

**A STUDY OF HIGH SENSITIVITY C-REACTIVE PROTEIN IN UNSTABLE ANGINA**Satish Kinagi<sup>1</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: BACKGROUND:** Unstable angina has a wide variability in its natural history, changing concepts of Pathophysiology, and newer approaches to its management strategies. So, unstable angina still has importance and prime interest in research work. Various ongoing research works has provided newer insights in pathophysiology of unstable angina syndrome and helps in recognition of clinical variability and unpredictability of it. C - reactive protein being the most sensitive acute phase reactant currently held. A recent previous study has estimated the levels and values of high-sensitivity C - reactive protein in both stable and unstable angina pectoris. Data provided by the study indicated need for further studies in this field. With all these facts, the present study is carried out to estimated Hs CRP levels as a marker of inflammation in patient of unstable angina. **AIMS AND OBJECTIVES:** The present study was carried out with the following Aims and Objectives. To estimate Hs-CRP levels as a marker of inflammation in patients of unstable angina. To compare Hs-CRP levels in cases of unstable angina, with Hs-CRP levels in patients of stable angina and in healthy age and sex matched controls. **MATERIAL AND METHODS:** This study was carried out at Basaveshwar Teaching and General Hospital, Gulbarga, MRMC Gulbarga. Approximate duration of study was 1 ½ year from June-2008 to November, 2010. **OBSERVATION:** Following are the conclusions drawn from the present study.

1. There were no statistically significant difference in age and sex distribution among three groups (UA, SA and normal control).
2. There were no significant difference in distribution of risk factors for ischemic heart disease present among UA (Gp A) and SA (Gp B).
3. The circulating level of TLC was significantly higher in patients of UA (Gp A) and SA (Gp B) than normal control (Gp C), but there was no significant difference in circulating levels of TLC between UA (Gp A) and SA (Gp B).
4. The circulating level of inflammatory marker HsCRP was significantly increased in patients of UA (Gp A) during attack of UA.
5. Comparison of HsCRP between three groups showed that levels of HsCRP was significantly higher in patients with UA (Gp A) than in either SA (Gp B) or control (Gp C). (P=0.000).
6. The circulating levels of HsCRP did not differ significantly between the SA (Gp B) and normal control (Gp C). (P=1.000)
7. The circulating levels of TLC did not significantly differ among subgroups of UA (UA Class I and UA Class II & III) and SA patients.
8. The circulating levels of HsCRP did not differ significantly between subgroups of UA i.e. in Class I UA and Class II and III UA, but HsCRP were significantly higher in both subgroups of UA than SA patients.

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In present study, the circulating elevated level of HsCRP was strongly associated with the clinical setting of Unstable Angina.

**KEYWORDS:** ACS, AMI, CAD, CRP, DM, HTN, HSCR, MI, NSTEMI, NQMI, STEMI, UA.

**INTRODUCTION:** The unstable anginal state, once expressed clinically may culminate in myocardial infarction or in sudden death or it may be turned to stable angina in few months. Prediction of outcome of any clinical episode of unstable angina has been extremely difficult.

The exact precipitating events at the atherosclerotic plaque of a patient with coronary artery disease, responsible for the attack of unstable angina, yet not fully defined. For better understanding of the pathophysiologic events occurring at the atherosclerotic plaque, various recent research works is continuing round the world.<sup>1</sup> Till date, various postulations for the precipitating events at the plaque site have appeared in the literature. Of them, only a few are well supported by various studies and currently accepted to have etiopathologic relations with precipitation of unstable anginal attack.

The role of inflammation at plaque site has been suggested by many workers.<sup>2-5</sup> According to Christopher P. Cannon and Braunwald, inflammation can play a major role in causing plaque instability.

C-reactive protein being the most sensitive acute phase reactant currently held. A recent study has estimated the levels and values of high-sensitivity C-reactive protein in both stable and unstable angina pectoris.<sup>5</sup>

Data provided by the study indicated need for further studies in this field. With all these facts, the present study is carried out to estimate HsCRP levels as a marker of inflammation in patient of unstable angina.

### **OBJECTIVES:**

**The present study was carried out with the following Objectives:**

1. To estimate Hs-CRP levels as a market of inflammation in patients of unstable angina.
2. To compare Hs-CRP levels in case of unstable angina, with Hs-CRP levels in patients of stable angina and in healthy age and sex matched controls.

**MATERIALS AND METHODS:** This study was carried out at Basaveshwar Teaching & General Hospital, attached to M. R. Medical College, Gulbarga during the period from 2008 to 2010.

**Selection Criteria:** Cases of unstable angina were taken for the study from patients admitted to ICCU or medical wards of Basaveshwar Teaching & General Hospital, Gulbarga with chest pain suggestive of angina.

### **Inclusion Criteria**

1. Angina occurring at rest (or with minimal exertion) and usually lasting more than 20 minutes (if not interrupted by nitroglycerine).
2. New onset angina, being severe and described as frank pain i.e., within 1 month.
3. Occurring with a crescendo pattern i.e., more severe, prolonged or frequent than previously.

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Any of these three criteria, singly or in combination were to be satisfied along with both of the following:

1. Presence of ST depression and/ or transient ST segment elevation and/ or T-wave inversion in ECG (ST segment depression  $\geq 1$  mm in one or more leads, with ST remaining horizontal or down sloping for  $\mu 0.08$  sec, symmetrical 'T' inversion  $\rho 5$  mm).
2. Absence of baseline evidence of myocardial infarction (New Q-wave or persistent ST elevation in ECG; three fold rise in levels of cardiac enzymes – CPKMB, SGOT, LDH).

### Exclusion Criteria:

1. Patient not willing to enroll in study.
2. Recent history of surgery or trauma within the preceding 2 months.
3. Renal insufficiency (creatinine  $>1.5$  mg/ dL).
4. Malignancy.
5. Liver cirrhosis.
6. History of recent infection.
7. History of acute myocardial infarction onset of  $<3$  months.

**HsCRP:** HsCRP (mg/dL) were measured by fully automated nephelometry-BN 100 technology by Dade Behring, Germany in all groups.

For estimation of HsCRP 2 ml of fasting blood will be collected by venupuncture in a sterile plain bulb and immediately send to collection centre of Thyrocare Laboratory, Mumbai.

**Normal ranges:** Adult is  $<0.30$  mg/dL.

### Risk of coronary heart disease:

0.01 – 0.07	Low.
0.07 – 0.11	Low risk (mild).
0.12-0.19	Moderate risk.
0.20 – 0.38	High risk.
$>0.38$	Highest risk.

All the clinical and investigational data will be entered in the proforma as given.

**OBSERVATIONS:** This study entitled “A Study of High Sensitivity C-Reactive Protein in Unstable Angina” was carried out at Basaveshwar Teaching & General Hospital, attached to M.R.Medical College, Gulbarga during the period from 2008 to 2010, which included a total of 150 subjects. Out of which, 50 were cases of unstable angina (Group-A); 50 were cases of stable angina (Group-B); and 50 were healthy controls (Group-C) selected after age and sex matching with the cases of UA Group-A constituted cases, subjects with SA (Group-B) and healthy controls (Group-C) constituted comparison group.

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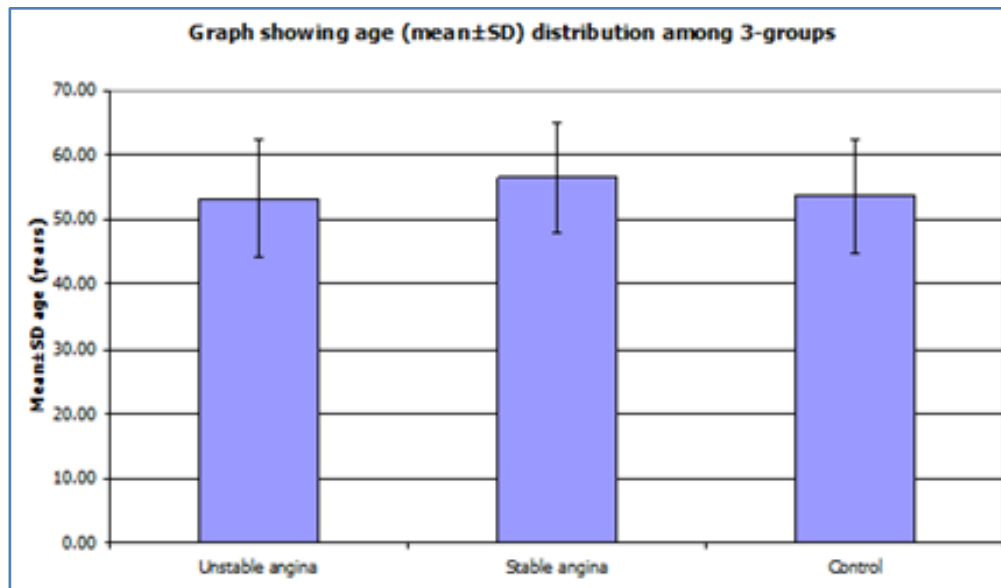
The following were the observations:

Group	Mean±SD Age (Years)	p-value
Unstable angina (group-A) (n=50)	53.36±9.11	0.1506
Stable angina (group-B) (n=50)	56.48±8.49	
Control (group-C)	53.64±8.83	

**Table 1: Age distribution among three groups**

Values are given as mean value±SD

In UA (Group-A) mean age was 53.36±9.11; in SA (group-B) mean age was 56.48±8.49; in control (group-C) mean age was 53.64±8.83. There were no significant difference in age distribution among three groups (p=0.1506).

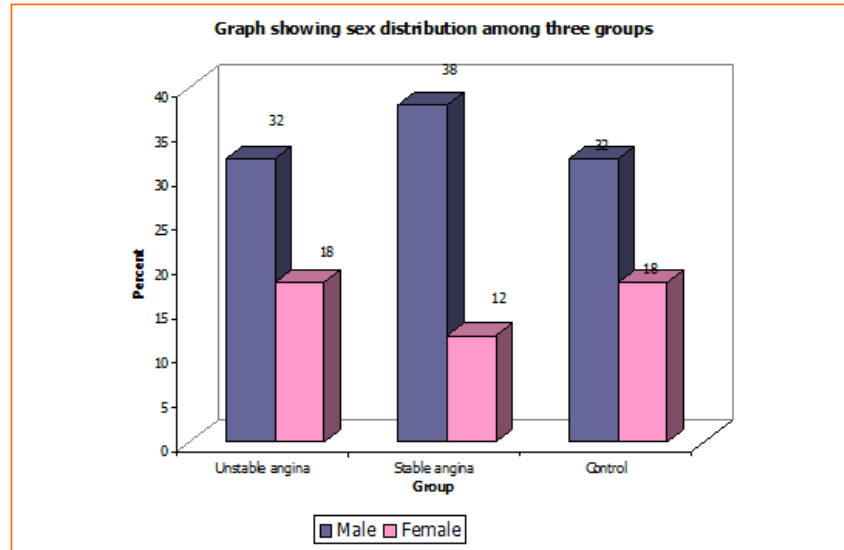


Sex	UA (Group-A) (n=50)	SA (Group-B) (n=50)	Control (Group-C) (n=50)	p-value
Male	32 (64%)	38 (76%)	32 (64%)	0.332
Female	18 (36%)	12 (24%)	18 (36%)	
<b>Total</b>	<b>50 (100%)</b>	<b>50 (100%)</b>	<b>50 (100%)</b>	

**Table 2: Sex Distribution among three groups**

There were total 32 (64%) male cases and 18 (36%) female cases in UA (group-A), 38 (76%) male and 12 (24%) female in SA (group-B) and in control (group-C) male and females were same as in UA (group-A). There were no significant difference in sex distribution among 3-groups (p=0.332).

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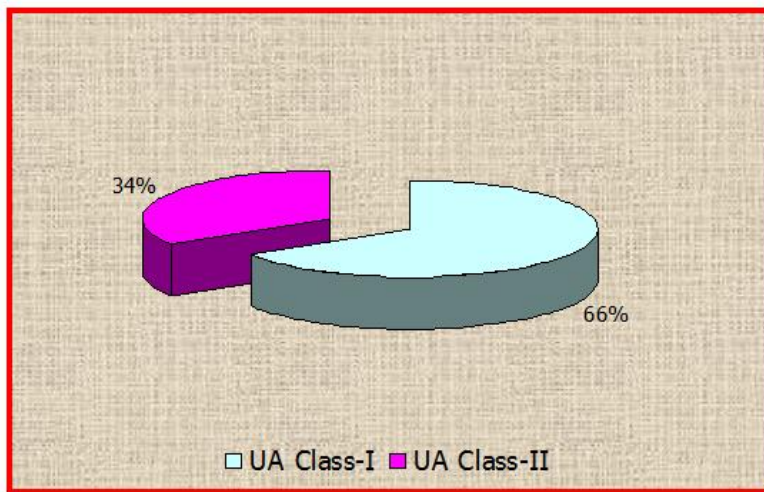


Out of 50 cases of UA, 33 (66%) had class-I angina i.e., angina with no rest pain and 17 (34%) had class-II and class-III angina i.e., angina at rest.

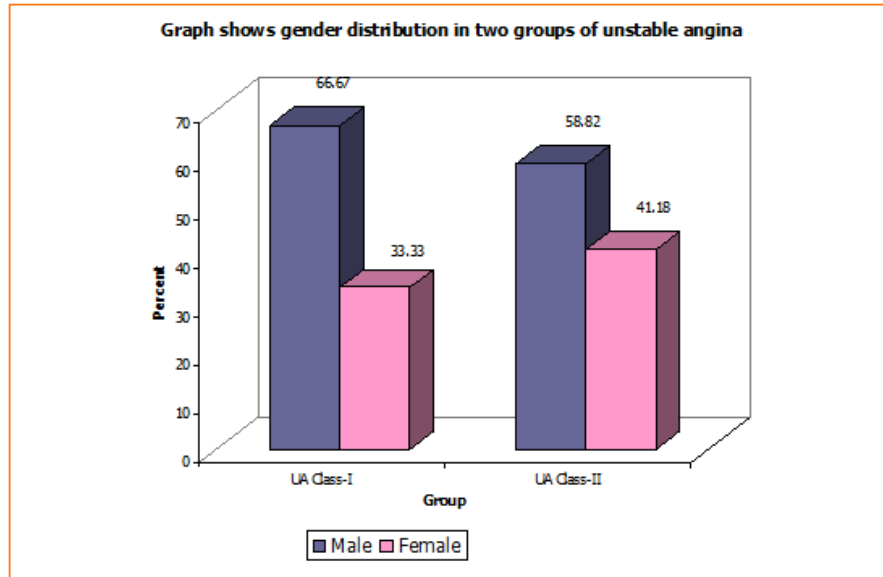
Sex	UA Class-I (n=33)	UA Class-II & III (n=17)
Male	22 (66.67%)	10 (58.82%)
Female	11 (33.33%)	7 (41.18%)
Total	33 (100%)	17 (100%)

**Table 3: Gender distribution in two-groups of unstable angina**

In UA Class-I, out of 33 there were 22 (66.67%) male and 11 (33.33%) female cases. In UA Class-II and III, out of 17 there were 10 (58.82%) male and 7 (41.18%) female cases.



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**Values and comparison of circulating levels of inflammatory marker. TLC and HsCRP among cases and control.**

**i) TLC**

Variable	UA (Group-A) (n=50)	SA (Group-B) (n=50)	Control (Group-C) (n=50)	p-value
TLC (count/mm <sup>3</sup> )	7178±844.74	6832±1020.89	5162±602	0.000

**Table 4: TLC Values among 3-groups**

Values given are mean±SD

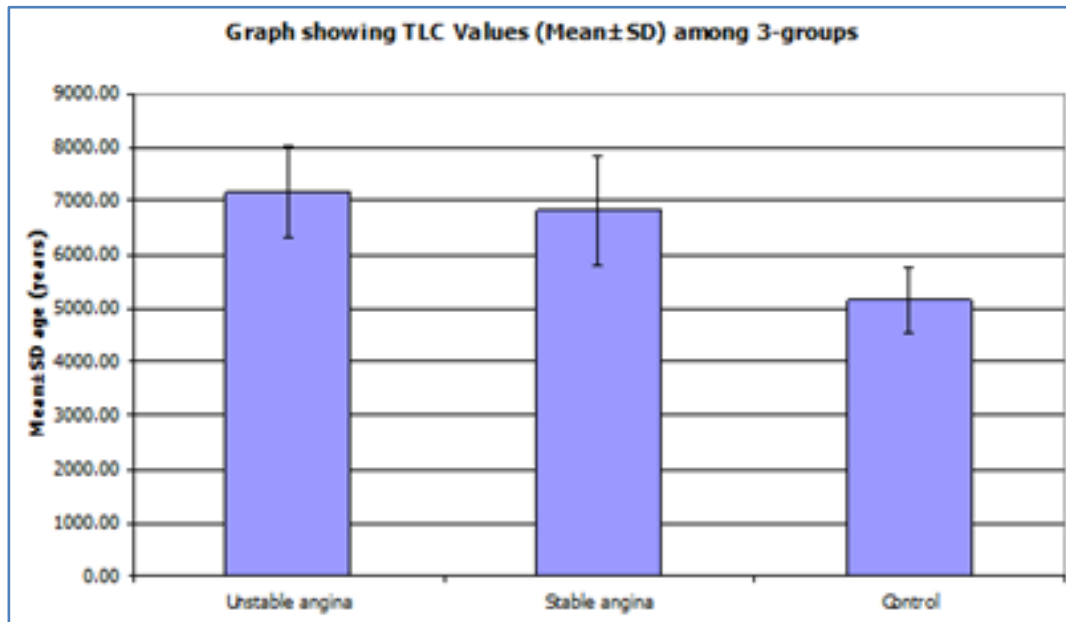
TLC (Mean±SD) among UA (group-A) was 7178±844.74; in SA (group-B) was 6832±1020.89; and in control (group-C) was 5162±602.00

Comparison groups	P value	Significant/ non-significant
UA (Group-A) Vs Control (Group-C)	0.000	Significant
UA (Group-A) Vs SA (Group-B)	0.124	Non-significant
SA (Group-B) Vs Control (Group-C)	0.000	Significant

**Table 5: Comparison of TLC among 3-groups**

Both the unstable angina (group-A) and stable angina (group-B) patients had significantly higher circulating levels of TLC than normal control (Group-C) subjects. However, there was no significant difference in the circulating levels of TLC between unstable (Group-A) and stable angina (Group-B) patients.

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### ii) HsCRP

Variable	UA (Group-A) (n=50)	SA (Group-B) (n=50)	Control (Group-C) (n=50)	p-value
HsCRP (mg/dl)	0.95±0.70	0.22±0.11	0.18±0.09	0.000

**Table 6: HsCRP Values among three groups**

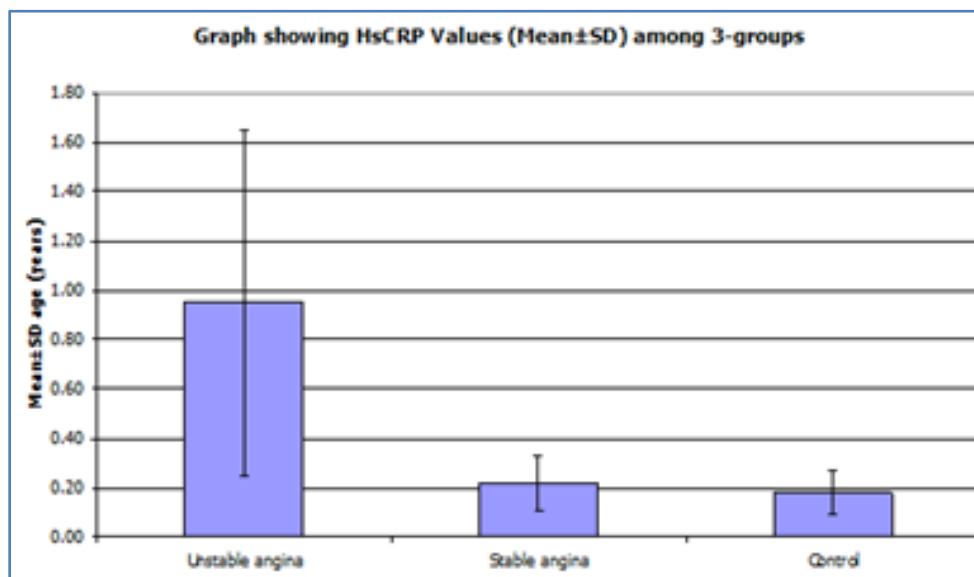
Values are mean±SD

HsCRP (mean±SD) in patients UA (Group-A) was 0.95±0.70; in SA (group-B) was 0.22±0.11 and in control (group-C) was 0.18±0.09.

Comparison groups	P value	Significant/ non-significant
UA (Group-A) Vs Control (Group-C)	0.000	Significant
UA (Group-A) Vs SA (Group-B)	0.000	Significant
SA (Group-B) Vs Control (Group-C)	1.000	Non-significant

**Table 7: Comparison of HsCRP among three groups**

The circulating levels of HsCRP was significantly higher in patients with UA (group-A) than in either SA (group-B) or normal control (group-C). The circulating levels of HsCRP did not differ significantly between the stable angina (group-A) and normal control (group-C) subject.



**iii) Values of inflammatory marker among patients with SA (group-B) and sub-groups of UA (UA class-I and UA class-II & III):** To test whether the two inflammatory markers differed between patients with UA Class-II and III, and patients with both UA class-I and stable angina (group-B), we further analyzed three groups of patients.

**DISCUSSION:** Cardiovascular disease will be the leading underlying cause of death in India by 2010. Social and lifestyle changes are responsible for the increased atherosclerotic coronary artery disease.

Management approaches to unstable angina syndromes have witnessed major changes over past two decades as our understanding of pathophysiology is being more definable with ongoing research.

Coronary atherosclerosis being the common root cause, many studies have been conducted to know any difference in severity and distribution of atherosclerotic lesions in coronary arteries from patients with stable and unstable angina.

Inflammation at the plaque site, triggering changes at the lesion, has been suggested by many workers to be responsible for the clinical episodes of unstable angina.

In a clinical setting, recently many studies<sup>5</sup> has been carried out to document inflammation during episodes of unstable angina. They measured a various markers of acute inflammation in unstable angina patients like WBC, ESR, fibrinogen, VCAM-I, Sr. Amyloid A protein and specially C-reactive protein and many of them consistently showed that C-reactive protein was significantly increased in patients with AMI and unstable angina patients.

Few of them showed that HsCRP were independently associated with clinical setting of unstable angina patients, few of them also suggested its prognostic value in severe unstable angina patients.

**SUMMARY:** Many research works suggest that inflammation plays an important pathogenic role in the initiation and progression of atherosclerotic plaque lesions. Still the reasons for uncertainty in otherwise predictable atherosclerotic plaques are yet to be fully revealed.



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The present study entitled “A Study of High Sensitivity C-reactive Proteins (HsCRP) in Unstable Angina Pectoris” was carried out in the Department of Medicine, M. R. Medical College and Basaveshwar Teaching & General Hospital, Gulbarga from June 2008 to November 2010. In the study, levels and values of an acute phase reactant HsCRP were estimated in patients of unstable angina, stable angina and healthy age and sex matched controls.

The study included total 150 subjects, there were 50 cases of unstable angina (Group-A); 50 were cases of stable angina (Group-B); and 50 were healthy controls (Group-C).

The aims of the study were to estimate HsCRP levels as a marker of inflammation in patient of unstable angina, stable angina and in control groups and to compare HsCRP levels in between three groups. The results subjected to tests of statistical significance.

The study design was hospital base, case control and multiple group comparison study. Detailed history, risk factors, clinical and physical examination was performed in each group. All routine investigations including ECG, RBS, KFT, total cholesterol, HsCRP were performed in each group. CPKMB was performed in UA (group-A) patients only.

The circulating levels of TLC was significantly higher in both UA (group-A) and SA (group-B) patients than normal control (group-C). However, there was no significant difference in the circulating levels of TLC between UA and SA patients.

The circulating levels of HsCRP was significantly higher in patients with UA (group-A) than in either SA (group-B) or normal control (group-C). However, the circulating levels of HsCRP did not differ significantly between the SA and normal control.

Multiple step wise logistic regression analysis showed that only HsCRP level was significantly, independently associated with unstable angina (odd ratio=36.56, 95% confidence interval 9.82-136.09,  $p=0.000$ ).

### **The following conclusions were drawn from the present Study:**

1. There was no statistically significant difference in age and sex distribution among three groups (UA, SA and normal control).
2. There were no significant difference in distribution of risk factors for ischemic heart disease present among UA (group-A) and SA (group-B).
3. The circulating level of TLC was significantly higher in patients of UA (group-A) and SA (group-B) than normal control (group-C), but there was no significant difference in circulating levels of TLC between UA (group-A) and SA (group-B).
4. The circulating level of inflammatory marker HsCRP was significantly increased in patients of UA (group-A) during attack of UA.
5. Comparison of HsCRP between three groups showed that levels of HsCRP was significantly higher in patients with UA (group-A) than in either SA (group-B) or control (group-C) ( $p=0.000$ ).
6. The circulating levels of HsCRP did not differ significantly between the SA (group-B) and normal control (group-C) ( $p=1.000$ ).
7. The circulating levels of TLC did not significantly differ among sub-groups of UA (UA class-I and UA class-II and III) and SA patients.

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8. The circulating levels of HsCRP did not differ significantly between sub-groups of UA i.e., in class I UA and Class II and III UA, but HsCRP were significantly higher in both sub-groups of UA than SA patients.
9. Multiple stepwise logistic regression analysis showed that only HsCRP level was significantly, independently associated with unstable angina (odds ratio = 36.56, 95% )

In the present study, the circulating elevated levels of HsCRP were strongly associated with the clinical setting of unstable angina.

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