Iron Deficiency Anemia & Adverse Events After ST Elevation Acute Myocardial Infarction

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Abstract

Objectives: Study objective was to look for the frequency of iron deficiency in ischemic heart disease patients presenting with acute ST elevation myocardial infarction and to see the association of adverse coronary events with iron deficiency among these patients

Methods: It was a cross-sectional study conducted on three hundred and seventeen patients at coronary care unit/Medical unit of services hospital Lahore. Serum ferritin, iron, and transferrin were measured by using automated immunoassays in patient admitted with acute myocardial infarction and adverse events developed after myocardial were recorded at 5th day of admission. Frequency of iron deficiency anemia was determined in these patients. Adverse events after acute myocardial infarction such as development of recurrent MI, unstable angina, arrhythmias, pericarditis, (EF <50%), adverse outcomes in the form of mechanical complications (ventricular septal defect or mitral regurgitation, and significant impairment of left ventricular functions, stroke and death rate was studied in these patients. Chi-square test was used to see association of iron deficiency anemia with adverse events developed after myocardial infarction.

Results: Frequency of iron deficiency was 82% among patients suffering from acute myocardial infarction. There was significant association of anemia with Post myocardial infarction heart failure (P=0.006), Low EF <50 %(P=0.00), increased mortality (0.076) and pericarditis (P= 0.069).Iron deficiency was associated with of adverse outcomes after myocardial infarction.

Conclusion: Increased frequency of iron deficiency anemia was recorded in patients suffering from acute myocardial infarction and it was significantly associated with the post myocardial infarction adverse events.

Keywords: Iron deficiency anemia, Acute myocardial infarction, Adverse outcomes

Introduction

Acute myocardial infarction is causing significant morbidity and mortality in patients suffering from cardiovascular diseases. Iron is essential for all physiological processes in body. Iron is not only required for erythropoiesis but is also important in oxygen storage & transport, Synthesis of deoxyribonucleic acid and so for the erythropoiesis, electron transport, oxygen transport and synthesis/ degradation of muscle protein. All the muscles in body including cardiac myocytes require iron for proper functioning.[1] Iron deficiency is of two types, one in which the iron stores are exhausted but the iron homeostasis is preserved, the second type of iron deficiency is called functional iron deficiency in which the total iron reserves are normal but the iron supply is not sufficient to fulfill the demands of body.[2] In functional Iron deficiency value of serum ferritin is normal but the transferrin saturation is low.[3]

Among cardiovascular diseases iron deficiency is seen in heart failure and in patients suffering from acute myocardial infarction.[4] Like many nontraditional novel cardiovascular risk factors, role of iron deficiency was studied in patients with cardiac illnesses.[5] There are many pathophysiological mechanisms for anemia in coronary artery disease. The hyperdynamic state contribute to left ventricular hypertrophy and arterial wall thickness if anemia is

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not get corrected.[6]

Anemia is a risk factor for ischemic heart disease and mortality associated with it.[7] Adverse prognosis is found in patients of anemia with acute coronary syndrome irrespective of type of anemia.[8] Effect of anemia on outcome is independent of other etiological factors and it can predict the survival in patients with cardiac diseases.[9] Myocardial necrosis resulting from acute obstruction of coronary artery results in acute myocardial infarction suggested by typical history ST segment elevation in two consecutive chest or limb leads or elevated cardiac biomarkers.[10] Heart failure is a clinical syndrome presenting with symptoms of dyspnea, paroxysmal nocturnal dyspnea, edema feet and signs such as elevated jugular venous pressure, and bibasilar crepitation. It is caused due to structural heart disease such as ischemia or due to any functional cardiac abnormality which is causing decreased in stroke volume.[11]

In this study we assessed the presence of iron deficiency and its association of with adverse outcomes/ events after acute myocardial infarction. Our aim was to look for the of iron deficiency in patients of ischemic heart disease presenting with coronary ischemia and to see the association of iron deficiency with adverse coronary events in these patients.

Methods

It was an observational cross-sectional study; the study duration was twelve months. The sample size for the study was calculated by taking most probable prevalence of iron deficiency as 29% and with 95% confidence interval. Three hundred and seventeen 317 patients were included in the study. These patients were admitted in coronary care unit of services hospital Lahore from July 2018 to July 2019 with acute ST elevation myocardialinfarction? Patients with cardiomyopathies, on anticoagulation therapy, cancer and fever were excluded. Informed consent was obtained by all and ethical approval was taken from institutional review board of services hospital Lahore.

Any hemoglobin level <12.0 g/dL is defined as anemia. Iron deficiency anemia was defined as hemoglobin level <12.0 g/dL in female and <13.5g/dl in male. Serum ferritin is a parameter for iron deficiency. Normal serum ferritin is 30-300ng/ml. Serum ferritin is an acute-phase reactant, and diagnosis of iron deficiency anemia was made if patient is anemic and serum ferritin was less than 30 ng/ml or serum ferritin less than 12 ng/dl.[12]

Baseline information was taken from hospital charts. Coronary artery disease was diagnosed as patient presenting with signs/symptoms of myocardial infarction, ECG changes, raised cardiac enzymes and Troponin I levels.[13] Other routine laboratory values were recorded. Complete blood count with red blood cell morphology and indices, Serum ferritin and iron was measured by using automated immunoassays on 5th day of admission. Adverse events/outcomes the patient developed after ST elevation myocardial infarction at 5th day of admission were recorded. The complications or adverse events after myocardial infarction studied were, recurrent Myocardial Infarction MI, unstable angina, arrhythmias(premature atrial & ventricular contraction, ventricular tachycardia, ventricular fibrillation and atrial fibrillation) stroke, pericarditis, significant impairment of left ventricular functions (EF <50%), the mechanical complications such as ventricular septal defect or mitral regurgitation due to papillary muscle ruptured and death. ECG changes, Troponin I and echocardiography was used to diag-nose the adverse events. The definition of iron deficiency was based on serum ferritin and hemo-globin levels.[14]

Results

Out of three hundred and fifty patients, mean age of patients was 54 years. 53%patients were male and 47%patients were female. Mean hemoglobin of patients was 10g/dl and mean serum ferritin was 25ng/dl. Mean ejection fraction of these patients was 45%. 88% of patients were found to be anemic. 82% patients had serum ferritin less than 30ng/dl and 18%patients has more than 30ng/dl(Table 1)

After myocardial infarction 62.1%patient developed adverse events like arrhythmias in the form of premature ventricular contractions (35%), atrial fibrillation (20%), ventricular tachycardia (23%), APC'S (10%) and ventricular fibrillation (7%), 23% patient had stroke, 15.5% patient had recurrent acute myocardial infarction, 97.1 %patient had unstable angina, 5% patient died, 20.5% patient had pericarditis, 74% patient had clinical heart failure and among these 68% patient had impairment of LV functions on echocardiography (EF <50%) (FIG.1), 0.3% patient patients had ventricular septal defect, 1.9% patient had mitral regurgitation due to papillary

Table 1: *Descriptive Statistics of Study Population*

Study parameters	N=total patients	Range	Minimum	Maximum	Sum	Mean		Std. Deviation	Variance
						Statistics	Std err		
Age	317	70	20	90	172.5	54.42	.867	15.435	238.245
Hemoglobin	317	8	6	14	3177	10.02	.115	2.042	4.171
Serum ferritin	317	152	4	156	8963	28.28	1.399	24.901	620.045
Ejection Fraction	317	55	9	64	14405	45.44	.388	6.913	47.792

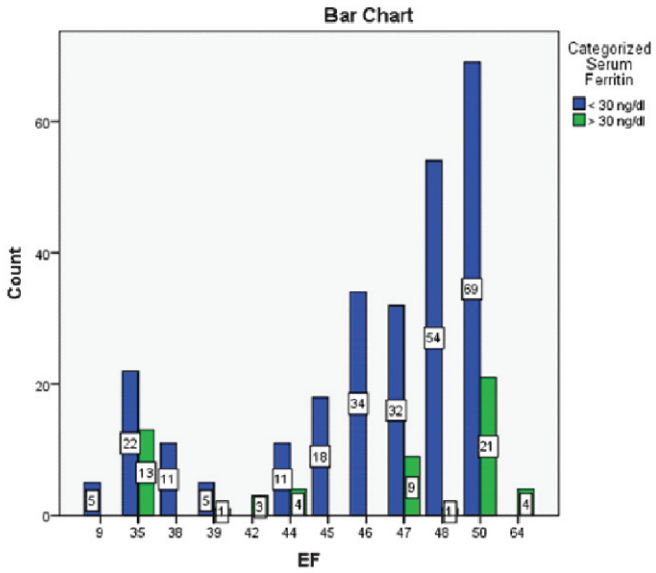

Figure 1: *Serum Ferritin and Ejection Fraction (P=0.00)*

muscle ruptured. The complications are listed in Table: 2

Recurrent acute myocardial infarction had no significant association with anemia (P=0.12). There was significant association of anemia with gender and males were having the significantly low levels of serum ferritin (P = 0.07), patients with diabetes mellitus were not found to have significantly low hemoglobin (P= 0.22). Stroke was not significantly related with serum ferritin levels (p=0.77), increased mortality was not seen in patients who were found to be anemic and had low serum ferritin (0.076). Hypertension was significantly related with anemia (P= 0.006). Obesity was not significantly related with anemia (P= 0.14).

The frequency of anemia in these patients was found to

Table 2: *Anemic Patients Who Developed Complications after Myocardial Infarction*

Study parameters	Serum Ferritin		Total no of patients	Types of Myocardial infarction
	N=< 30 ng/dl	N=> 30 ng/dl		
Diabetes mellitus	123	30	153(48.3%) P=(0.22)	Anterior wall myocardial infarction Total No of patient = 178(56.2%)
Hypertension	122	37	159(50.2%) P=(0.006)	
Obesity	24	11	45(14.2%) P=(0.14)	
Unstable Angina	224	52	276(97.1%) P=(0.11)	Inferior wall myocardial infarction Total No of patient = 8(2.5%)
Recurrent acute Myocardial infarction	37	12	49(15.5%) P=(0.12)	
Death	13	0	13(5%) P=(0.076)	
Pericarditis	58	7	65(20.5%)	Lateral wall myocardial infarction Total No of patient = 8(2.5%)
Clinical heart Failures	199	38	237(74%)	
Mechanical complications	7	0	7(2.3%)	
Stroke	63	11	74(23.3%) P=(0.77)	Posterior wall myocardial infarction Total No of patient = 8(2.5%)
Arrhythmias	159	38	197(62.1%)	

found with adverse events after myocardial infarction.

Discussion

Results of our study showed high frequency of iron deficiency anemia in patients with acute myocardial infarction and significant association was found between anemia and adverse events after myocardial infarction. It is shown in the previous studies that iron deficiency is associated with adverse coronary outcomes. These patients are prone to develop cardiovascular diseases in future and the role of iron replacement is not clear in these patients.[15]

A cross sectional study done on stable patients of ischemic heart disease by obtaining bones marrow aspirates. The results of the study showed bone marrow depletion of iron stores in patients with ischemia but not in control group.[16]

It has been shown in some studies that intravenous iron replacement helps to alleviate the symptoms of heart failure in patients suffering from iron deficiency. This suggests that early correction of iron deficiency after myocardial infarction can reduce the adverse outcomes in these patients.[17]

Iron deficiency is seen in patients with heart failure and is causing increased morbidity. The role of anemia in progression of disease is not clearly understood. Erythropoietin treatment did not improve the clinical status and associated complications. Anemia is common in patients with heart disaeses. This leads to poor outcomes in these patients. Whether to take anemia as markers of heart failure severity or a factor that mediate heart failure progression is not entirely clear. Erythropoiesis-stimulating agents did not lead to clinical improvement and at times causing the serious side effects. Treatment of anemia was studied in patients both with absolute and functional iron deficiency. It is seen that treatment of iron deficiency is beneficial in patients with absolute iron deficiency and it appears to be unclear whether we should treat the functional iron deficiency or not.[18] All these findings are supporting the results of our study. Hemoglobin abnormalities have been described as a cause of poor prognosis in patients with ischemic heart disease based on retrospective cohort studies.[19] Our study also showed increased mortality in patients who was suffering from anemia due to iron depletion.

In a patients of chronic kidney disease hemoglobin abnormalities can lead early coronary intervention.[20] It is an independent risk factor for prediction of risk of recurrent myocardial infarctions and bleeding during the procedure. Anemia is also an important factor for risk stratification of these patients. Incresed risk of recurrent ischemic events demands for early correction of anemia.[9]

In patients who undergo coronary stenting after myocardial infarction, hemoglobin, serum creatinine levels and ADP induced residual platelet activity is found to be an independent factors for in hospital adverse cardiovascular outcomes.[21]

It is an observation in a study that patients of pulmonary hypertension and heart failure and coronary artery disease undergoing bypass surgery, one third to half of patients were affected by iron deficiency and symptomatic improvements was shown after intravenous iron administration even in the absence of anemia. There is increased risk of early hospital readmission associated with absolute iron deficiency.[22]

The patient undergoing percutaneous coronary intervention after myocardial infarction does not get benefited from erythropoietin and increase risk of thrombotic events were observed in these patients and iron preparations are recommended only in those patients who are having the iron deficiency or the blood loss.[23]

A study done in patients with heart failure and pulmonary hypertension showed that one third of patients with heart failure and fifty percent patients with pulmonary hypertension demonstrated iron deficiency. This observation suggests that iron deficiency is a risk factor for all cardiovascular events.[8]

Sixty one percent prevalence of iron deficiency in patients of coronary artery disease was seen and it persisted at some point in next thirty days. This effect appears to be associated with antiplatelet treatment and increased inflammation. High frequency of iron deficiency in patients of acute myocardial infarction need to deter-mine the hemorrhagic risk factors in patients. Anti-platelet treatment and subsequent coronary interven-tion can be a cause of iron deficiency in these patients. Also there is a need to

required for those patients who are requiring early coronary intervention.[7]

It has been shown that red cell distribution width is a risk factor and is poor prognostic factor after coronary events. Ferritin level is a marker of inflammation and poor prognostic factor for left ventricular systolic function. Coronaryy artery disease is associated with increase in other markers of inflammation such as C - reactive protein. [24]

Conclusion

The frequency of iron deficiency anemia is very high in patients suffering from acute myocardial infarction and it is associated with significantly increased complications after myocardial infarction.

Limitations of Study: The patients were only followed during hospital stay. Further studies are required for post myocardial infarction follow up and risk stratification in patients with iron deficiency anemia.

Author's Contribution

NM: Data Collection
MR: Research Proposal, writing discussion
ZS: Statistical Analysis & Research Proposal writing

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