# ORIGINAL ARTICLE CAUSES OF LOW HAEMOGLOBIN LEVEL IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Background: Anaemia is common in patients admitted with acute myocardial infarction (AMI) and can badly affect the short and long term outcomes. Hospital acquired anaemia (HAA) is a type of anaemia which develops in patients during hospitalization with a normal haemoglobin level at the time of admission. There is very scant data regarding the causes for hospital acquired anaemia. This study was conducted in order to determine the causes and baseline characteristics of low haemoglobin level in AMI. Methods: This descriptive study was performed in Lady Reading Hospital Peshawar from 1st June 2013 to 31st May 2014. All the patients with AMI having normal baseline haemoglobin level at admission were included. Haemoglobin was rechecked on 5th day of admission to see whether patient develops HAA or not. Results: A total of 456 consecutive patients with AMI were screened for low haemoglobin. Low haemoglobin level (haemoglobin <12 g/dl in female and <13 g/dl in male) on 4<sup>th</sup> day of admission was found in 84 patients. The mean age of these 84 patients were  $59.4\pm12.4$  years, 39 (46.4%) were female and 45 (54%) were male. Patients with age >70 years were 12 (14.3%). hypertensives were 34 (40.5%), diabetics were 24 (28.6%), CKD was seen in 11 (13.1%), dyslipidemia in 17 (20.2%), and smokers were 16 (19%). Upper GI bleed was found in 23 (27%), lower GI bleed in 7 (8.3%), hematuria in 6 (7.1%), possible coronary intervention in 7 (8.3%), and more than one cause in 14 (16.6%) patients, while no cause was found in 27 (32.14%) patients. Conclusion: One third of patients had no discernible cause of low haemoglobin, while one fourth of patients had isolated upper GI bleed as the main cause for hospital acquired low Hb.

Keywords: Acute MI, Hospital acquired anaemia (HAA), GI bleed, Haemoglobin Pak J Physiol 2017;13(2):22–4

#### **INTRODUCTION**

Anaemia can worsen the coronary artery disease. Anaemia may be a marker of bleeding which further predisposes to adverse outcome and increase morbidity and mortality. There is a possibility that acute myocardial infarction (AMI) patients having low haemoglobin are managed differently than patients with normal haemoglobin level, which can contribute to adverse outcomes. May be these patients are exposed to the extensive investigations, cardiac catheterization and other invasive treatment. This is true for the patients who need invasive treatment with AMI where the bleeding associated with the invasive treatment may outweigh the risk versus benefit associated with early coronary vascularization.

Chronic anaemia mostly have multiple different causes which includes chronic inflammation, nutritional deficiency of iron, vitamin  $B_{12}$ , folic acid, renal, bone marrow disorders and other chronic disorder which may be difficult to manage. In contrast, the usual causes of hospital acquired anaemia (HAA) may be inhospital treatments and blood taken for investigations. HAA is preventable and it may cause worsening of the myocardial ischemia. If associated with adverse outcomes, HAA may be preventable and could represent an actionable target for hospital-based quality improvement efforts. Potential benefits of preventing

HAA may include reducing patient's exposure to the risks from acute anaemia treatments such as blood transfusion, improving clinical outcomes, and reducing costs. However, before resources are directed to HAA prevention, it is necessary to better understand the incidence and predictors of HAA and its association with clinically relevant outcomes.<sup>1,2</sup>

Identifying potentially modifiable risk factors for hospital acquired anaemia and its short-term outcomes in terms of mortality and morbidity is becoming increasingly important. New onset HAA represents a potentially important target for hospitalbased interventions with the goal of improving patient's outcomes. Hospital-acquired anaemia is common during admission with AMI and is associated with greater long term mortality and poorer health status.

# MATERIAL AND METHODS

It was a descriptive, observational cross-sectional study done at Department of Cardiology, Lady Reading Hospital, Peshawar from 1<sup>st</sup> June 2013 to 31<sup>st</sup> May 2014. Data was collected from 456 patients by using consecutive non-probability sampling technique using 20% frequency of hospital acquired anaemia (HAA)<sup>3</sup> in patients with acute myocardial infarction, 95% confidence interval and 5% margin of error under WHO formula for sample size calculation. Patients of both genders aged 18–75 years who had acute myocardial infarction and were not anaemic at admission (i.e., haemoglobin more than 13 gm/dl in males and more than 12 gm/dl in females) were included in study. Patients with elevated cardiac biomarkers from elective coronary revascularization and those who had undergone CABG during hospitalization were excluded. Informed written consent was taken from all the patients with ethical approval from ethical committee of Postgraduate Medical Institute, Lady Reading Hospital Peshawar. Baseline haemoglobin was checked at the time of admission and was repeated on day 5 after initial admission. Bias in the study was controlled by checking haemoglobin from the same laboratory, on Sysmax KX 21<sup>®</sup>.

Data was collected on specially designed proforma and was entered and analyzed using SPSS-17. Frequencies and percentages were calculated for qualitative variables like gender and HAA, and Mean±SD were calculated for quantitative variables. Hospital acquired anaemia (HAA) was stratified among age and gender. Post-stratification Chi-square test was applied, and  $p \le 0.05$  was taken as significant.

### RESULTS

A total of 456 consecutive patients with acute myocardial infarction (AMI) were screened for hospital acquired anaemia. Hospital acquired anaemia (HAA) (Hb <12 g/dl in females and <13 g/dl in males) on 5<sup>th</sup> admission day was found in 84 patients.

The mean age of these 84 patients were 59.4 $\pm$ 12.4 years. In patients found having HAA, 39 (46.4 %) were female and 45 (54%) were male. Patients with age >70 Years were 12 (14.3%) in HAA and 27 (7.2%) in non-HAA (p=0.04). Hypertensives were 34 (40.5%) in HAA and 142 (38.1%) in non-HAA (p=0.05); diabetics were 24 (28.6%) in HAA and 101 (27.1%) in non-HAA (p=0.05). Patients with chronic kidney disease (CKD) were 11 (13.1%) in HAA and 18 (4.8%) in non-HAA (p=0.01). Dyslipidemia was seen in 17 (20.2%) in HAA and 46 (12.4%) in non-HAA (p=0.005). Smokers were 16 (19%) in HAA and 37 (10%) in non-HAA (p=0.04). (Table-1).

The mean age of the rest of 372 patients was  $56.7\pm11.8$  years in patients found to have HAA, 171 (46.1 %) were female and 201 (54%) were male. Upper GI bleed was found in 23 (27%), Lower GI bleed in 7 (8.3%), Hematuria in 6 (7.1%) and possible coronary intervention in 7 (8.3%) and more than one cause was found in 14 (16.6%) while no cause was found in 27 (32.14%) (Table-2).

Mean baseline haemoglobin was  $13.4\pm1.2$  g/dl in males, and  $13.1\pm1.31$  g/dl in females. Mean followup haemoglobin was  $10.9\pm1.72$  g/dl in males and  $10.0\pm1.67$  in females (Table-3).

| Table-1: Characteristics of subjects with and |
|---|
| without hospital acquired anaemia with acute  |
| myocardial infarction [n(%)]                  |

| my ocar diar infar celon [n( / 0)] |            |                |       |  |
|------------------------------------|------------|----------------|-------|--|
| Characteristics                    | HAA (n=84) | No HAA (n=372) | р     |  |
| Male                               | 45 (54)    | 201 (54)       | 0.68  |  |
| Female                             | 39 (46.4)  | 171 (46.1)     | 0.52  |  |
| Diabetics                          | 24 (28.6)  | 101 (27.1)     | 0.05  |  |
| Hypertensive                       | 34 (40.5)  | 142 (38.1)     | 0.05  |  |
| Smokers                            | 16 (19)    | 37 (10)        | 0.04  |  |
| Age >70 Years                      | 12 (14.3)  | 27 (7.2)       | 0.04  |  |
| CKD                                | 11 (13.1)  | 18 (4.8)       | 0.01  |  |
| Dyslipidemia                       | 17 (20.2)  | 46 (12.4)      | 0.005 |  |

| Table-2: Causes of hospital acquired anaem | Table-2: | e-2: Causes | s of hospital | acquired anaemia |
|--|----------|-------------|---------------|------------------|
|--|----------|-------------|---------------|------------------|

| Cause                                      | Frequency | Percentage |
|--|-----------|------------|
| Isolated upper GI bleed                    | 23        | 27.0       |
| Isolated lower GI bleed                    | 7         | 8.3        |
| Isolated hematuria                         | 6         | 7.1        |
| Bleeding during/from coronary intervention | 7         | 8.3        |
| Causes more than one                       | 14        | 16.6       |
| Unknown                                    | 27        | 32.14      |

Table-3: Haemoglobin levels of the subjects

| Characteristics                      | Group A        |
|--------------------------------------|----------------|
| Mean Baseline Haemoglobin in male    | 13.4±1.2 g/dl  |
| Mean Baseline Haemoglobin in female  | 13.1±1.31 g/dl |
| Mean Follow up Haemoglobin in male   | 10.9±1.72 g/dl |
| Mean follow up Haemoglobin in female | 10.0±1.67 g/dl |

### DISCUSSION

Although the main cause of anaemia in this part of the world is nutritional but as we have excluded the base line anaemic patient so our study was mainly focus on the acquired causes in hospital set up. In most of the patients there is usually no obvious cause for anaemia. Increased blood removal for various investigation by phlebotomist may be possible cause for hospital acquired anaemia in acute myocardial infarction specially those patients which needs highest level of care in Intensive cardiac care setting .It has been found that almost one fourth to one fifth of patients who had normal haemoglobin at admission developed anaemia by hospital discharge in our study cohort. Although inpatient bleeding is a strong predictor for HAA, most of these patients did not have obvious bleeding event during hospital admission, suggesting that HAA is not simply because of in hospital bleeding events. Similarly in our study no documented cause is found in about one third of patients with hospital acquired anaemia. Importantly, moderate-severe HAA is also was associated with increased short term and longterm mortality, independent of AMI severity and regardless of the presence and extent of bleeding, suggesting that HAA is prognostically important in its own right and may represent a target for prevention efforts in multiple studies.<sup>1-3</sup>

In our study the most frequent cause for HAA was upper GI bleed which was found in about 27% of patient. While about 17% of patients have multiple causes for HAA. Most of patient in our set up is treated with fibrinolytic therapy as compare to western

population where most of them are treated with percutaneous coronary interventions. The streptokinase is mainstay of treatment in our hospital. So GI and urinary tract bleeding is most common with streptokinase. Also most of the time there is bleeding and oozing from cannulation site also. Also in our setup only those patient are treated with percutaneous coronary interventions that have recurrent symptoms in spite of thrombolytic therapy. Our findings support prior observations by Sattur et al<sup>4</sup>, who reported, in a his study, that incident anaemia in PCI patients was independently associated with long-term mortality. In our study PCI were performed in about 8.3% of the patients. The anaemia threshold used in that study (Hb  $\leq 10$  g/dl) was relatively low, potentially leading to overestimation of the association between anaemia and outcomes. Our study produced similar results with that of Selisbury et al, i.e., HAA is more frequent in patients with low BMI, old age, diabetic, CKD and those with coronary interventions. Our study provides new insights by examining a large, contemporary cohort, focusing on patients with AMI and using standard definitions of anaemia. Moreover, our analysis provides new data about variability of HAA. Our findings have important clinical implications. Several of the correlates of HAA are also associated with chronic anaemia and bleeding in AMI patients (such as age, female sex, acute heart failure, and chronic kidney disease)5-8 and probably identify a high-risk population with poor haematopoietic reserve. On the other hand, some independent correlates are hospital-based processes and complications (use of glycoprotein IIb/IIIa inhibitors and bleeding) and could be targets for prevention efforts. Several of these variables are associated with bleeding, 7-9 and the use of bleeding avoidance measures, such as radial artery access for percutaneous coronary intervention, closure devices, smaller sheaths, or alternative antithrombotic agents such as bivalirudin in place of heparin and a glycoprotein IIb/IIIa inhibitor, present potential opportunities for improvement.<sup>10-13</sup>

# CONCLUSION

About one third of anaemic patients on  $5^{\text{th}}$  day of admission had no discernable cause while 27% of patients had isolated upper GI bleed. Most of the anaemic patients were of old age, dyslipidemic, and/or having chronic kidney disease.

#### REFRENCES

- Salisbury AC, Alexander KP, Reid KJ, Masoudi FA, Rathore SS, Wang TY, *et al.* Incidence, correlates, and outcomes of acute hospital-acquired anemia in patients with acute myocardial infarction. Circ C ardiovasc Qual Outcomes 2010;3:337–46.
- Salisbury AC, Amin AP, Reid KJ, Wang TY, Masoudi FA, Chan PS, *et al.* Hospital-acquired anemia and in-hospital mortality in patients with acute myocardial infarction. Am Heart J 2011;162:300–9.
- Salisbury AC, Reid KJ, Alexander KP, Masoudi FA, Lai SM, Chan PS, *et al.* Diagnostic blood loss from phlebotomy and hospitalacquired anemia during acute myocardial infarction. Arch Intern Med 2011;171:1646–53.
- Sattur S, Harjai KJ, Narula A, Devarakonda S, Orshaw P, Yaeger K. The influence of anemia after percutaneous coronary intervention on clinical outcomes. Clin Cardiol 2009;32(7):373–9.
- Wu WC, Rathore SS, Wang Y, Radford MJ, Krumholz HM. Blood transfusion in elderly patients with acute myocardial infarction. N Engl J Med 2001;345:1230–6.
- Aronson D, Suleiman M, Agmon Y, Suleiman A, Blich M, Kapeliovich M, *et al.* Changes in haemoglobin levels during hospital course and long-term outcome after acute myocardial infarction. Eur Heart J 2007;28:1289–96.
- Subherwal S, Bach RG, Chen AY, Gage BF, Rao SV, Newby LK, et al. Baseline risk of major bleeding in non-ST-segment elevation myocardial infarction: the CRUSADE (Can rapid risk stratification of unstable angina patients suppress adverse outcomes with early implementation of the ACC/AHA Guidelines) Bleeding Score. Circulation 2009;119:1873–82.
- Moscucci M, Fox KA, Cannon CP, Klein W, Lopez-Sendon J, Montalescot G, *et al.* Predictors of major bleeding in acute coronary syndromes: the Global Registry of Acute Coronary Events (GRACE). Eur Heart J 2003;24:1815–23.
- Rao SV, O'Grady K, Pieper KS, Granger CB, Newby LK, Van de Werf F, *et al.* Impact of bleeding severity on clinical outcomes among patients with acute coronary syndromes. Am J Cardiol 2005;96:1200–6.
- 10. Rao SV, Ou FS, Wang TY, Roe MT, Brindis R, Rumsfeld JS, et al. Trends in the prevalence and outcomes of radial and femoral approaches to percutaneous coronary intervention: a report from the National Cardiovascular Data Registry. JACC Cardiovasc Interv 2008;1(4):379–86.
- 11. Cantor WJ, Mahaffey KW, Huang Z, Das P, Gulba DC, Glezer S, *et al.* Bleeding complications in patients with acute coronary syndrome undergoing early invasive management can be reduced with radial access, smaller sheath sizes, and timely sheath removal. Catheter Cardiovasc Interv 2007;69:73–83.
- 12. Mehran R, Lansky AJ, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, *et al.* Bivalirudin in patients undergoing primary angioplasty for acute myocardial infarction (HORIZONS-AMI): 1year results of a randomized controlled trial. Lancet 2009;374:1149–59.
- 13. Stone GW, White HD, Ohman EM, Bertrand ME, Lincoff AM, McLaurin BT, *et al.* Bivalirudin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a subgroup analysis from the Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trial. Lancet 2007;369:907– 19.

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