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A STUDY ON PREVALENCE OF ELEVATED HsCRP IN ACUTE VASCULAR EVENTS

General Medicine

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ABSTRACT

The Acute vascular events remain an important health problem and merits continued attention from clinical researchers, epidemiologists and practising physicians. The role of inflammation pathogenesis of atherosclerosis has been firmly established in past two decades. High sensitive CRP is a sensitive marker of inflammation and tissue injury in arterial wall. In clinical studies, circulating hsCRP has been bound to correlate with prognosis of acute vascular events.

AIMS AND OBJECTIVES : To determine prevalence of elevated hsCRP in Acute Vascular events and to determine its role in morbidity and mortality.

METHODOLOGY:STUDY SAMPLE : 50 CASES STUDIED DURING MARCH 2018 TO AUGUST 2018

INCLUSION CRITERIA: Age more than 15 years and less than 60,Acute myocardial infarction, Ischemic stroke, Unstable angina.

EXCLUSION CRITERIA: Age less than 15 and more than 60 years ,Smoking,Alcoholism,Patient with previous attacks ,Other inflammatory conditions,Immunosuppresant therapy.

METHODS : Clinical history, complete clinical examination, investigations.

OBSERVATION AND RESULTS:

CONCLUSION: There is Very high prevalenc of elevated hsCRP among patients with acute vascular events.

KEYWORDS

hsCRP (high sensitivity C Reactive Protein), Atherosclerosis

INTRODUCTION :

Atherosclerosis possess a fundamental chronic inflammatory aspect, and the involvement of numerous inflammatory molecules has been studied in this scenario, particularly C-reactive protein (CRP).

In view of epidemiologic evidence associating high CRP levels with cardiovascular risk, measurement of serum levels of high-sensitivity CRP has been proposed as a tool for assessment of cardiovascular risk.

The Third Report of the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (ATP III)[1] categorizes cardiovascular risk factors as (a)non modifiable, such as age, gender, and ethnicity; (b)modifiable, including Diabetes mellitus, Hypertension, Dyslipidemia, and Smoking; and (c) emerging risk factors, encompassing triglycerides[2], homocysteine[3], and various inflammatory markers. CRP an acute phase reactant, remains the most studied molecule.

C - reactive protein Structure and Metabolism:

CRP was first described in 1930 by Tillet and Francis, named after its ability to precipitate and interact with phosphorylcholine residues of the C polysaccharide derived from teichoic acid within the cellular wall of *Streptococcus pneumoniae*, as well as its ability to precipitate with calcium ions[4]. CRP is associated with various chronic inflammatory processes, such as certain rheumatologic conditions, cancer, and CVD[5].

C-reactive protein is predominantly synthesized in the liver (1q23.2)[6], typically within the transcriptional phase of the response to pro-inflammatory cytokines. IL-6 appears to be the main regulator, by promoting de *novo* synthesis of CRP via up regulation of C/EBPβ and C/EBP , key transcription factors in this process[7]. In addition, IL-6 signalling may be reinforced by IL-1β and TNFα, both of which increase transcription rate of CRP [8]. CRP has been shown to be expressed in adipocytes in response to pro-inflammatory mediators, representing yet another link between obesity and chronic inflammation[9].

Following synthesis and release into circulation, serum CRP levels tend to increase significantly 6–8 hours after initial stimulation, peaking at 24–48 hours, with a half-life of approximately 19 hours. CRP concentration in circulation is determined by its synthesis rate[10].

C - reactive protein: From Pentameric to Monomeric:

CRP has been described to adopt two different conformational forms: the native pentameric isoform (pCRP) and the monomeric isoform (mCRP)[11], which possess distinct antigenic, electrophoretic, and biological features[12]. pCRP is the main form detected in serum [13] and is a very stable molecule, there is evidence pCRP can be dissociated, both in vitro and in vivo, into individual mCRP units.

In vivo generation of mCRP : by local expression of mCRP mRNA in various extra hepatic tissue like adipocytes, smooth muscle cells, and inflammatory cells within atheromatous plaques and by local dissociation of pCRP into mCRP has been observed in atherosclerotic plaques [14].

CRP actively participates in atherogenesis by directly influencing processes such as activation of the complement system, apoptosis, vascular cell activation, monocyte recruitment, lipid accumulation, and thrombosis. pCRP can generate inflammatory responses binding to the Phosphatidylcholine on the exterior of LDL- ox and the surface of apoptotic cells[15], while mCRP is able to modulate platelet function inducing aggregation and contributes to athero-thrombosis.

The American Heart Association and the Centers for Disease Control and Prevention issued guidelines in 2003 for the use of hsCRP in clinical practice[16].

Briefly, the vascular risk as per hsCRP level is classified as:

1) **LOW RISK - <1mg/L**
2) **INTERMEDIATE RISK - 1 - 3mg/L**
3) **HIGH RISK - > 3 mg/L**

Respectively, when considered along with traditional markers of risk. This critical finding has corroborated studies conducted worldwide; all studies of adequate sample size have found the risk of hsCRP to be independent of and additive to traditional risk factors [17-22].

Values of hsCRP in excess of 8 mg/L may represent an acute-phase response caused by an underlying inflammatory disease or intercurrent infection and should lead to repeat testing in approximately 2 to 3 weeks; consistently high values, however, represent very high risk of future cardiovascular disease[23]. Because hsCRP levels are stable over long periods, have no circadian variation, and do not depend on prandial state, screening can easily be done on an outpatient basis at the time of cholesterol evaluation.

hsCRP has prognostic usefulness in cases of acute ischemia, even without troponin level elevation, suggesting that an enhanced inflammatory response at the time of hospital admission can determine subsequent plaque rupture[24].These findings help explain why individuals with elevated hsCRP levels are also more likely to benefit

from aggressive interventions compared with those with low hsCRP levels.

AIMS AND OBJECTIVE :

1. To determine the prevalence of elevated hsCRP in 50 patients with acute vascular events.
2. To compare with 50 controls of non vascular acute event.
3. To determine role of hsCRP in determining the morbidity and mortality.
4. To analyze the levels of hsCRP in patient without any other specific CVS risk factors.

MATERIALS AND METHODS

STUDY POPULATION

A 50 cases were selected for the study, who attended the in patient clinics satisfied all the inclusion and exclusion criteria and who were admitted in the Department of Internal Medicine and Department of Cardiology, Guntur Governament Hospital. With consent obtained.

Age and sex matched controls (50) were also studied for comparison and meaningful interpretation of data. The controls were recruited from other acute cases that were recruited from the wards.

METHODS

Detailed clinical history was taken from each patients and a complete review of their case notes performed. A complete clinical examination of the nervous system and cardiovascular system was done for each patient.

LABORATORY METHODS :

To all selected patients, following investigations were done**.**

ECG
ECHO
CPK MB
CT BRAIN
FBS
FLP
HsCRP

Other relevant investigations were done

hsCRP was measured after admission in hospital within 1st 24hrs hsCRP were estimated by VITROS 5.1 chemistry system and VITROS 5600 integrated system to quantitatively measure CRP in human serum or plasma. As per the normative data from VITROS 5600 system, manual and current literature, the cardiovascular risk was determined. For our study we considered hsCRP level of ≥ 3 mg/L as high risk

INCLUSION CRITERIA

FOR CASES

1. Age more than 15 years and less than 60
2. Acute myocardial infarction : Evidenced by ECG, elevated CK MB, or ECHO
3. Ischemic stroke : Evidenced by Two CT BRAIN taken at least 3 days gap showing signs of ischemia
4. Unstable angina : Evidenced by ECG or elevated CK MB

FOR CONTROLS

1. Age more than 15 less than 60 years.
2. Presence of any illness
3. Event should be acute
4. No cardiovascular risk factors

EXCLUSION CRITERIA

1. Age less than 15 and more than 60 years
2. Smoking
3. Alcoholism
4. Patient with previous attacks
5. Other inflammatory conditions

a. SLE
b. Scleroderma
c. Rheumatoid arthritis
d. Other Connective Tissue Disorders

6. Immunosuppresant therapy

OBSERVATIONS AND RESULTS

In our study of 50 patients were selected as cases and 50 patients as controls selected to analyzed the following:

1. To determine the prevalence of elevated hsCRP patients with acute vascular events
2. To compare with 50 controls of non vascular acute event.
3. To determine role of hsCRP in determining the morbidity and mortality
4. To analyse the levels in patient without any other specific CVS risk factors

When we divide and analyze as follows

i) With risk factors and elevated hsCRP
ii) Without risk factors only elevated hsCRP
iii) Controls.

OBSERVATIONS ARE AS FOLLOWS

TABLE 1: BASELINE CHARACTERS

Sl.No	Baseline features	cases	Control
1	Male	34	25
2	Female	16	25
3	Family History	18	0
4	Hypertension	29	0
5	Diabetes mellitus	26	0
6	LDL>100	25	0
7	HDL<50 for Female <40 for Male	20	0
8	TGL	20	0
9	FBS	26	0
10	2D ECHO	35	0
11	CT Brain	15	0
12	CKMB	35	0
13	Death	5	1

Table 2: CONTROLS

No. of patients	Diseases
15	Fever
5	LRI
10	Trauma
4	Post operative
8	DKA
2	Acute abdomen
2	Pancreatitis
4	UTI

TABLE 3: AVERAGE ELEVATED CRP

Normal	Total Cases	Cases without risk factors	Cases with risk factors	Control
<0.3	2.217	1.84	2.37	1.46

TABLE 4: CLASSWISE DISTRIBUTION WITHOUT RISK FACTORS

Type of disease	Low	Intermediate	High
Myocardial Infarction	0	2	0
Unstable Angina	4	6	0
Stroke	2	1	0

TABLE 5: CLASS WISE DISTRIBUTION FOR ALL CASES

Type of diseases	Low	Intermediate	High	Total
Myocardial infarction	1	14	2	17
Unstable angina	5	13	0	18
Stroke	9	5	1	15

TABLE 6: MORTALITY AND ASSOCIATED RISK FACTORS

Type	No. of patients
Death	5
Hypertension	3
Diabetes mellitus	3
Hyperlipidemia	4

CONCLUSION :

High sensitive CRP is a new method which determines lower levels. We used the hsCRP method this study and showed significant differences in the CRP level between patients and controls. The mean serum levels of hsCRP to be significantly higher in patients.

IN OUR STUDY ,

- most of the cases were between age 40 and 60 years ,we had found that mean age of cases is 51.4years ,with male predominance and, Sex distribution is male 34(68%), female 16(32%).
- 35(70%) cases have underlying risk factors, 15(30%) patients have no risk factors. 18(36%) cases have family history of vascular

events, 29(58%) with Hypertension, 26(52%) with Diabetes, 25(50%) with LDL>100, 20(40%) with HDL<50 in females<40 in males and 20(40%) with TGL>150. Hypertension, followed by Diabetes is major risk factor associated with elevated hsCRP.

- There is an elevated level of hsCRP seen in 46(92%) cases normal levels in 4 cases and in controls elevated hsCRP found in 43(89%) and 7 cases normal value. The average elevated level of CRP in cases with risk factors and without risk factors are significantly above level of controls.
- The average elevated hsCRP in total cases is 2.217mg/l, in cases with risk factors 2.37mg/l, in cases without risk factors 1.84mg/l, and for controls 1.46mg/l. In our study, the average elevated hsCRP is more for cases with risk factors than without risk factors, elevation of hsCRP parallel to conventional risk factors.
- 50 cases are taken, among them MI cases are 17(34%) and unstable angina 18(36%) and ischemic stroke 15(30%). Overall more number of cardiovascular cases are studied. In 17(34%) MI cases, 14 cases have intermediate risk levels of hsCRP i.e, 1 to 3mg/dl, 2 cases have high risk levels, 1 case have low risk levels of hsCRP.
- In 18(36%) unstable angina cases, 13 cases have intermediate risk levels of hsCRP, 5 cases have low risk levels.
- In 15(30%) of stroke cases, 9 cases have low risk level of hsCRP, 5 cases intermediate risk level and 1 low risk level.
- From the above analysis it is observed that intermediate risk levels of hsCRP more associated with cases in MI & Unstable angina.
- hsCRP levels in ischaemic stroke more on low risk level side and elevation of hsCRP more in cardiovascular cases than stroke cases. And hsCRP have association with cardiovascular events than stroke.
- Regarding the distribution of cases without risk factors, 2 MI cases, 10 unstable angina, 3 ischemic stroke, total 15 cases.
- All MI have intermediate risk levels of hsCRP, in unstable angina 6 cases intermediate risk and 4 cases low risk levels of hsCRP. In ischaemic stroke 2 with low risk hsCRP levels, 1 with intermediate risk level. In total, among cases without risk factors, 9 with intermediate risk value i.e., CRP between 1 and 3mg/l. 6 cases are with low risk value.
- From the above analysis it is clearly shows that the cases without risk factors also have elevated hsCRP and elevated hsCRP is associated with MI and stroke.
- Regarding the distribution of cases over all, 32(64%) cases are in intermediate risk group, 15(30%) cases are with low risk group and 3 patients are in high risk group. Most of cases fall in intermediate risk value group and clearly show the hsCRP association with the vascular events.
- Regarding the mortality, total death in our study 5, 3 deaths in MI, 1 death each in unstable angina and ischaemic stroke. Most of the patients who were died i.e. 3(9.3%) in number belong to intermediate (32 cases) risk group, 1 (6.6%) with low risk(15 cases) and 1(33%) with high risk(3 cases).
- Most of deaths in cases occurred in intermediate risk. On comparing the mortality in patients with various risk factors, hyperlipidemia plays a major role i.e. Nearly 4 of the 5 deaths. Hypertension and diabetes are second most leading comorbid condition.

LIMITATIONS :

hsCRP increase occurs during times of infection, trauma ,systemic inflammatory, post infarct conditions thus may limit clinical utility.

CONCLUSION

In our study it is clearly shown that most of patient selected had:

1) Very high prevalence (92%) of elevated hsCRP among patients with acute vascular events.
2) Level of elevated hsCRP More in vascular events than compared to non vascular events
3) Elevated hsCRP is no Role in mortality and morbidity vascular events
4) A high prevalence (93.3) of elevated HsCRP patients with acute vascular events without risk factors.

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