Original Article

Coronary Artery Disease

Estimation of Monocytes in Patients with Coronary Artery Disease

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ABSTRACT

Objective: To evaluate the role of monocyte count in patients presenting for coronary artery heart disease and to assess its significance as a risk factor.

Design: Cross sectional study.

Place and Duration of Study: This study was carried on the patients taken from Coronary Care Unit (CCU) Department of Isra University Hospital, Dewan-e-Mushtaque CCU and from Red Crescent Hospital CCU from May 2011 to October 2011.

Materials and Methods: In this study 140 individuals were enrolled to observe the monocyte count in patients with coronary artery disease. In control group 42, Stable Coronary Artery Disease (CAD) 34 and Acute Myocardial Infarction (AMI) 64 individuals were taken. Three ml of blood was collected in EDTA bottles for differential leukocyte count (DLC) from each patient presenting with chest pain in coronary care unit. The total leukocyte count (TLC) and other parameters were determined by different automatic analyzers in the clinical laboratory.

Results: In all three groups male predominance with 70%, 64% and 64% in Stable CAD, control, and AMI group was seen respectively. In stable CAD group highest percentage (53%) of patients were seen in 56 to 65 years age followed by 50% of patients of 35-45 years and 42% of patients of 46-55 years in control and AMI group respectively. Both in stable CAD and AMI groups; monocyte count was highly significant in diabetic patients however in individuals with higher BMI; monocyte count was significantly increased in AMI group than stable CAD and control groups.

Conclusion: It is concluded from the present study that monocyte count has significant relationship between clinical stages of CAD and diabetic patients. However individuals with higher BMI showed significant high levels of monocyte count in AMI group only.

Key Words: Atherosclerosis, monocytes, Coronary artery disease, Acute myocardial infarction.

INTRODUCTION

Multiple factors including dyslipidemia, dysglycemia, smoking, and genetic predisposition all contribute to the coronary artery disease[1]. Pathogenesis of atherosclerosis is mainly supposed due to endothelial injury. This results in the inflammatory reactions and activation of immune system.[2,3]

Multi-centric studies have reported decreased fibrinolytic response in patients presenting for coronary artery disease having increased count of WBC and ultimately leads to higher mortality[2]. Coronary artery heart disease is the most frequent cause of mortality worldwide and these patients urgently require medical services to manage and for evaluation of acute-onset chest pain in emergency department[4].

As it is categorized under inflammatory disease, some inflammatory markers have been used / proposed for evaluation of cardiovascular risk[5]. From all those markers suggested the total leukocyte count (TLC) has been the most productive and clinically applicable and also being practiced[1], due to its low cost and easy and wide availability[5]. Pathogenesis of atherosclerosis involves important cells of inflammation however very little literature is available about the role of these inflammatory cells particularly monocytes in CAD. Some studies also highlighted the role of peripheral monocyte count in patients with variant angina[6].

Monocytes/macrophage plays very crucial role in development of atherosclerosis. The circulating monocytes are named as lipid laden foam cells when they engulf the fatty acids and reach inside the vessel wall. Hence this event is the earliest in the atherosclerotic plaque formation. Later these lipid laden foam cells secrete several proteolytic enzymes causing rupture of the plaque and plaque instability. Subsequent sequence of changes leads to unstable angina or acute myocardial infarction (MI). Also in the infracted area monocytes are recruited rapidly, where they enhance the wound healing, damage to the extracellular matrix and reperfusion injury[7]. Monocyte potentiates the inflammatory process in atherosclerosis by plaque formation and rupturing the fibrous cap thus their role could be taken as a risk factor for coronary artery heart disease. Some studies have also shown that increased number of leukocytes during coronary artery disease is linked with decreased epicardial blood flow in myocardium following reperfusion, thrombo- resistance

and adverse outcome[8]. Some of the studies have reported the association of left sided heart function recovery with monocyte count with high predictive value. Also the St segment elevation was related with monocyte count[9,10].

Although the current available data has shown that monocyte count is predictive for long term cardiovascular risk but sufficient documented data is not yet available for its role in coronary heart disease. The present study was designed to evaluate the role of monocyte count in patients who are admitted with angina and acute myocardial infarction and to assess its significance as a risk factor.

MATERIALS AND METHODS

A total number of 140 patients selected were divided into three groups for this study according to criteria mentioned below. The study was carried out from May 2011 to October 2011. All the patients included in this study; presented in Coronary Care Unit (CCU) Department of Isra University Hospital, Dewan-e-Mushtaque CCU and from Red Crescent Hospital CCU Hyderabad. All patients were interviewed and detailed information regarding the disease was recorded on a printed Performa. A prior permission was obtained from the respective CCU Incharge and consent was obtained from attendants before interview.

140 patients selected for this study were divided into

1. **Control Group:** Consisted of 42 individuals with chest pain with normal electrocardiogram (ECG).
2. **Stable-CAD Group:** Consisted of 34 patients with angina pectoris typical at mild to moderate exertions. With no previous myocardial infarction or any electrocardiogram findings.
3. **Acute Myocardial Infarction Group:** Consisted of 64 patients of acute myocardial infarction (AMI).

The diagnosis of AMI was based on the presence of at least two of the following criteria:

A. Typical pain with duration of more than 20 minutes; increased CK-MB or increase in Trop-T levels.

B. An elevation of the ST segment ≥ 1 mm for at least two frontal leads or ≥ 2 mm for at least two precordial leads on the electrocardiogram at rest or appearance of new Q waves on the electrocardiogram at rest.

Inclusion Criteria: All the patients of either gender (male and female) with age over 18 years, presenting at emergency department / CCU with acute chest pain.

Exclusion Criteria:

- Patients under 18 years of age.
- Patients of chronic renal failure (serum Creatinine ≥2.0 mg/dl)
- Patients with a history of trauma, surgery, neoplasia & infectious diseases in the 30 days prior to admission.
- Patients using immune-suppressive therapy.
- Clinically significant endocrine, hematologic or respiratory disease.

Samples Collection Procedure

- Three ml of blood was collected in EDTA bottles for differential leukocyte count (DLC) from each patient presenting with chest pain in coronary care unit. The TLC and other markers were determined by different automatic analyzers in the clinical laboratory.
- The slides stained with Leishmann's stain were used for counting DLC manually.

RESULTS

In this study 140 individuals were enrolled to observe the monocytes count in patients of coronary artery disease. In control group (n=42), Stable CAD (n=34) and AMI (n=64) individuals were taken. In all three groups the number of male patients was found to be higher 64% in control, 70% in Stable CAD and 64% in AMI group respectively. (Figure: 01)

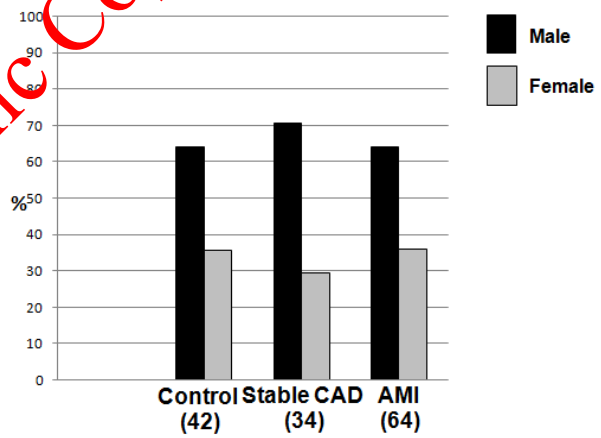

Figure No.1: Gender distribution between cases and controls

Table No.1: Age distribution (years) between cases and controls

Age (Years)	Control Group	Stable-CAD Group	AMI Group	Total
35-45	21	2	12	35
46-55	14	10	27	51
56-65	7	18	21	46
>65	---	4	4	8
TOTAL	42	34	64	140

Among the AMI group highest proportion of the patients were recorded between the ages 46-55 years

(27 out of 64). In control group highest recorded patients were between ages 35-45 years i-e: 21 individuals out of 42. In stable CAD group 18 patients out of 34 were between 56 to 65 years of age (Table: 1).

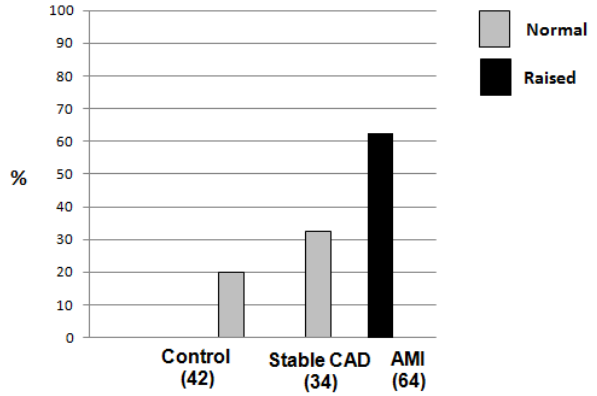

Figure No.2: Comparison of cardiac marker (Trop-T) between cases & controls

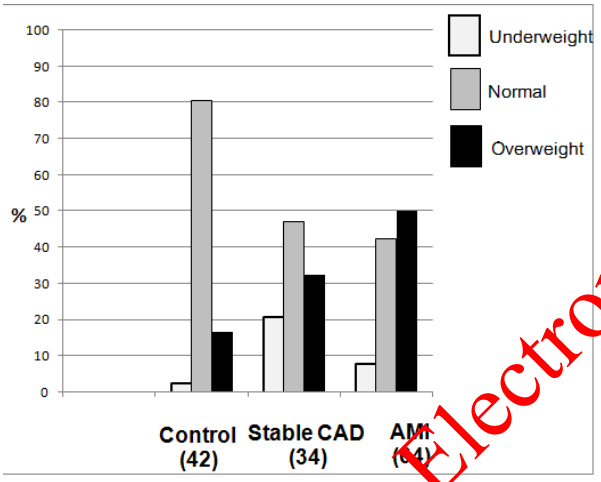

Figure No.3: Comparison of BMI between cases & controls

Table No.2: Association of BMI with Monocyte Count in cases and controls

	BMI		
	Over Weight	Normal	Under Weight
Control	17%	81 %	2%
Monocyte Count / mm2	(600-800)	(400-600)	(200-400)
Stable CAD	32%	47%	21%
Monocyte Count / mm2	(800-1000)*	(400-800)	(200-600)
AMI	50%	42%	8%
Monocyte Count / mm2	(800-1000)**	(800-1000)*	(800-1000)*

* = Significant ($p < 0.05$) ** = Highly significant ($p < 0.04$)

Trop-T was measured in all three groups (control, stable CAD and AMI). In control group, levels of Trop-T was investigated in only in 20% of the individuals and results showed normal levels, in remaining 80% of control group individuals, the Trop-T were not investigated on the basis of clinical findings. In stable CAD Trop-T levels were noted in 33% and were found normal, the rest of the individuals were not preferred for Trop-T. However in AMI group Trop-T levels were significantly increased in about 63% of individuals ($p= 0.005$) (Figure: 2).

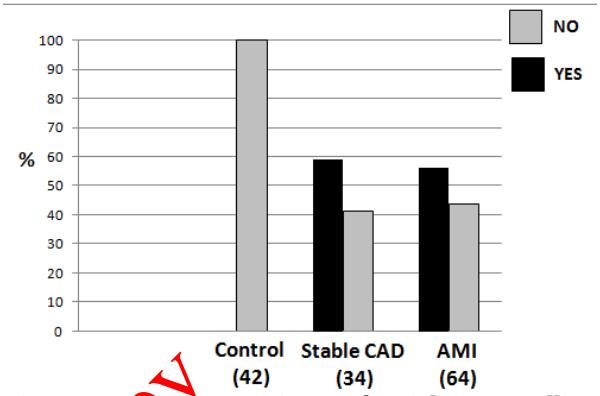

Figure No.4: Comparison of Diabetes Mellitus between cases & controls

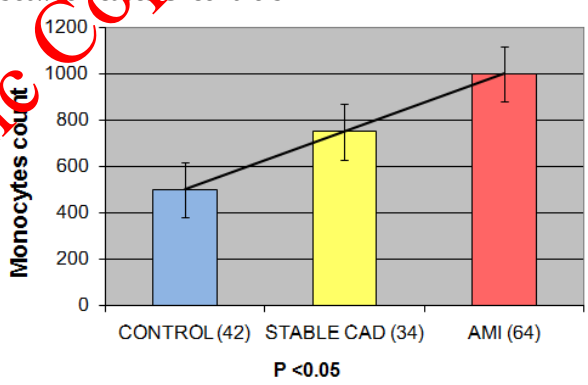

Figure No.5: Comparison of monocyte count between cases & controls

Table No.3: Association of diabetes with monocyte count

	Diabete Mellitus	
	Diabetic	Non Diabetic
Control	NIL	100%
Monocyte Count / mm2	(200-800)	(200-800)
Stable CAD	59%	41%
Monocyte Count / mm2	(800-1000)**	(800-1000)
AMI	57%	43%
Monocyte Count / mm2	(800-1000)**	(800-1000)

** = Highly significant ($p < 0.01$)

BMI analysis results revealed that in control group, BMI was normal in 81% individuals, 2% were underweight and around 17% individuals were overweight. In stable CAD about 47% individuals were having normal BMI while 21% of the individuals were underweight and 32% were overweight. In AMI 42% individuals were of normal weight, 8% of individuals were underweight and 50% of individuals were overweight (Figure 3).

In control group individuals who were overweight monocyte count were found to be in normal range and similar results were noted in normal and underweight individuals. In stable CAD group, the monocyte count was significantly increased in overweight individuals while it was normal in underweight and normal group individuals. In AMI group, in overweight individual monocyte count was highly significant with $p < 0.04$. Similarly significant results were also found in normal and underweight individuals where p value turns out to be $p < 0.05$ (Table: 2).

The ratios of diabetic patients were also noticed in study individuals. In control group all 42 individuals were non diabetic while in stable CAD about 59% of individuals were diabetic while 41% of individuals were non diabetic. In AMI group about 57% of individuals were having diabetes and 43% of individuals were non diabetic (Figure: 4).

In control group, consisting of all non diabetic individuals; the monocyte count was found normal. Both in stable CAD and AMI groups, monocyte count was highly significant in diabetic and in non diabetic patients it showed significant values with P value ($p < 0.01$ and $p<0.05$ respectively) (Table: 3).

After revealing and analyzing all the risk parameters it was found that monocyte count is significantly and greatly increasing from control to stable CAD and the AMI group respectively ($p <0.05$) (Figure: 5).

DISCUSSION

The aim of the present research is that increase in the levels of monocyte count is directly associated with poor prognosis and vaso-occlusive events in patient of coronary artery disease, the experimental data suggest a direct role of monocyte count in micro vascular obstruction. The only way to test whether monocyte count contribute directly to poor outcome in ischemic cardiovascular disease is to assess its levels in blood in patients who presented with chest pain secondary to coronary artery disease. The increase in monocyte count will correlate with the patient clinical stage and underlying risk factors of CAD. Hence, it turns out to be one of the prognostic tools for the prediction of an increased risk of CAD due to atherosclerosis. This view was also proposed by Pamukcu B, et al.

In present study it is also discovered that monocytosis is an independent risk marker for severity of atherosclerosis which is totally consistent with the work done by Burkhard L, et al.

In the present study, the monocytes were found to be (one of the most important components of the inflammatory process) an independent marker for the prognosis of stable CAD and AMI. These results are in agreement with Abrahão Afiune Neto, et al who also states that the increases in the number of monocyte count are related to the CAD and AMI.

Another study by Furman MI et al, showed a higher incidence of congestive heart failure and higher intra-hospital mortality rate in both men and women was observed with leukocytosis ($\geq$ 10,000/mm3). This correlates with our present study that, monocytosis is strongly associated with CAD which in turns is the common cause of congestive heart failure.

Hung MJ et al reported that, peripheral monocyte count is increased in the patients with variant Angina. The study is consistent with our present study, in which we also observed that levels of monocytes are elevated in patients of stable angina comparatively to the control group of individuals.

This research has also discovered that a very high incidence of monocytosis was visible in patients with Stable CAD and AMI group and these results are consistent with the studies done by Sposito AC, et al, who reported that leukocytosis is more severe in patients with stable CAD that have had a prior AMI; than those with just stable CAD.

As in this study, gradual increase in monocyte count was noted in a comparison between the control group and the stable CAD and AMI groups, which correlate with the study of Barron HV et al, indicating a gradual increase in the level of monocyte count which is associated with level of severity of atherosclerosis, the coronary blood flow, and high mortality in patients of CAD.

The study of Mariani et al, also highlighted the importance of monocytes count independently related to the recovery of left ventricular function at six months following AMI which strongly associate with this present study indicating monocytosis is strongly associated with AMI and it's a independent risk marker for CAD.

Simcha R. Meise et al observed a significant increase in monocyte count 2–3 days following acute myocardial infarction (AMI); the study is consistent with our present study.

Findings of Panutsopulos D et al display a statistically significant association of the increased in the levels of endothelial growth factor (VEGF) and transforming growth factor β1 (TGF-β1) levels in peripheral monocytes, with stable angina and diabetes in coronary artery disease. The study is consistent with our present study which shows association between monocyte count and diabetes in Stable CAD group and AMI group of individuals.

Grau AJ et al reported that Neutrophilia is an independent risk variable for cardiovascular disease; however this study have shown that the monocytosis works better prognostic tool for Cadiovascular disease than any other isolated subtypes of leukocytes.

CONCLUSION

It is thus concluded from the present study that monocyte count has important role, which is directly related to the clinical stages of CAD, accounting for the slightly higher values of AMI group in comparison with the stable CAD group and also between the stable CAD group compared with the control group.

Hence it is recommended that in the rural areas of underdeveloped countries where best diagnostic methods are not readily available, the TLC and DLC being simple, inexpensive, and widely could be made available even at remote areas. Thus it may be tuned into an additional parameter for the preliminary approach of patients with suspicion of CAD.

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