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LEVEL OF HIGH-SENSITIVITY C-REACTIVE PROTEIN IN PATIENTS WITH CHRONIC STABLE ANGINA

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ABSTRACT

Objective: To determine the serum levels of high sensitivity C-reactive proteins (hs-CRP) in our local patients with chronic stable angina.

Material and Methods: This cross sectional descriptive study was conducted in the Department of Cardiology Lady Reading Hospital, Peshawar, between January 2010 and January, 2011. We studied 125 consecutive patients of any gender with chronic stable angina. Base line characteristics, fasting levels of hs-CRP and lipid profile of patients were determined and recorded on predesigned research proforma. Data was analyzed using SPSS version 16.

Results: Mean age was 53.1 ± 7.6 years (range 40-70), and 53.6% (n=67) were females. Majority 47.2% (n=59) were having Canadian Cardiovascular Society function class-II (CCS-II) angina. Mean hs-CRP levels were 3.17 ± 2.45 (0.4-9.5). Majority of patients 41.6% (n=52) were having their hsCRP levels in the intermediate risk category. Mean total cholesterol levels were 187.42 ± 36 (112-275). Mean LDL cholesterol was 118.84 ± 31.32 (49-176). Mean HDL cholesterol was 32.84 ± 10.59 (16-65). Mean Triglycerides level was 237.31 ± 129.84 (73-628). Mean CPK level was 108.20 ± 65.76 (46-333).

Conclusion: Patients with chronic stable angina have elevated levels of hs-CRP.

Key Words: hs-CRP, chronic stable angina, lipid profile.

INTRODUCTION

Chronic stable angina is the most frequent manifestation of coronary artery disease, with its prevalence in middle-aged individuals estimated to be between 4 and 12%[1]. A large body of evidence suggests that inflammation plays a key role in the pathogenesis of atherosclerosis[2]. The chronic inflammatory process can develop to an acute clinical event by the induction of plaque rupture and therefore cause acute coronary syndromes[3]. Patients with chronic stable coronary artery disease are having elevated base line hsCRP levels as compared to healthy population[4]. Research has shown that elevated baseline levels of hs-CRP are associated with rapidly progressive coronary artery disease in patients with stable angina[5].

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According to American Heart Association (AHA) Statement[6] hs-CRP levels, using standardized assays, categorize patients as follows: Relative Risk for future cardiovascular events is low for Patients with average hsCRP Level i.e. <1 mg/L. Risk is average for levels 1.0 to 3.0 mg/L and high for hsCRP >3.0 mg/ L[6]. In patients with stable coronary disease or acute coronary syndromes, hs-CRP measurement may be useful as an independent marker of prognosis for recurrent events, including death, MI, and restenosis after PCI. The benefits of therapy based on this strategy remain uncertain. (Class IIa, Level of Evidence B)[6]. The aim of this study was to determine the serum levels of circulating hsCRP and frequency of different risk levels distribution according to AHA Statment[6] in our local patients with chronic stable angina.

MATERIAL AND METHODS

This cross sectional study was conducted in the Department of Cardiology, Lady Reading Hospital, Peshawar, between January 2010 and January, 2011. We studied 125 consecutive patients, age 40 years or above, of any gender with chronic stable angina after taking informed written consent.

Patients with inflammatory conditions such as recent acute illness (one month or lesser duration), severe arthritis, lupus, or inflammatory bowel disease were excluded, patients with acute coronary syndrome or any sort of coronary intervention within one month from the time of induction to study, a period adequate for any residual effects of acute ischemia or stress on hs-CRP levels, to disappear, were also excluded.

The diagnosis of chronic stable angina was made in the presence of at least one of the following criteria[7]; (1) a history of characteristic chest pain or discomfort (constricting in nature, radiating to jaw and or left arm for < 30 min) provoked by exercise, relieved on rest and/or nitrates (up to 1.5 mg sublingual) administration, or (2) evidence of reversible ischemia on exercise electrocardiography or imaging modality. Canadian Cardiovascular Society functional class (CCS) was used for the assessment of severity of angina[9].

Patients selected for study were interviewed through a pre-designed research proforma. Base line levels of hsCRP, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and creatine phosphokinase (CPK) were measured on fasting serum in hospital laboratory. Patients with baseline levels more than 10mg/l were reevaluated after minimum of 3 weeks. The Tina-quant CRPHS immunoturbidimetric assay for hsCRP from Roche was used. Hitachi P-800 System Pack performed all analysis. Data was analyzed using statistical package for social sciences (SPSS) version 16. Categorical variables like sex and angina functional class were presented as frequencies and percentages. Numerical variables like age, serum fasting level of high-sensitivity C-reactive protein and lipid profile were presented as Mean ± SD. Correlation between continuous and categorical variable were determined by Pearson's correlation test and chi-square tests respectively. P value < 0.05 was considered significant.

RESULTS

A total of 125 chronic stable angina patients were evaluated. Clinical characteristics of patients are shown in Table 1. Mean age of our patients was 53.10 ± 7.64 and female were slightly more 53.6%. About 26.4% (33) of patients were having no traditional risk factor for CAD other than age and gender, while 37.6% (47) patients were having multiple risk factors. Majority of patients 47.2% (59) were having Canadian Cardiovascular Society functional class II symptoms.

Mean hsCRP levels was 3.17 ± 2.45mg/l (0.4-9.5) with Interquartile range of 0.9-4.85 (median=2.4). Mean total cholesterol levels was 187.42 ± 36 (112-275). Mean LDL cholesterol was 118.84 ± 31.32 (49-176). Mean HDL cholesterol was 32.84 ± 10.59 (16-65). Mean Triglycerides levels was 237.31 ± 129.84 (73-628) and mean CPK levels was 108.20 ± 65.76 (46-333). HsCRP had no significant correlation to age (r=-0.06, p=0.06) total cholesterol (r=0.025, p= 0.786), LDL Cholesterol (r= 0.005, p= 0.954), HDL Cholesterol (r= 0.019, p= 0.829), Triglyceride (r=0.063, p=0.482) or CPK (0.034, p=0.708). Majority of patients were having hsCRP levels in the range of average risk category 41.6% (n=52) as in Table 2. HsCRP levels based risk categories were statistically significantly correlated to the angina function class P<0.000 as in Table 3.

Table 1: Clinical Characteristics of patients

Total No. of patients	125
Age ……..yr ± SDRange	53.10±7.6440-70
Female….% (no.)Male	53.6% (67)46.4% (58)
Heart rate ± SD	75.66 ± 7.18
Systolic BP mmHg	139.63 ± 21.19
Diastolic BP mmHg	85.20 ± 9.46
current or ex smoker	11.2% (14)
History of DM	17.6% (22)
History of HTN	22.4% (30)
Family history of Premature CAD	20.8% (26)
No Risk Factor except age & gender	26.4% (33)
More than one Risk Factor*	37.6% (47)
Angina functional class	
CCS-Class-I	35.2% (44)
CCS-Class-II	47.2% (59)
CCS-Class-III	15.2% (19)
CCS-Class-IV	2.4% (3)

CCS= Canadian Cardiovascular Society

*having more than one conventional risk factors other than male gender & age.

Table 2: Distribution of different Risk Categories based on HsCRP Levels

Risk Categories	Standard Risk* Levels mg/L	Frequency (%age)
Low	<1	37 (29.6%)
Average	1-3	52 (41.6%)
High	>3	36 (28.8%)

* As per AHA 2007 guidelines[6]

Table 3: Angina Function Class* Risk category baseline Crosstabulation

		Risk category			Chi-square test
		low risk	inter-medi-ate risk	high risk	
Angina function class	CCS-I	25	14	5	P<0.000
	CCS-II	11	29	19	
	CCS-III	1	8	10	
	CCS-IV	0	1	2	
Total		37	52	36	

DISCUSSION

Mean age of our patients with chronic stable angina was much younger (mean 53±7.2 yrs) as compared to the European population[8]. We observed that majority of our patients (41.6%) hsCRP levels were in the intermediate risk category (hsCRP= 1-3mg/l) while another 36% were in the higher risk category as defined in ACC/AHA guidelines. The mean hsCRP levels of our patients were 3.17 ± 2.45mg/l which also reflects higher risk category (hsCRP >3mg/l). These frequencies are consistent with internationally published data from other population[8]. Sabatine et al found that majority of their patients 39.61% (n=1494) with chronic CAD were having hsCRP levels in the intermediate risk category, with another 29.45% (n=1109) in the higher risk category. They further reported that higher baseline hsCRP levels (>1mg/l) were associated with a significantly greater risk of the composite end point of cardiovascular death, MI, or stroke in patients with chronic stable angina, during an average of 4.8 years of follow-up (P<0.001). The absolute event rate of cardiovascular death, MI, or stroke over the course of follow-up was 7.4% in those with hsCRP levels <1 mg/l, 11.3% in those with an hsCRP of 1 to 3 mg/l, and 12.8% in those with an hsCRP >3 mg/l. Higher baseline hsCRP levels also were associated with a significantly greater risk of new-onset diabetes mellitus and heart failure (P<0.001). Habib S et al reported almost similar frequency of average risk category CRP levels (40.1%) in Saudi patients with chronic stable coronary artery disease[4]. Rapid CAD progression in patients with stable angina pectoris is associated with elevated base line C-reactive protein levels. This was found in several studies while evaluating CAD angiographically[5]. In the present study hsCRP levels had no significant correlation to either age or lipid profile. Munir et al reported that age or base line lipid profile had no relation to hsCRP levels in patients with acute coronary syndrome[9]. Majority of our patients were having Canadian Cardiovascular Society angina function class II (CCS-II) and statistically there was significant (p<0.000) correlation between severity of symptoms and hsCRP based undesirable risk category (intermediate and high risk categories).

In the subgroup analysis we found that 23 patients were having LDL cholesterol below the currently recommended threshold (<100mg/dl) for treatment in patients with chronic stable angina while their levels of hsCRP were in the intermediate risk category (n=8) or in the high risk category (n=15). Thus elevated levels hsCRP predict the risk level independent of LDL cholesterol levels. This was previously observed in the Jupiter trial[10]. In current strategies of global risk assessment in patients with known CAD disease[1], lipid testing is the only blood test routinely recommended. But hsCRP level is an independent risk predictor for functional status of the patients, future vascular events and even arterial remodeling in patients with chronic coronary artery disease[11,12,13]. Therefore, hsCRP evaluation may have the potential to improve cardiovascular risk prediction models in secondary prevention of CAD.

The present study has certain limitations. First, it was single centre non randomized trial. Second, levels of hsCRP are not known for normal individual in the local population. Third, objective methods for evaluation of anginal symptoms and ischemia were not followed in the present study.

CONCLUSION

Patients with chronic stable angina have elevated levels of hsCRP.

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