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In Hospital Prognosis in Patients Treated with Primary Percutaneous Coronary Intervention, Role of Admission Hemoglobin Level

Amro Elnagar[1], Neama Elmelegy[1], Ahmed Abdelmonaem[1], Ahmed Magdy[2]

[1]Cardiology Dept., Faculty of Medicine, Benha Univ., Benha, Egypt

[2]Cardiology Dept., the National Heart Institute, Giza, Egypt

Corresponding Author's Email: a.magdy92@gmail.com

Abstract

Purpose: Hemoglobin level is associated with outcomes and complications in ST segment Myocardial Infarction (STEMI) patients. The aim of the study is was to evaluate the correlation between admission Hemoglobin level and the incidence of in hospital complications in patients with STEMI treated with primary Percutaneous Intervention (pPCI).

Methodology: This was an observational study recruiting STEMI patients at the National Heart Institute. Admission Hemoglobin level withdrawn and the patients receiving pPCI was followed up during their hospital stay for incidence of complications including new significant arrhythmias, no reflow, stroke, contrast induced nephropathy (CIN). Duration of hospital stay was used as an overall indication of incidence of complication. Patients receiving lytic therapy, parenteral antiplatelet, receiving urgent CABG were excluded from the study. Out of 173 patients presented with STEMI to the National Heart Institute in Egypt and recruited for the study, 106 patients only were included in the study.

Findings: Significant correlation between admission Hemoglobin level and incidence of new significant arrhythmias, no reflow and prolonged duration of hospital stay P-value ($P < 0.009$, $P < 0.000$, Prob > chi2 = 0.001) respectively. There was a significant association between hemoglobin level at the time of admission in STEMI patients and incidence of in-hospital complications including different types of arrhythmias, no reflow phenomenon, and prolonged duration of hospital stay.

Recommendation: All the precautions should be taken by health care providers with efficient team work to avoid no reflow in anemic and polycythemic patients presenting with STEMI in primary intervention.

Keywords: *Hemoglobin, STEMI, PCI*

1.0 INTRODUCTION

Cardiovascular disorders are the number one cause of death worldwide [1]. Acute Coronary Syndrome represents a high risk situation that requires prompt management. Acute Myocardial in the form of Non-ST segment Myocardial Infarction (NSTEMI) or ST segment Myocardial Infarction (STEMI) represents the highest risk and properly timed management is mandatory to save lives. Several guidelines and algorithms have been developed and under continuous update to provide the utmost management strategies for Acute Myocardial Infarction specially STEMI patients.

Primary Percutaneous Intervention (PCI) remains the best choice in treatment of patients presenting with ST segment Myocardial Infarction (STEMI) within 12 hours from chest pain onset [2]. Many patients undergoing Primary PCI develop several complications during their hospital stay despite the revascularization with Primary PCI. These complications could be mechanical such as Ventricular septal rupture, acute mitral regurge, rupture mitral valve chorda. Complications could also be acute heart failure or electrical as different types or arrhythmias such as Atrial Fibrillation or Ventricular tachycardia [3]. The occurrence and immediate management of such complications highly affects the mortality and morbidity of Acute coronary syndrome (ACS) patients specially STEMI patients. Anemia is a frequent comorbidity in cardiovascular disease and is associated with higher mortality as well as increased hospitalization after myocardial infarction, [4] even under mild anemia. There is accumulating evidence that anemia is related to a series of severe complications in cardiovascular diseases (CVD) such as thromboembolic events, bleeding complications, uncontrolled hypertension, and inflammation characterized by elevated levels of inflammatory cytokines [4].

Additionally, polycythemia is much expected in the cardiovascular patients [5]. This could be due to associated chronic decreased oxygen level due to smoking or other factors. Polycythemia might lead to hyper viscosity, and increased thromboembolic risks. This means higher incidence of complications in already a risky group of patients. The objective of this study was to assess the correlation between Hb level whether high or low levels, and the in hospital complications after STEMI in patients undergoing Primary PCI.

2.0 MATERIAL AND METHODS

This was an observational study that included patients presenting with STEMI to the emergency room. Admission Hemoglobin (Hb) level was withdrawn as a part of the regular procedures without delaying the time to revascularization. Only patients receiving pPCI with Drug Eluting Stents (DES) were included and followed up during their hospital stay. The study excluded patients who received lytic therapy, parenteral antiplatelet, coronary thrombus aspiration or who were decided to have emergent coronary artery bypass graft (CABG). This was to keep the sample homogenous and not to impact the study outcomes. The patients were followed up for incidence of major complications including no reflow, new significant arrhythmias, stroke, Contrast Induced Nephropathy (CIN), and finally the total duration of hospital stay was used as a reflection of incidence of complications.

The study included 173 patients who presented to the National Heart Institute directly without transfer from other cardiac centers to avoid delay in presentation time to the emergency room. Total number of 67 patients was excluded from the study sample. The reasons for exclusion were: presentation after the window of 24 hours for intervention, there intervention was decided to be not including primary intervention with drug eluting stents either in the form of urgent Coronary artery Bypass Graft (CABG) or aspiration due to large thrombus burden. This

has made the study group more homogenous and the intervention procedure more identical in almost all the patients. The remaining sample was formed of 106 patients. The patients were recruited at the National Heart Institute in Egypt with more than 173 patients. After applying the exclusion criteria (Lytic therapy, parenteral antiplatelet, urgent CABG, CKD) a homogenous sample of 106 patients was assessed.

2.1 Statistical Analysis

The data was reviewed in light of the aim of the study. Certain comparison points have been defined as the hemoglobin level and incidence of no reflow, hemoglobin level and incidence of new significant arrhythmias, hemoglobin level and incidence of Contrast Induced Nephropathy (CIN), hemoglobin level and incidence of new stroke, and finally hemoglobin level with the duration of hospital stay. The patients were categorized based on Hb level to 3 groups (Polycthemia with Hb level > 16 gm/dl for men and 15 gm/dl for women, Anemia with HB level <12gm/dl for men and <11 for women, Normal if the Hb level is <16, >12gm/dl for men and <15, >11 gm/dl for women) [6].

The analysis was done through Stata software version 6 program. The data was normally distributed when viewed before categorization. The hemoglobin level was categorized as anemic, normal and polycythemic and was compared to the other points of comparison using Chi2/Fischer's exact tests when comparing categorical/ categorical data and ANOVA test was used when the data was categorical/ continuous. Bonferroni test was used following ANOVA test to localize the difference in between the groups. The level of confidence was set to be 95% with a P-value of 0.05.

3.0 RESULTS

There were 82 males and 24 females. The mean age was 56.7 years with a standard deviation of 10.2 years. The youngest age presented was 28 years old and the oldest age was 85 years old. Risk profile of the patient showed 50 patients to be hypertensive and 56 non- hypertensive. Additionally, 45 patients were diabetic while 61 were non- diabetic. Also, 61 patients were smokers in different ranges from mild to heavy smoking habits while 45 patients denied smoking at all. Only 19 patients had previous history of ischemic heart disease either with previous coronary intervention or on chronic medical treatment without intervention.

Regarding incidence of new significant arrhythmias there was a statistically significant difference in between the groups using Fischer's exact test and Pearson chisquare test. This showed higher incidence of arrhythmias in the anemic group more than the normal or the polycythemia groups (P <0.009). Regarding the group with normal hemoglobin level 42 patients showed no significant arrhythmias, while only 17 showed significant arrhythmias with a percentage of only 27%. In the anemic group 18 out of total 29 patients developed significant arrhythmias with more than 62%. In the polycythemia group 9 patients out of 18 total developed significant arrhythmias with 50%.

No reflow was a point of comparison. There has been a highly significant statistical difference between the 3 groups based on the hemoglobin level with the TIMI flow result of the primary percutaneous intervention (P <0.000). There has been a higher incidence of no reflow associated with higher levels of hemoglobin (Polycythemia) group. From 18 patients showing Hb level 16 mg/dl or higher, 12 patients showed less than TIMI 3 flow with a percentage of 67%. In the anemic group, 11 out of 29 patients had TIMI flow results less than 3 with a percentage of 37%. In the group with normal hemoglobin level, only 8 patients out of 59 had no reflow with a percentage of 13.5%. The incidence of stroke was very rare happening in only one patient of the total sample of 106 patients who had normal hemoglobin level. Based on

that, the study results that there is no enough evidence to declare or refuse a significant association between the admission hemoglobin level and cerebrovascular stroke post primary coronary intervention in STEMI patients.

Additionally, there has been no statistically significant difference in between the groups based on hemoglobin level and incidence of Contrast induced nephropathy after primary percutaneous intervention in patients with STEMI (P <0.3). There have been 4 patients of the anemic group exposed to contrast induced nephropathy with a percentage of 16%. The group with normal hemoglobin level showed 3 patients out of 56 with only 5% of the group. Finally only one patient had polycythemia experienced CIN.

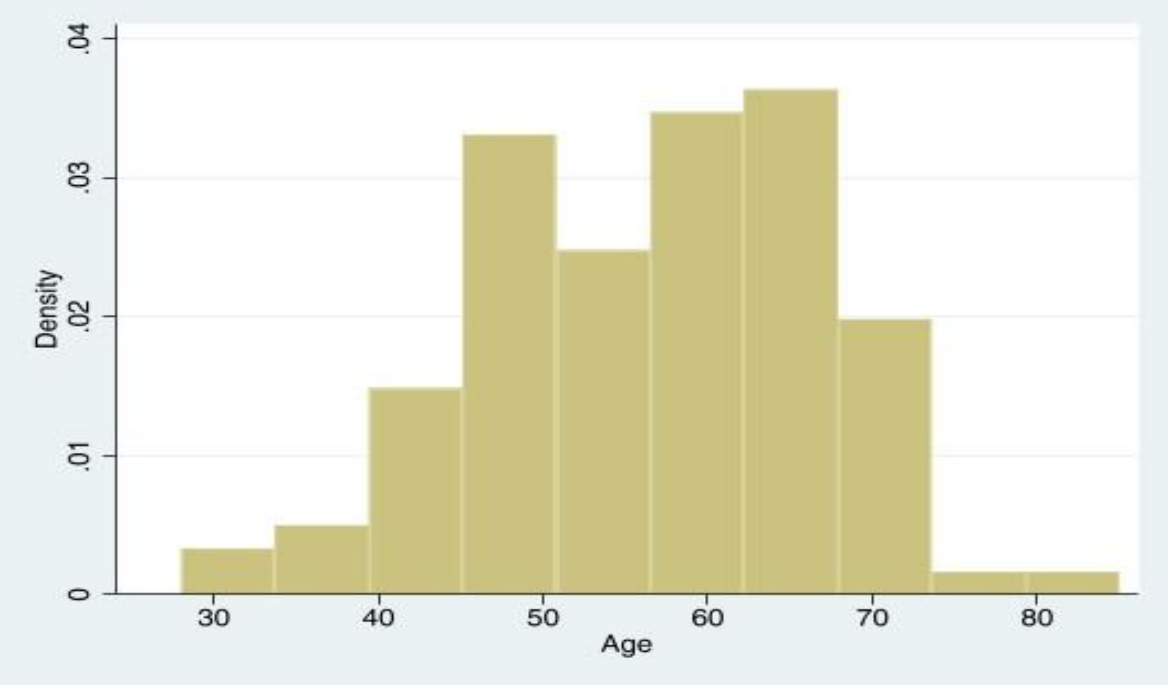

Figure 1: Age distribution

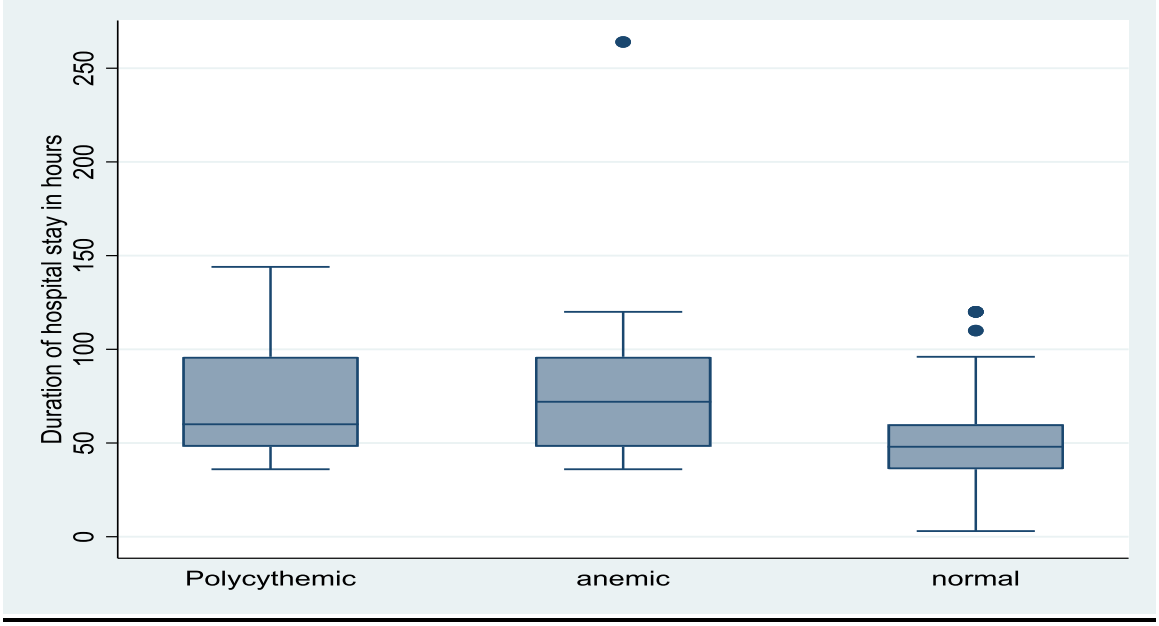

Figure 2: Duration of hospital stay

Table 1: Risk profile

Risk factor	Yes	%	No	%
DM	45	42	61	58
HTN	50	47	56	53
Smoking	61	58	45	42
Previous IHD	19	18	87	82

Table 2: Fischer's exact test

	New significant arrhythmias		
Hemoglobin	**No**	**Yes**	**Total**
Polycythemia	9	9	18
Anemic	11	18	29
Normal	42	17	59
Total	**62**	**44**	**106**

Table 3: Fischer's exact, Pearson Chi square test

	No reflow		
Hemoglobin	**Yes**	**No**	**Total**
Polycythemia	**12**	**6**	**18**
Anemic	**11**	**18**	**29**
Normal	**8**	**51**	**59**
Total	**31**	**75**	**106**

Table 4: Peasrson's Chi square, Fischer's exact test

	New onset of stroke		
Hemoglobin	**Yes**	**No**	**Total**
Polycythemia	**0**	**18**	**18**
Anemic	**0**	**29**	**29**
Normal	**1**	**58**	**59**
Total	**1**	**105**	**106**

Table 5: Peasrson's Chi square, Fischer's exact test

	Contrast Induced Nephropathy (CIN)		
Hemoglobin	**Yes**	**No**	**Total**
Polycythemia	**1**	**17**	**18**
Anemic	**4**	**25**	**25**
Normal	**3**	**56**	**56**
Total	**8**	**98**	**106**

Table 6: One way ANOVA, Bonferroni tests

	Analysis of Variance				
Source	**SS**	**df**	**Ms**	**F**	**Prob > F**
Between groups	14220.8238	2	7110.4119	6.89	0.0016
Within groups	106343.412	103	1032.46031		
Total	**120564.236**	**105**	**1148.23082**		

Barlett's equal variances test: Chi2(2) = 15.0387 Prob > chi2 = 0.001

Table 7: Bonferroni test

	Polycythemic	Anemic
Anemic	11.4253	0.716
Normal	-15.0452	-26.4705
	0.255	0.001

The duration of hospital stay has been considered as an overall estimate of complication incidence. The more prolonged the patients' hospital stay the higher incidence of complications they had. There has been a statistically significant difference between the groups according to the hemoglobin level with a longer duration of stay in the anemic group with hemoglobin level less than 12 mg/dl (P <0.0016).

4.0 DISCUSSION

The sample size was homogenous excluding death as an end point as it is related to multiple variables not just the hemoglobin level, but time to presentation, complexity of coronary anatomy and intervention, performing team experience and available resources, coronary care unit post intervention capacities and complication management. All these factors play major role in determining survival rates post primary intervention especially in STEMI patients.

There were different types of arrhythmia that was reported in the sample during hospital stay. This ranged from infrequent extra systoles either atrial or ventricular till ventricular tachycardia either sustained or non-sustained depending on the period it lasted. The significant arrhythmias -considered in the study- included new incident atrial fibrillation, ventricular tachycardia either

monomorphic or polymorphic. Also, Brady arrhythmias such as Mobitz type 1 or 2, and complete heart block were considered .

Hemoglobin level affected the incidence of significant arrhythmias post Primary percutaneous intervention in STEMI patients. The anemic group with blood hemoglobin level less than 12 mg/dl had the highest incidence of significant arrhythmias (62% of anemic group compared to 50% in the polycythemia group and only 27% in the normal Hb level group, (P value <0.009). This matched with data from similar studies conducted internationally [7]. A recent study published 2022 in Switzerland with a sample size of 1931 patients concluded that anemia is strongly correlated with new onset atrial fibrillation (NOAF) in Intensive Care Unit (ICU) patients. Incidence of NOAF was 12.8% in the anemic group while it was only 9.9% in the total population of study. Despite the fact that causality couldn't be determined, several justifications could lead to this effect.

Myocardial- supply mismatch and atrial ischemia could be an underlying cause of the NOAF. This cause is believed to be very evident in the study dealing with acute coronary syndrome (STEMI patients). The mentioned study determined a stimulatory cut-off value for the incidence of NOAF with Hb level of 9.96 g/dL.[8] Another large perspective cohort study from Japan followed up a cohort of 132,250 Japanese patients for a mean period of 13.8 years. They reached a conclusion that anemia is associated with higher incidence of AF. Despite the fact that their study cohort was all about Chronic Kidney Disease (CKD) patients, the Multivariate Hazard ratio (HR) for the anemic group only was 1.5 with a confidence interval (1.24-1.83) [9].

A large population based nationwide study from Korea published 2020 reached a conclusion that both high and low hemoglobin levels were associated with higher incidence of AF. That conclusion applies to both men and women. Anemia was associated with higher incidence of AF by 11% and 3% in men and women respectively. Additionally, Polycythemia was associated with an elevation of AF incidence by 21% and 36% in men and women respectively. They drew a U-shaped curve of association between Hb levels and AF incidence. This study was conducted on stable patients without ischemic burden, so in acute stress in the form of myocardial infarction abnormal Hb levels were expected to be major determinants of arrhythmia incidence and general outcomes. [10]

In trial to define a causality relationship between anemia and AF, another Korean study published in 2020 performed a Mendelian randomization analysis over 2627 patients who underwent catheter ablation for AF and appropriate medical treatment during a follow up period. They could detect a higher incidence of recurrence of AF in anemic patients post catheter ablation (hazard ratio [HR] 1.45 [1.17–1.80], p = 0.001), yet they failed to detect a genetic bases for that association. [11] The association between abnormal hemoglobin level including both anemia and polycythemia need further research to detect the possible underlying reasons for that association with arrhythmias.

No reflow has been defined in many studies as less than TIMI III flow. Several underlying mechanisms have been described to explain the incidence of no reflow. One major explanation was the damage to microvasculature and endothelia dysfunction taking place due to the ischemic process. Another explanation was the closure of the microvasculature with platelets, leukocytes, and fibrin debris. Different factors play roles in the no reflow phenomenon. This includes duration of ischemia, leukocytes, platelets, micro thrombi, and reperfusion onset. [12] [13] This study focused on Hemoglobin level correlation with incidence of no reflow. A highly statistically significant association between Hemoglobin level and incidence on no reflow in

STEMI patients with primary PCI was detected (P <0.000). This included both the anemic and polycythemia groups with an incidence of 37.5% and 67% respectively .

This matched with results from other international studies. Many studies have been discussing the Hb level and its associations with no reflow. Some studies have gone further in evaluating the Complete Blood Count (CBC) parameters and the incidence of no reflow. A study from Turkey has detected a significant correlation between the Reticulocyte Distribution Width (RDW) at the admission time with incidence of no reflow in STEMI patients. They concluded that RDW more than 14% was 70% sensitive and 64% specific for prediction of no reflow in STEMI patients receiving pPCI (OR 5.89, <95% CI 1.63 -21.24; p value 0.007). [14]

Another study from Turkey that evaluated 3804 patients reached a conclusion that could predict the incidence of no reflow in STEMI patients treated with pPCI (P value <0.001). They went further with determination of a cut off Hb level below which the incidence of no reflow is believed to be the highest. This is Hb level 11.5 mg with a sensitivity of 83% and specificity of 80%. (AUC = 0.844,95% CI: 0.821–0.867; p < 0.001).[15] The noteworthy point here is that 11.5 g/dl level is considered mild type of anemia in many scales. Thus, even mild degrees of anemia are associated with higher incidence of no reflow.

The incidence of both cerebrovascular stroke and contrast induced nephropathy was low with only one patient suffering stroke post pPCI for treatment of STEMI. In addition to that, CIN occurred in only few cases with no statistically significant difference between the different groups of hemoglobin levels. Other studies have detected statistically significant correlation between anemia and incidence of CIN, but this was in patients already known to have Chronic Kidney Disease (CKD). They concluded that the lower the Glomerular Filtration Rate (GFR), the higher the risk of CIN in anemic patients. [16] [17] The difference in the proposed study from these ones is the studied group. While these studies were focusing mainly on the CKD patients in elective settings where coronary angiography was planned, the studied group in this study was patients presenting with STEMI in acute setting where the situation is lifesaving. According to the European Society of Cardiology (ESC) STEMI guidelines the renal function tests are not required before primary intervention.

A study published in the American Heart Journal in 2019 detected a significant correlation between anemia and stroke in anemic acute coronary syndrome patients on the long term after 180 days. [18] Since this is a long term effect, it is believed to be explained by different mechanisms from the stroke occurring in the acute setting. The scope of this study was to assess the in hospital complications only. Duration of hospital stay was used as an overall estimate of the incidence of complications after pPCI in STEMI patients. Longer duration of hospital stay was detected in the anemic group. Several justifications could explain this difference. In anemic group, the stay was prolonged because of the patients' need to receive blood transfusion in severe forms. This was also the case in cases complicated by bleeding either Gastrointestinal or hematoma at the puncture site since almost all the causes included were through femoral access. Follow up period was needed for such patients. Patients with less than TIMI III flow usually were prescribed Tirofiban which was infused over 18-24 hours. A similar follow up day was required in this group of patients .

Patients who experienced significant new arrhythmias such as atrial fibrillation, Ventricular arrhythmias or advanced degrees of heart block required different interventions. These interventions included antiarrhythmic drugs such as amiodarone infusion, electrical cardio-version, and temporary or permanent pacemaker insertion. Long durations of follow up were needed for these cases according to the corresponding guidelines.

5.0 CONCLUSION

There is a significant association between hemoglobin level at the time of admission in STEMI patients and incidence of in-hospital complications including different types of arrhythmias, no reflow phenomenon, and prolonged duration of hospital stay.

6.0 RECOMMENDATIONS

All the precautions should be taken by health care providers with efficient team work to avoid no reflow in anemic and polycythemic patients presenting with STEMI in primary intervention. Further research is needed to assess the correlation between hemoglobin level and in hospital complications.

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