies and the in-hospital management of stroke patients. Jaume Roquer et al[16] documented mean age for stroke was higher in women than in men.

In contrast to above studies, we documented the increased incidence of acute thrombotic stroke in both males and females after the age of 60 years with slight predominance in males. We also documented the incidence of thrombotic stroke after 60 years of age in males and females were 73% and 76.9% respectively.

Smoking is widely accepted as one of the risk factors for cerebral infarction in western populations. Smoking is thought to affect lacunar infarction mainly through reversible factors, such as increased platelet aggregation and arterial vasoconstriction induced by sympathetic activity rather than through atherogenic factors and this relationship has not been observed in most Japanese epidemiological studies[17].

Contrary to the above study, the above relation of smoking with acute ischaemic stroke is not observed in our population.

Manson JE et al[18] in their study had proved that stroke in diabetics is more likely to be fatal,when compared to anyother novel risk factors.

In terms with that of the above study,we also observed that mortality was highest among the diabetic group when compared to hypertensive group or diabetic and hypertensive group.

Thomas S.Bowman et al[19] documented that TC, HDL and Triglyceride level were not independent risk factors for ischemic stroke and TC: HDL ratio did not have a linear association with the risk of ischemic stroke.

In contrast to the above study we did notice the much significance rise in TC, LDL and TG and decrease in HDL in relation to ischemic stroke when compared to controls in our study.

CRP, one of the acute phase reactants, is an indicator of underlying systemic inflammation[19] and a novel plasma marker of atherothrombotic disease[20-22]. It is likely that CRP has many pathophysiological roles in the inflammatory process,including binding of phosphocholine and recognition of foreign pathogens and phospholipid constituents of damaged cells[19].

Kerstin winbeck et al[23] study documents, rised CRP in 127 patients without thrombolysis with a first ischemic stroke no more than 12 hours after symptom onset. In contrast, a CRP increase between 12 and 24 hours after symptom onset predicts an unfavourable outcome and is not a best parameter to predict outcome which is estimated before 12 hours of onset of symptoms.

In the present study, CRP was measured only after CT image confirmation of infarction which was done after 24 hours of onset of symptoms. So CRP level was estimated after CT confirmation and before 72 hours of onset of symptoms.

In the present study, CRP was elevated in 54 patients out of 60 study group which is statistically significant.

Mario Di Napoli et al[24] studied, the risk of CRP in 72% of patients (P<0.0001) out of 473 first ever ischemic patients and suggested the CRP as a independent marker of underlying chronic inflammatory process in atherosclerosis.

Montaner et al[25] described a peak level of interleukin-6 after 24 hours of symptom onset.

Recently, Di Napoli[26] observed an increase of CRP within 3 hours after stroke compared with the prestroke value.

Mahapatra SC et al[27] observed CRP value 76 mg/L in 64 patients out of 80 total thrombotic stroke patients (P< 0.001). The study was undertaken to assess the role of inflammation in pathogenesis of ischemic stroke.

Rathore HS et al[28] performed a study to measure and compare CRP levels in the cortical and lacunar infarct and to find out their diagnostic importance at an early stage of stroke. CRP was estimated in 25 cases of lacunar and 25 cases of cortical infarct. The CRP was considered positive if its value was more than 6mg/L, observed rise of CRP in 12% cases of lacunar infarct and 88% cases of cortical infarct.

In the present study the CRP rise was 82.4% in cortical and 26.6 in subcortical. It was clearly observed in our study that CRP was raised in all subtypes of cerebral infarct without much difference.

In Irene M et al[29] study, CRP levels were measured in a random sample of 773 subjects 55 years of age and follow-up was done for the next 6.5 years. They documented the progression of subclinical atherosclerosis and CRP predicts myocardial infarction and stroke.

In our control study involved age and sex matched healthy individuals; elevation of CRP level was noted in 12% of cases. The prediction of myocardial infarction and stroke couldn't be done since it needs longer follow-up.

In L.Masoti et al[30] study they retrospectively measured CRP values in 196 elderly patients for relationship between CRP and short term prognosis and concluded that elevation of CRP could represent a negative prognosis in elderly patients with ischaemic stroke, in particular, for short term prognosis.

In the present study, there were 14 deaths, 10 were males and 4 were females and in all of them CRP >6mg/dl which is in terms with that of the above study reiterating that elevated CRP levels were a bad prognostic indicator.

CONCLUSION

In this study mean C-Reactive protein levels were significantly higher in patients with ischemic stroke when compared to controls.It is also observed that by elevated C-Reactive protein in ischemic stroke can be diagnosed positively but subtypes (cortical, subcortical) of cerebral infarction cannot be differentiated at the time of early diagnosis. C-Reactive protein levels were raised in all cases who expired.

REFERENCES

1. Wade S. Smith, S. Claribone Johnston et al Cerebrovascular diseases, Harrisons principles of internal medicine, 19th edition, chapter 446, page no 2559-2586.
2. Allan. H. Ropper, Martin. A. Samuel et al., Cerebrovascular Diseases, Adams and Victors Principles of Neurology, 10th Edition, Page No. 778-884.
3. SK Das, TK Banerjee, ABiswas et al., Aprospective community based study of stroke in Kolkata, India, Stroke: 2007; 38(3); 906-910.
4. D. Nagaraja, G. Gururaj et al., Feasibility study of stroke surveillance: data from Bangalore, India. IJMR, 2009 October 130:396-403.
5. Feign V, laws L,Bennet D, barber cello S, Parag V, worldwide stroke incidence & early case fatalities in 56 population based studies a systematic review. Lancet neurol 2009; 8 (4);355-369.
6. Brains disease of nervous system,10th edition-walton, page 197-268.
7. Praveen kumar.P, Priyanka devi N, A Retrospective study of clinical profile of stroke victims in Coimbatore medical college hospital IOSR-JDMS, vol 15,issue 8,ver 3(august 2016), page 67-70
8. Ridker et al. Inflammation, atherosclerosis, ischemic episode exploring hidden side of the moon", NEJM 1997, Vol. 336: 1014.
9. Tillet WS, Francis T. Serological reactions in pneumoniae with a non-protein somatic fraction of pneumococcus. J. Exp. Med. 1930; 52: 561-571.
10. Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: Global burden of disease study. Lancet 1997; 349: 1269-1276.
11. Murray CJR, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global burden of disease study. Lancet 1997; 349: 1498-1504.
12. Kristensen B et al. Epidemiology and etiology of ischemic stroke in young adults aged 18-44 years in Northern Sweden. Stroke 1997; 28: 1702- 1709.
13. Tsong-Hai Lee et al. Etiologic study of young ischemic stroke in Taiwan. Stroke 2002; 33: 1950-1955.
14. Bousser MG. Stroke in women. Circulation 1999; 99: 463-467.
15. Bonita R. Epidemiology of stroke. Lancet 1992; 339: 342-344.
16. Jaume Roquer, Ana Rodriguez Campello, Meritxell Gomis. Sex differences in first-ever acute stroke. Stroke 2003; 34: 1581-1585.
17. Yumihiro Tanizaki et al. Incidence and risk factors of subtypes of cerebral infarction in a general population. The Hisayama Study. Stroke 2000; 31: 2616-2622.
18. Manson JE et al. A prospective study of maturity onset diabetes mellitus and risk of CHD and stroke in women. Arch. Intern Med 1991; 151: 1141- 7.
19. Gaby C, Kushner I. Acute phase proteins and other systemic responses of inflammation. N Engl J Med 1999; 340: 448-454.
20. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen C-RP, albumin or leukocyte count with coronary heart disease. JAMA 1998; 279: 1477-1482.
21. Wilson PWF. Metabolic risk factors for coronary heart disease. Current and future prospects. Curr Opin Cardiol 1999; 14: 176-185.
22. Ridker PM. Evaluating novel cardiovascular risk factors: Can we better predict heart attacks? Ann Intern Med 1999; 130: 933-937.
23. Kerstin Winbeck et al. Prognostic relevance of early serial C-reactive protein measurements after first ischemic stroke. Stroke 2002; 33: 2459-2464.
24. Mario Di Napoli, Francesca Papa. Inflammation, hemostatic markers and antithrombotic agents in relative to long-term risk of new cardiovascular events in first-ever ischemic stroke patients. Stroke 2002; 33: 1763-1771.
25. Montaner J et al. Correlation between the expression of proinflammatory Cytokines and matrix metalloproteinases in the acutephase of an ischemic stroke. Rev Neurol 2001; 33: 115-118.
26. Di Napoli M. Early inflammatory response in ischemic stroke. Thromb Res. 2001; 103: 261-264.
27. Mahapatra SC et al. C-reactive protein in thrombotic stroke. JAPI Dec 2002; 50: 1512.
28. Rathore HS et al. Role of C-reactive protein estimation in early diagnosis of cortical and lacunar infarct. JAPI Dec. 2002; 50: 1516.
29. Irene M et al. C-reactive protein predicts progression of atherosclerosis measured at various sites in the arterial tree. The Rotterdam Study. Stroke 2002; 33: 2750-2755.
30. L.Masotti et al. Prognostic role of C-reactive protein in very old patients with acute ischaemic stroke. Journal Of Internal Medicine 2005; 258: 145- 152.