Biomedical Research 2015; 26 (3): 467-470 *ISSN 0970-938X*
www.biomedres.info

Role of microalbuminuria and C - reactive protein as a marker of coronary artery disease.

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Abstract

The aim of present study was to quantify Serum - CRP and microalbuminuria in patients of acute chest pain and to find out correlation between CRP and microalbuminuria with chest pain. A hospital based cross sectional study was conducted on patients admitted in Emergency wards of Medicine Department of SGRRIMHS and Shri Mahant Indiresh Hospital, Dehradun (Uttarakhand). A total of 100 participants were included in the study. Out of which fifty patients of acute chest pain (33 male, 17 female) and 50 clinically healthy volunteers (29 male, 21 female) of similar age and sex were included in this study. Patients with respiratory diseases like pulmonary embolism, tuberculosis and pleurisy, gastro esophageal diseases like gall bladder, gastric and/or duodenal ulcer and diabetes mellitus, hypertension were excluded from the present study. All the participants were subjected to urinary examination for microalbuminuria and serum CRP estimation. Fifty patients in the age group 30-70 years and fifty clinically healthy age and sex matched volunteers (mostly staff members, their families and relatives of patients) were included in this study. Microalbumin in urine and CRP in serum was estimated by turbidometric methods. The mean serum CRP levels for male and female chest pain patients was calculated to be 33.91 ± 12.65 mg/l and 33.65 ± 15.57 mg/l respectively which was quite high as compared to the normal males 5.31±3.84 mg/l and female 6.39 ± 4.02 mg/l counter parts. Increase was more marked in female patients in comparison to their healthy counterparts exhibiting a gender differentiation in terms of CRP levels. The mean urinary albumin levels for male and female patients of acute chest pain was 29.39± 10.32 mg/l and 33.47±12.98 mg/l respectively which was found to be increased as compared to normal males with a value of 14.23 ± 9.92 mg/l and normal females 9.86 ± 5.96 mg/l respectively. Here again, the increase was more marked in female patients exhibiting gender differentiation again in terms of measured variables.

Keywords: Coronary artery disease**,** acute chest pain, microalbuminuria, C-reactive protein

Accepted April 04 2015

Introduction

Microalbuminuria is a term used to describe a moderate increase in the level of urine albumin. It occurs when the kidney leaks small amounts of albumin into the urine. It is also a marker for generalized vascular dysfunction. It's prevalence in United States and European general population surveys ranges from 6% to 10% [1]. Microalbuminuria is a common finding in patients with cerebrovascular disease. It is a risk factor for stroke in men and women, independent of other risk factors for cerebrovascular disease [2-3]. A significant association between microalbuminuria and carotid artery initima- media thickness has been observed in patients with Type II diabetes and in those with hypertension, suggesting that microalbuminuria may be a marker for early development of carotid artery atherosclerosis [4-5]. These correlations indicate a link between microalbuminuria and atherothrombotic stroke.

Inflammation appears to be pivotal in all phases of atherosclerosis from fatty streak lesion to a mature plaque. CRP is an important downstream marker of inflammation. CRP is produced by liver and increases whenever there is an activation of immune system. Immune system cells secrete inflammatory mediators and CRP is produced in response to elevation of these inflammatory mediators. CRP is an independent predictor of future cardiovascular events and its knowledge can be used as an adjunct for global risk assessment [6]. In the setting of acute coronary ischemia and unstable angina, the role of CRP is rapidly evolving. Multiple studies demonstrate that CRP levels predict early and late mortality in acute coronary ischemia and add to the predictive value of cardiac troponin [7-11].

There are few reports regarding quantification of various inflammatory mediators in cardiovascular diseases in In-

dian population. Microalbuminuria and CRP are intimately involved with the pathogenesis of chest pain. Therefore, the present study was designed to correlate microalbuminuria and CRP with acute chest pain and assess their prognostic value for cardiovascular diseases.

Materials and Methods

Fifty patients in the age group of 30-70 years and 50 normal healthy volunteers were selected randomly from patients admitted in Emergency & Medicine wards of SMIH, Patel Nagar, Dehradun. The present study was conducted in the department of Biochemistry in collaboration with department of Medicine. This study was divided into two groups:

Group A: Fifty clinically healthy volunteers.
Group B: Fifty patients of acute chest pain suffering from cardiovascular diseases.

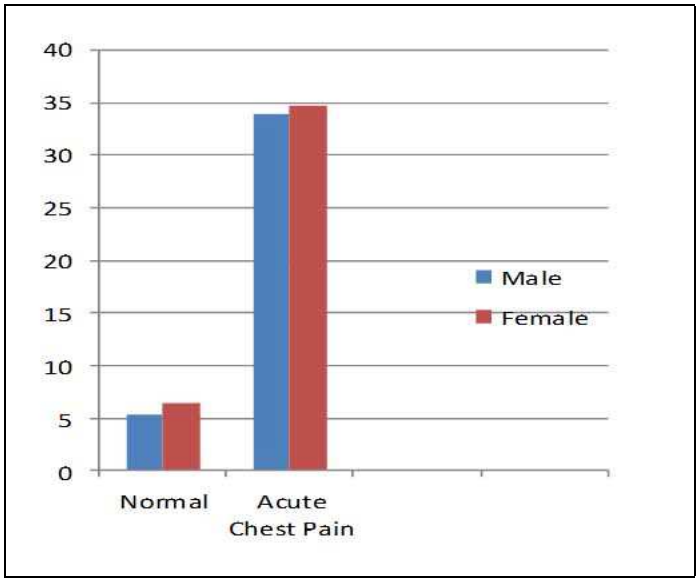
Patients having chest pain for more than 30 minutes, with more than 1 mm ST elevation in at least 2 contiguous ECG leads (Lead II & V1- V6 chest leads) were included in this study. Patients with respiratory diseases like pulmonary embolism, pulmonary tuberculosis and pleurisy, gastro esophageal diseases like gall bladder, gastric and/ or duodenal ulcer and diabetes mellitus, hypertension and acute infections were excluded from the present study. A written consent was obtained from all studied group patients and the present study was approved by the Institutional Ethical Committee. 5ml venous blood was collected from antecubital vein under aseptic conditions and subjected to routine investigations like CK-MB and serum CRP and routine urine examination. Haemolysed and lipemic blood samples were not analyzed. Serum CRP was measured by quantitative turbidometric method as described by Hokama and Nakamura [12]. The microalbumin levels were measured using semi autoanalyzer using immunoturbidometric procedure [13] through Kit provided by Agappe Diagnostics Ltd., Kerala. All values were calculated and expressed as Mean ± SD. All analysis was performed using SPSS computer program version 16.0.

Results

The mean serum CRP levels for male and female acute chest pain patients was (33.91 ± 12.65 mg/l) and (33.65 ± 15.57 mg/l) respectively which was quite high as compared to the normal male (5.31 ± 3.84 mg/l) and female (6.39 ± 4.02 mg/l) counterparts, as shown in Table 1 and depicted graphically in Figure 1. Increase was more marked in female patients in comparison to their healthy counterparts exhibiting a gender differentiation in terms of CRP levels. Mean urinary albumin in healthy volunteers was found to be 14.23 ± 9.92 mg/l in males and 9.86 ± 5.96mg/l in female participants which increased significantly in patients with a mean of 29.39 ± 10.32 mg/l in men and 33.47 ± 12.98 mg/l in women as shown in Table 1 and depicted graphically in Figure 1. Here again the increase was more marked in female patients in comparison with their healthy counterparts.

Table 1.

Variable	Group A (Normal)		Group B (Acute Chest Pain)	
	Male (29)	Female (21)	Male (33)	Female (17)
CRP	5.31±3.84 mg/l	6.39 ± 4.02 mg/l	33.91±12.65mg/l	33.65±15.57mg/l
Microalbuminuria	14.23±9.92mg/l	9.86±5.96mg/l	29.39±10.32mg/l	33.47±12.98mg/l



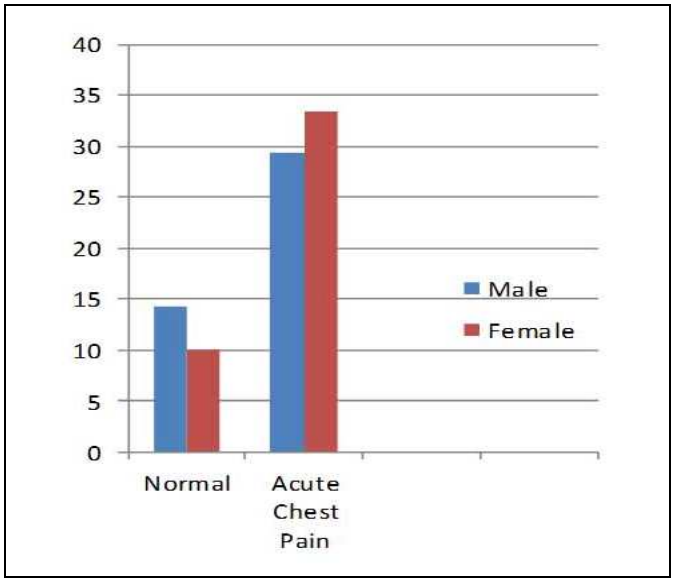


Figure: 1 *Serum CRP in mg/l* *Microalbuminuria in mg/l*

Discussion

Chest pain accounts for up to 5% to 10% of the consultations in emergency departments [14]. Quantification of CK-MB is a well established biomarker for diagnosis of coronary artery diseases which is helpful in management and treatment of the disease. CK-MB is a known biomarker, which increases in myocardial ischemia and unstable angina. CK and CK-MB were once the primary tests ordered to detect and monitor heart attacks, but they have now been largely replaced by the troponin test which is more specific for damage to the heart. All individuals with infarction developed raised CRP levels and there was a significant correlation between the peak CRP and CK-MB values. The CRP, however, reached a maximum concentration around 50 hrs after the onset of pain at a time, when CK-MB, which peaked after about 15 hrs, had already returned to normal. Angina alone or coronary arteriography did not cause a rise in CRP or CK-MB concentrations. Increased CRP production is a nonspecific response to tissue injury and raised CRP levels in cases of chest pain with a normal CK-MB indicated a pathological process other than myocardial infarction (15).

Mean CRP in healthy volunteers was found to be 5.76 ± 3.9 mg/l which increased significantly in acute chest pain ($p<0.01$). Taking cut off value of CRP 14.90 mg/L, the Sensitivity in patients was 98%, Specificity 96% and Positive Predictive value was 97%. Increase was more marked in female patients in comparison with their healthy counterparts, exhibiting a gender differentiation. CRP stimulate production of tissue factor by mononuclear cells, the main initiator of blood coagulation [16]. An elevated Serum CRP signifies ongoing activation of inflammation that characterizes unstable CAD [17]. Hach et al tested that measurement of CRP in patients could be a marker of acute coronary syndrome. They have found that concentration of CRP was elevated in 59 of the patients with final diagnosis of Acute M I and in 5% of patients with unstable angina.

In the present study we also estimated albumin in urine. Mean urinary albumin in healthy volunteers was found to be 12.40 ± 12.81 mg/l which increased significantly in patients with a mean of 30.78 ± 11.33 mg/l. Here again the increase was more marked in female patients of either group in comparison to their healthy counterparts exhibiting a gender differentiation in terms of microalbuminuria. Monitoring microalbuminuria might also be helpful for clinical decision making and further management. Taking cut off value of urinary albumin 20.90 mg/l, the sensitivity in patients was 82%, specificity was 92% and positive predictive value was 87%. Microalbuminuria assessment is valuable not only for prognostic value but also for monitoring efficacy of treatment [18]. It has been reported that markers of inflammation such as CRP, Interleukin-6 and Tumor necrosis factor-α, indicate that low grade inflammation is associated with the progression of microalbuminuria and with an increased risk of atherosclerotic disease [19].

Conclusion

The field of cardiovascular medicine has become a progressively competitive and costly field for the development of novel therapies and establishing clinical benefits over currently available therapies. Cardiovascular disease is the leading health concern and warrants continued research and development for novel treatment options to address this still unmet need. An undeniable need exists for novel biomarkers to fully understand the disease process and identify new treatment targets for the improvement of clinical outcomes in patients with cardiovascular diseases. Whether the aforementioned cheaper putative biomarkers prove useful still up to debate and more clinical trials are necessary to establish their validity. None the less, new biomarkers are sure to play a critical role in both clinical practice and research.

Conflict of Interest: None

Acknowledgement

The authors are grateful to Honorable Chairman, Shri Guru Ram Rai Education Mission for his kind support, guidance and favor.

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