



THE POSITIVE PREDICTIVE VALUE OF ABSOLUTE NEUTROPHILIA FOR DEVELOPMENT OF EARLY CONGESTIVE HEART FAILURE IN PATIENTS OF ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

BACKGROUND: Leukocytosis and neutrophilia is associated with post MI mortality and Heart Failure. The presence of absolute neutrophilia during first 12 hours after AMI can predict the occurrence of CHF which may help to identify high risk individuals who can then be benefited from more aggressive treatment

OBJECTIVE: To determine the positive predictive value of absolute neutrophilia for development of early congestive heart failure in patients of acute myocardial infarction

METHODS: This was a cross sectional study conducted at Department of Cardiology Mayo hospital Lahore from November 2013 to April 2014. A total of 260 patients were included in the study after their informed consent. Demographic data (name, age, gender, weight, height) was noted. Information about history of smoking, hypertension and diabetes was taken and blood was drawn at admission to determine absolute neutrophil counts. Patients were divided into two groups on the basis of raised or normal absolute neutrophil count (ANC) values. Echocardiography was done 4 days after admission to determine ejection fraction and label early CHF as per operational definitions. All patients were managed according to standard protocol for acute MI. Data entry and analysis was done by using SPSS 13.

RESULTS: Mean age of all these 260 patient was 52.12 ± 8.86 years. Gender distribution of patients showed that there were 120 female and 140 male patients. 86(33%) patients were diabetic, 82(32%) were hypertensive and 37% were smokers. In 184(70%) patients, absolute neutrophilia was observed. Heart failure was observed in 128(69%) of these patients. The positive predictive value for absolute neutrophilia turns out to be 69.57%.

CONCLUSION : Positive predictive value for absolute neutrophilia is high for heart failure in these patients.

KEY WORDS: Absolute neutrophilia, Early congestive heart failure, Acute myocardial infarction

INTRODUCTION

Coronary heart disease is the leading cause of mortality worldwide. In 2008, an estimated 7,70,000 Americans had a new coronary event and about 4,30,000 had a recurrent event.¹ Acute myocardial infarction (AMI) accounts for about half of all the coronary heart disease hospital admission and is the cause of approximately 75% of all coronary heart disease deaths.²

Acute myocardial infarction promotes inflammation. White blood cells (WBCs) are the major mediators of inflammation so WBCs and their differential have been studied to predict cardiovascular outcome after a cardiac event. Increased

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neutrophils are associated with poor functional recovery after coronary angioplasty and extension of infarct size upon reperfusion in acute coronary syndrome (ACS) patients.³ Inflammatory biomarkers have been identified as an important tool for risk stratification in post-MI patients³. The incidence of congestive heart failure (CHF) after AMI, either in the intensive care unit or before discharge is 22%. A 2010 update from the American Heart Association estimated that there were 5.8 million people with heart failure in USA in 2006.⁴

Leukocytosis and neutrophilia is associated with increased mortality and HF in post-MI patients and improved risk stratification over the traditional predictors.⁵

The presence of absolute neutrophilia [neutrophil count > 7500/mic/lit] during first 12 hours after AMI can predict the occurrence of CHF. This may help identify high risk individuals who might benefit from more aggressive treatment. In a cross-sec-

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tional study by Rashidi, et al, 312 patients diagnosis with AMI were studied, 202 patients (68.9%) had absolute neutrophilia (neutrophil count > 7500/mic/lit) of which 121(79.6%) were reported as cases of CHF.⁶

After adjustment for age, sex, serum creatinine level, CK-MB and location of MI, the relationship between the absolute neutrophil count (ANC) and the presence of CHF remained significant (OR=2.14;95%CI= 1.19-3.84,p=0.011).The positive predictive value of absolute neutrophilia for development of early CHF in patients with AMI was found to be 60% in study by Rashidi et al.⁶

No study had so far been reported regarding such topic in Pakistan. As positive predictive value changes with prevalence of disease, so we want to conduct this study to generate magnitude for our local population.

OBJECTIVE:

To determine the positive predictive value of absolute neutrophilia for development of early congestive heart failure in patients of acute myocardial infarction

MATERIAL AND METHODS:

This was a cross sectional study conducted at Department of Cardiology Mayo hospital Lahore from November 2013 to April 2014. 260 patients were included in the study. Patients with ejection fraction (EF) less than 40% were labeled as cardiac failure patients.

SELECTION CRITERIA:

Following inclusion and exclusion criteria were observed:

INCLUSION CRITERIA:

Patients with AMI presenting within 12 hours as per operational definition ,age 40-70 yrs, both genders, Patients with absolute neutrophil count more than 7500 units.

EXCLUSION CRITERIA:

History of chest pain for more than 12 hours before admission, previous history of myocardial infarction, non ST-Elevation MI patients, history of exogenous steroid use one month before admission, evidence of infection within a week before admission diagnosed on the basis of history and laboratory tests, history of malignancy within the past three years diagnosed on standard investigations, history of gastrointestinal bleeding within a week before admission diagnosed clinically, major trauma or surgery within a week.

DATA COLLECTION:

Patients meeting the inclusion criteria were en-

rolled in study from Emergency Department, Mayo hospital Lahore. Informed consent was obtained. Demographic data (name, age, gender, weight, height) was noted. Information about history for smoking, hypertension and diabetes was taken and blood was drawn at admission to determine absolute neutrophil counts. Patients were divided into two groups on the basis of raised or normal ANC values.

Echocardiography was done at 4 days after admission to determine ejection fraction and label early CHF as per operational definitions. All patients were managed according to standard protocol for acute MI. All information obtained was recorded on a standard proforma.

DATA ANALYSIS PROCEDURE:

Data was entered and analyzed by using computer software SPSS version 13.0.The positive predictive value of absolute neutrophilia for development of early congestive heart failure in patients of acute myocardial infarction was calculated and presented in the form of frequency and percentage. Data was stratified for the variables like diabetes, hypertension and smoking to address the effect modifier.

RESULTS:

In this study a total 260 patients were included. Mean age was 52.12±8.86 years. Minimum and maximum age of patients was 40 and 70 years respectively.(Table-1).Gender distribution of patients showed that there were 120 female and 140 male patients. 86(33%) were diabetic.

82(32%) patients were hypertensive. 37% patients were smokers.(Table -2)

There were 184(70.8%) patients who had absolute neutrophilia. i.e. Neutrophil count >7500(Table-3).Patients echocardiography was done to assess the ejections fraction. There were 128(49.2%) patients whose ejection fraction was <40% and the 132(50.8%) patients ejection fraction was >40%.(Table-4).There were 184 patients who had absolute neutrophilia. In patients with absolute neutrophilia, 128(69%) had heart failure. The positive predictive value for absolute neutro-

Table-1:Descriptive statistics for age (years) in relation to gender of patients

	<i>Male</i>	<i>Female</i>	<i>Total</i>
<i>N</i>	140	120	260
<i>Mean</i>	53.10	50.97	52.12
<i>SD</i>	8.50	9.17	8.86

Table-2: Age and risk factors distribution among 260 patients

<i>Gender</i>	<i>Male</i>	<i>Female</i>
		140(53.84)
Diabetic	Diabetic	No Diabetic
	86(33%)	174(67%)
Hypertensive	Hypertensive	Non Hypertensive
	82(32%)	176(68%)
Smoker	Smoker	Non Smoker
	37%	63%

Table-3: Absolute neutrophilia among patients

		<i>Frequency</i>	<i>Percent</i>
<i>Absolute Neutrophilia</i>	<i>Present</i>	184	70.8
	<i>Absent</i>	76	29.2
Total		260	100.0

Table-4: Heart failure among patients

		<i>Frequency</i>	<i>Percent</i>
<i>Heart Failure</i>	<i>Yes</i>	128	49.2%
	<i>No</i>	132	50.8%
Total		260	100.0

Table-5: Postive predivive value of absolute neutrophilia

		<i>Heart Failure</i>		<i>Total</i>
		<i>Present</i>	<i>Absent</i>	
<i>Absolute Neu-trophilia</i>	<i>Yes</i>	128(100%) ^{TP}	56(42.4%) ^{FP}	184(70%)
	<i>No</i>	0(%) ^{FN}	76(57.6%) ^{TN}	76(30%)
Total		128	132	260

philia for development of early congestive heart failure in patients of acute myocardial infarction was 69.57% (Table-5).

DISCUSSION:

Although the diagnosis and management of acute myocardial infarction (AMI) has improved a lot over the past decades, it is still a major public health problem worldwide. According to World Heart Federation the burden of disease in developing countries will become closer to developed countries, due to the accelerated economic development and life style changes. Atherosclerosis is the underlying basic mechanism of cardiovascular disease.

An elevated leukocyte count is associated with poor clinical outcome in patients treated with thrombolytic therapy for AMI⁷. A major component of the leukocytosis associated with AMI is an elevated neutrophil count, Recent studies have suggested that an elevated neutrophil count is related to early development of congestive heart failure (CHF)⁸. Impaired microvascular perfusion,⁹ and left ventricular(LV) dysfunction¹⁰. During acute myocardial ischemia and reperfusion, neutrophils, together with platelets cause mechanical plugging of the coronary microvasculature and damage to endothelial function, resulting in a reduction of coronary vasodilator reserve. Neutrophil platelet interactions are also a cause of development of a thrombus¹¹.

Furthermore, it is proved that neutrophils release proinflammatory cytokines, leading to impaired microvascular perfusion¹².

In a study by Takahashi, 260 patients with primary PCI and neutrophilia were assessed at admission and were to have increased risk of in-hospital cardiac deaths and HF. 57% of the patients with high neutrophil counts had heart failure (in hospital cardiac events)¹³. There are very few studies regarding the predictive value of absolute Neutrophil count for the prediction of heart failure after acute myocardial infarction. However, in a cross sectional study conducted by Rashidi, et al, 202 patients (68.9%) out of 312 patients with AMI had neutrophilia (neutrophil count> 7500/mic/lit). 121(79.6%) patients were reported as cases of CHF and 81(57.4%) had no CHF. The positive predictive value of absolute neutrophilia for development early CHF in patients of acute MI was found to be 60%⁶.

In this study 184(70.8%) patients had absolute Neutrophilia, heart failure was observed in 128 (69%) patients, The positive predictive value of absolute Neutrophilia was 69%, which is a bit high as compared to the PPV reported by Rashidi in his study. However Rashidi reported absolute neutrophilia as 79.6% among patients which is quite lower as compared to the results of our study. In this study all patients who had heart failure among them all patients with heart failure were having absolute neutrophilia.

Studies reporting data from secondary analyses of clinical trials which enrolled patients with ST elevation MI have demonstrated conflicting findings regarding the association between peripheral neutrophil count and 30-day post-MI outcomes.



In a large randomized trial of clopidogrel versus placebo in ST elevation MI patients undergoing fibrinolysis, the neutrophil count in the highest quartile was independently associated with the risk of cardiovascular death and HF at 30 days. However, in another trial of fibrinolysis in ST elevation MI, there was no significant association between cell counts and clinical outcomes⁹.

Also, the subsequent development of HF was consistently found to be related with neutrophilia in selected studies with both short and long-term follow-up periods. A very recent study by Arruda-Olson et al done on 2,047 MI patients neutrophil count was independently associated with death and HF after a mean follow-up period of 4.9 years¹⁴.

Increased neutrophil count has been reliably associated with increased MI size and decreased left ventricular function. Evidence of congestive heart failure with elevated BNP levels is associated with poor prognosis due to increased myocardial damage¹⁵.

Samad Ghaffari in his study concluded that higher neutrophil count was found to have the best predictive value for both mortality and heart failure¹⁶.

Khatri, in his study reported the sensitivity as 82.3% and specificity of 64.8%. of Neutrophilic Leucocytosis for the prediction of CHF. Among the patients with heart failure 93.5% had neutrophil count >65% and only 6.5% of cases had count <65%. Positive predictive value of Neutrophil for the prediction of heart failure after acute myocardial infarction was 63%¹⁷.

The positive predictive value of absolute neutrophilia was 69% which is almost comparable to the positive predictive value reported by Khatri. In this study, among patients with heart failure all patients had absolute neutrophilia which is also comparable to the results of Khatri. i.e. (93.5%)

Furman et al who demonstrated a strong and consistent association between leucocyte count and all causes mortality including congestive heart failure from AMI, independent of other therapeutic and prognostic factors. Furman et. Al, in their multinational study, also demonstrated that, in patients with full spectrum of acute coronary syndrome, WBC count is independently associated with the development of congestive heart failure¹⁸.

Also the subsequent development of HF was consistently found to be related with neutrophilia. The potential detrimental role of neutrophils in myocardial injury after ischaemia and reperfusion has been suggested many years ago, and there is evidence that these cells directly damage myocardial tissue besides being part of the acute inflammatory response to tissue injury. In ACS, these cells are functionally activated, and local neutrophil infiltration has been documented in plaque lesions. This suggests that neutrophils play a role in mediating destabilisation of atherosclerotic plaques¹⁹.

A cross-talk between neutrophils and platelets has been recognised and neutrophils are recruited to the injury sites both through the classical recruitment cascade or by adhering to platelets which are attached to the endothelial cells. Moreover, microparticles derived from stimulated polymorphonuclear leukocytes may enhance coagulation and perpetuate thrombus formation because they can activate platelets and enhance platelet P-selectin expression²⁰.

CONCLUSION:

Absolute neutrophilia is simple and widely available test which can be helpful to identify STEMI patients who are at a higher risk of death and developing heart failure. This study also helps in discrimination of high risk patients presenting with STEMI who will benefit from revascularization in the form of angioplasty or coronary artery bypass graft.



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