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C-REACTIVE PROTEIN AND SERUM LIPID PROFILE IN ACUTE ISCHEMIC STROKE

General Medicine

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ABSTRACT

INTRODUCTION: Stroke is an episode of acute atraumatic infarction of brain, retina or spinal cord in a defined vascular distribution which may be due to arterial thrombosis, intracranial or subarachnoid hemorrhage or cerebral venous thrombosis. Inflammation and elevated plasma lipids leading to atherosclerosis have been implicated in the development of atherothrombotic stroke. The present study evaluates the acute phase reactant namely C-reactive protein and lipid levels in the patients suffering acute ischemic stroke and their correlation with patient outcome in hospital.

MATERIALS AND METHODS: 50 patients admitted within 72 hours of stroke symptom onset with CT evidence of first ischemic stroke were evaluated clinically, investigated for CRP levels and lipid profile and their outcome was recorded.

RESULTS: Our stroke patients had a mean age of 64.76 years with 34%females and 66%males. The risk factors noted were hypertension (60%), smoking (58%) and diabetes mellitus (26%).Common presentations included hemiparesis/plegia (72%), aphasia (28%), and cranial nerve involvement (26%).The mean CRP level was 6.034 mg/dl. In 78% of patients CRP level exceeded 0.6 mg/dl. The mean serum cholesterol was 179.02 mg/dl and a mean serum LDL-C level of 110.6 mg/dl. A CRP level >0.6 mg/dl was associated with higher mean serum cholesterol and LDL cholesterol levels. Patients with CRP >0.6 mg/dl and LDL-C more than116.7mg/dl had 7 fatalities out of 39 as compared to no fatalities in those with CRP <0.6 mg/dl and LDL-C <80.09 mg/dl.

CONCLUSION: A C-reactive protein level exceeding 0.6 mg/dl may be an important risk factor for ischemic stroke . A CRP level > 0.6mg/dl with LDL-C >116.7mg/dl was associated with poor outcome in ischemic stroke.

KEYWORDS:

C-reactive protein, Lipid profile, Ischemic stroke

INTRODUCTION

WHO defines stroke as "rapidly developing illness characterized by clinical symptoms and/or signs of focal or global disturbances of cerebral function with symptoms lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin"[1]

In 2013 AHA/ASA defined stroke as an episode of acute CNS infarction or ischemic cell death in brain, retina or spinal cord in a defined vascular distribution which is diagnosed on clinical, pathological or radiological grounds with symptoms lasting 24 hours or more or resulting in fatal outcome.[2] In Transient ischemic attack an acute episode of neurologic dysfunction typically lasts less than 24 hours and results from focal cerebral, spinal cord, or retinal ischemia, but is not associated with tissue infarction. The risk of stroke increases to11% in the next 7 days and 24-29% over the following five years after an episode of TIA.[3]

Every year 5 million persons die worldwide while 5 million are permanently disabled due to stroke.4 In India the reported incidence of stroke is 119-145/lakh population and the prevalence in rural and urban areas is 84-262/lakh and 334-424/lakh population respectively. 5 In 80-85% of cases strokes are ischemic due to the thrombosis of extra or intracranial arteries or due to cardioemboli in the cerebral circulation.Haemorrhagic stroke are due to hemorrhage in intracranial or subarachnoid vessels which is not due to trauma. Thrombosis of cerebral venous structures can also produce stroke. The risk factors predisposing to stroke include hypertension, diabetes mellitus, heart disease, smoking, male gender, African- American ancestry, heredity, advanced age, arteriovenous malformations, obesity, alcohol, cocaine and amphetamine use .Identification and management of risk factors may prevent strokes. The treatment of stroke includes antiplatelet agents, intravenous thrombolysis, endarterectomy and stenting of intracranial vessels as well as control of blood pressure and intracranial pressure. Stroke management is now an evolving field due to the development of new medical, surgical and endovascular treatment modalities aided by widely available imaging techniques.

Since cardiovascular disease and cerebrovascular disease have important risk factors like hypertension, diabetes and smoking in common atherosclerosis is believed to be involved in the genesis of stroke. An increasing body of evidence has linked inflammation and elevated plasma lipids with pathogenesis of atherothrombotic stroke. Infection and inflammation cause increased levels of leucocytes with production of cytokines, clotting factors and fibrinogen, as well as alteration of endothelial cell function and activation of monocytes and macrophages. These changes combined with elevated circulating plasma lipids promote atherosclerosis and thrombosis. Hence markers of inflammation and plasma lipids have been the focus of scientific interest in this scenario.

In 1930 Tillet and Francis observed that the serum of acutely ill patients caused precipitation of pneumococcal somatic C polysaccharide, thus behaving as a marker of acute inflammation. Named C-reactive protein, this factor disappeared soon after inflammation subsided and was absent in healthy individuals. C-reactive protein exerts a profound pro-inflammatory effect by activating the production of monocyte chemotactic protein-1 (MCP-1). Using MCP-1 activation as an assay, Edward T.H. Yeh, showed that both statins and fenofibrates can inhibit C - reactive protein induced MCP-1 induction, whereas acetylsalicylic acid cannot. Thus some of the anti atherosclerotic drugs may exert their effect through C - reactive protein axis.[6]

Lipids, a heterogeneous group of compounds related to fatty acids which circulate in plasma in the form of lipoproteins. The Framingham Heart Study7 ,Verschuren et al[8] and PROCAM 9 study categorically implicated raised serum cholesterol to be the principal risk factor in coronary artery disease (CAD) and established a direct relationship between a rise in serum cholesterol with increased risk of CAD. Serum triglycerides and LDL-cholesterol levels are also recognized as risk factors for coronary artery disease.(10,11) Almost all classes of lipoproteins that contain Apo B (VLDL, B-VLDL, LDL, Lp (a), and oxidized LDL) are considered to be atherogenic. Lipids play a role in

all three stages of atheroma development, viz. fatty streak, fibro fatty plaque, and advanced or complicated plaque. Thus hyperchol esterolemia is a well recognized risk factor for ischemic heart disease but a clear association of increased cholesterol levels with stroke has not been established,[12] with only nonembolic thrombotic strokes being correlated to hypercholesterolemia, while lacunar strokes, cardioembolic strokes and hemorrhagic strokes showing none or possibly negative correlation. Where thrombotic strokes were confirmed by angiography, a positive correlation was shown for total serum cholesterol, LDL-cholesterol and triglycerides and a negative correlation was found with HDL –C.[13] An Indian report studying young patients, where hyperlipidemia was found to be a significant risk factor for nonembolic ischemic stroke.14 Ridker et al reported that in case of cardiovascular disease LDL-C was minimally correlated with CRP levels. They also reported CRP was superior to LDL-C as a predictor of cardiovascular disease and that both CRP and LDL-C levels taken together predict cardiovascular disease better than either factor taken alone. They concluded that statin therapy may confer benefit in primary prevention for patients with low LDL-C due to its inhibitory effect on C-reactive protein induced inflammation.[15]

In the present study we have attempted to study the levels of C - reactive protein and lipid profile in patients of acute thrombotic stroke and to correlate them to patient outcome.

AIMS AND OBJECTIVES

1. Semi Quantitative calculation of C - reactive protein in CT proven patients of acute ischemic stroke.
2. Quantitative assessment of lipid profile in the same group.
3. Co -relating the CRP and lipid profiles with patient outcome in acute ischemic stroke.

METHODS

50 Patients of both sexes older than 18 years with a CT proven diagnosis of ischemic stroke who were admitted to Maharishi Markandeshwar Hospital Mullana, Ambala within 72 hours of onset of stroke symptoms were included in the study and subjected to a detailed history, physical examination and investigations including CRP and lipid profile estimation. Their outcome while in hospital was recorded. Patients suffering from acute infectious disease, angina pectoris, acute myocardial infarction, immunological or neoplastic disorders, recent trauma, surgery, burns, osteoarthritis, rheumatoid arthritis and Ankylosing Spondylosis were excluded from the study.

OBSERVATIONS AND RESULTS

In our study, out of 50 patients 16% were in age group 40-50 years, 26% were 51-60 years old, 24% were in age group 61-70 years whereas the 34% of patients were above 70 years of age. The mean age of our patients was 64.76 years (SD+/- 11). Out of 50 patients 34% were females and 66% were males. The most common presentation was hemiplegia/hemiparesis observed in 72%, whereas cranial nerve involved were observed in 26% and aphasia in 28% followed by vomiting, headache and altered sensorium.Seizure was not the presenting symptom in any patient. A history of TIA in the past was present in 52% of patients. Hypertension was the leading risk factor being present in 60% of our stroke patients followed by smoking (58%) and diabetes mellitus(36%).The mean CRP levels in our patients were 6.034 mg/dl (SD +/-5.21).A positive CRP level (>0.6 mg/dl)was seen in 78% of patients and in 22% it was below this level. The total serum cholesterol level was 179.2 mg/dl (SD +/-28.62) with only 20% cases having serum cholesterol >200mg/dl while in 80% patients it was <200mg/dl.The mean HDL –C level was 43.42mg/dl (SD+/- 4.11).The mean serum Triglyceride level was 143.31 mg/dl (SD +/- 46.93) .The mean LDL-C level in our patients was 110.6 mg/dl (SD+/- 31.14) with LDL-C being more than 100 mg/dl in 72% of patients and <100 mg/dl in 28%. In patients who had CRP levels >0.6 mg/dl the mean serum cholesterol level was 183 mg/dl (SD +/- 29.7) and those who had CRP negative the mean serum cholesterol was 164.7 mg/dl (SD+/- 17.6).CRP positive patients also had a mean LDL-C level of 116.7 mg/dl whereas those who were CRP negative had mean LDL-C of 80.09 mg/dl.There was no significant difference in VLDL-C levels between CRP positive and negative patients. Among those 39 patients in whom CRP was positive and mean LDL-C level was >116.7 mg/dl, there were 7 fatalities while 29 survived and 3 left. In patients with CRP level below 0.6 mg/dl and mean LDL-C below 80.09 mg/dl all 11 patients survived.

DISCUSSION

The present study was a hospital based prospective study on CRP levels and Lipid profile in patients suffering from acute ischemic stroke and their impact on the in- hospital outcome. In our study the mean age of the patients was 64.years(SD +/-11.5) as compared to 58.1 years reported by Curb et al16, 65.3 years by Agarwal et al17 and 69.7 years by Rost et al.18 Hypertension was the risk factor identified in 60% of our patients as compared to 27% of patients reported by Curb et al. Diabetes mellitus was identified in 36% of our patients as compared to 27% by Curb et al and 9.5% by Rost et al.58% of our patients were smokers as compared 54.4% in those of Curb et al and 22.7% reported by Rost et al.The mean CRP levels were 6.034 mg/dl as compared to 5.8 mg/dl reported by Rost et al, 14.3 mg/dl by Curb et al and 25.0mg/dl by Agarwal et al. CRP levels of > 0.6 mg/dl was present in 78% in our study and raised in 80% of those studied by Mahapatra et al19 and 77.7% of those studied by Dhamija et al.20 The mean serum cholesterol was 179.2 mg/dl in our study and it was 72.mg/dl Garg et al21 ,222mg/dl in that of Curb et al and 232 mg/dl in that of Hachinski22. The mean LDL-C level was 110.6 mg/dl while Curb et al reported a value of 106.02mg/dl. The mean serum HDL-C levels in our patients were 43.42 mg/dl and were comparable to those reported by Garg et al and Hachinski et al which were 35.57 mg/dl and 41.0 mg/dl respectively. Serum triglycerides were 110.63 mg/dl in our study and compared well with 106.02 mg/dl reported by Garg et al. Additionally in our study patients with CRP >0.6 mg/dl and LDL-C >116.7 mg/dl there were 7 fatalities out of 39 cases as compared to no fatalities in 11 patients with CRP levels below 0.6 mg/dl and LDL-C below 80.09 mg/dl.

CONCLUSION

C - reactive protein exceeding 0.6mg/dl was found to be associated with increased the risk for acute thrombotic stroke. More than 50 % of the patients suffering from acute ischemic stroke who had CRP> 0.6 mg/dl also had LDL-C more than 100 mg/dl. There appears to be no significant correlation between other lipid parameters (serum total cholesterol levels HDL, triglycerides, VLDL) with C-reactive protein level. A CRP level > 0.6 mg/dl along with LDL-C > 116.7 mg/dl appears to be associated with poor prognosis in acute thrombotic stroke. Measures to reduce both LDL and CRP levels will probably help in a significant way in stroke prevention. Further studies in larger sample size are required to prove the role of CRP as a prognostic marker in acute ischemic stroke.

TABLES

TABLE 1: Age Distribution

Age (years)	No. of cases	Percent
40-50	8	16.0
51-60	13	26.0
61-70	12	24.0
>70	17	34.0
TOTAL	50	100.0

Table 2: Showing Symptom Analysis

Symptoms of Strokes	Present	Absent
Hemiplegia	36 (72%)	14 (28%)
Aphasia	14 (28%)	36 (72%)
Cranial nerve palsy	26 (52%)	24 (48%)
Vomiting	6 (12%)	44 (88%)
Headache	3 (6%)	47 (94%)
Altered sensorium	3 (6%)	47 (94%)

Table no 3: Risk Factors of stroke

Risk Factor	No. of Cases (%)	
	Present	Absent
Diabetes Mellitus	18 (36%)	32 (64%)
Hypertension	30 (60%)	20 (40%)
Smoking	29 (58%)	21 (42%)

Table 4: Showing C - reactive protein distribution among cases

	No. of cases	Percentage
C-Reactive Protein		
> 0.6 mg/dl	39	78%
< 0.6 mg/dl	11	22%

Table 5: Showing distribution of total cholesterol as > 200 mg/dl and < 200 mg/dl (ATP-III guidelines)

Group	Total cholesterol (mg/dl)	No. of cases	Percentage
Cases	> 200	10	20%
	< 200	40	80%

Table 6: Showing distribution of LDL values (mg/dl)

Group	LDL (mg/dl)	No. of cases	Percentage
Cases	> 100	36	72%
	< 100	14	28%

Table 7: Showing correlation of mean total cholesterol levels with serum C - reactive protein levels

	Total cholesterol (mg/dl)		
C –Reactive Protein			Number of Cases
(mg/dl)	Mean	SD	
(> 0.6 mg /dl)	183	29.7	39
(< 0.6 mg/dl)	164.7	17.6	11

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