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FREQUENCY OF HOSPITAL ACQUIRED ANEMIA (HAA) IN ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Objective: To determine the frequency of hospital acquired anemia in patients of acute myocardial infarction.

Methodology: This cross sectional observational study was conducted from 6th June 2014 to 6th December 2014 at Cardiology Department, Lady Reading Hospital Peshawar. In this study, patients who were admitted with acute myocardial infarction and normal baseline hemoglobin level at the time of admission (according to WHO criteria) were included. Hemoglobin was rechecked on 5th day of admission to see whether patient develops hospital acquired anemia.

Results: A total of 246 patients with acute myocardial infarction (AMI) were included in the study. Of these patients 137(55.69%) were males. Mean age was 57.9±11 years. About 58 (27.57%) were hypertensive while 48(19.5%) were diabetics. Chronic kidney disease was found in 9(3.65%). Mean baseline hemoglobin was 14.3±1.2 g/dl in males and 13.42±1.31 g/dl in females while on follow up it was found to be 11.4±1.72g/dl and 10.3 ±1.67g/dl in males and females respectively. Hospital acquired anemia (HAA) (hemoglobin< 12g/dl in females and <13g/dl in males) on 5th admission day was found in 50(20.32%). Patients found to have HAA, 23 (46%) were females and 27 (54%) were males.

Conclusion: HAA is common in AMI patients who are treated medically or with percutaneous coronary intervention.

Key Words: Acute Myocardial Infarction, Hospital Acquired Anemia (HAA), GI Bleed

INTRODUCTION

Anemia at admission is a frequent finding in patients with acute coronary syndrome (ACS), and has been observed in up to 15% of the patients with myocardial infarction, reaching 43% in elderly patients. Anemia can adversely influence prognosis in these patients through various mechanisms; by reducing oxygen in the blood and, by increasing myocardial oxygen consumption due to elevated cardiac output to maintain appropriate tissue oxygenation.

Anemia in patients hospitalized with acute myocardial infarction (AMI) is associated with increased mortality, higher hospitalization, and worse health-related quality of life. However, most prior studies of anemia in the setting of AMI have evaluated chronic anemia (present at admission) or short-term changes in hemoglobin during hospitalization. Little research has focused on hospital-acquired anemia (HAA), which develops acutely during AMI admission in those with normal baseline hemoglobin (Hb). Given that the etiology of HAA, an acute phenomenon, is likely to be different from that of chronic anemia. It is important to understand the risk factors for its development and its prognostic implications. In contrast to chronic anemia, which portends a poor prognosis, HAA may be preventable by modifying processes of care, such as using measures to prevent peri-procedural bleeding and limiting diagnostic blood loss from phlebotomy. HAA develops in about 20% of patients admitted with acute myocardial infarction. Both chronic anemia and hospital-acquired anemia (HAA) are associated with greater mortality and worse health status in patients with acute myocardial infarction (AMI). HAA could potentially be prevented by implementing strategies to reduce blood loss in high risk patients. Although in-hospital bleeding is a risk factor for HAA and is already recognized as an important target for quality improvement, HAA seems to be multifactorial and commonly develops in the absence of bleeding. Several factors other than bleeding might be associated with HAA, including blunted hematopoetic response and phlebotomy.

Limiting scheduled phlebotomy, use of pediatric blood tubes, and more frequent use of stored serum specimens in high-risk patients may all minimize diagnostic blood loss (DBL) and could reduce the incidence and severity of HAA.[1]

It is unclear to what extent HAA during AMI hospitalization resolves quickly in follow-up or persists after the acute episode of care. Moreover, it is unknown whether clinically important outcomes, such as mortality and health status, differ between patients with transient and persistent HAA. Understanding the patterns of HAA recovery and their association with clinical outcomes, would further support the importance of preventing and recognizing HAA. Furthermore, it may help identify patients at risk of poor recovery after AMI who may benefit from more intensive follow-up.[2]

The aim of this study is to determine the frequency of hospital acquired anemia in patients admitted with acute myocardial infarction whose hemoglobin level was normal at the time of admission.

METHODOLOGY

This is a cross sectional observational study, which was conducted at Department of Cardiology, Lady Reading Hospital, Peshawar from 6th June 2014 to 6th December 2014. Sampling was done by consecutive non probability technique. All patients of both genders with age 18-75 years who fulfilled the criteria of acute myocardial infarction were included. AMI was defined as typical rise and fall of biochemical markers of myocardial necrosis with at least one of the following:

Ischemic symptoms (severe chest pain radiating to left jaw and arm, associated with sweating and nausea or vomiting). Development of pathologic Q waves in the ECG. Electrocardiographic changes indicative of ischemia (ST-segment elevation or depression). Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

Patients who were not anemic at admission (i.e. hemoglobin more than 13gm/dl in males and more than 12gm/dl in females), while patients with elevated cardiac biomarkers from elective coronary revascularization or patients who had CABG during hospitalization were excluded.

Hospital Acquired Anemia (HAA) was defined with the criteria of the World Health Organization (hemoglobin <13 g/dL in men and <12g/dL in women) on 5th hospital day in patients who were having normal hemoglobin at the time of admission.

Informed written consent was taken from all the patients. Baseline hemoglobin was checked at the time of admission and was repeated on day 5 after initial admission. Bias in the study was controlled by checking hemoglobin from the same laboratory i.e. main laboratory of Lady Reading Hospital Peshawar using same analyzer machine (sysmax KX 21). Exclusion criteria was strictly followed to reduce the bias. The data was entered in specially designed proforma. Data was entered and analyzed by SPSS version 17. Frequencies and percentages were calculated for qualitative variables like gender and HAA, while mean $\pm$ standard deviation were calculated for quantitative variables like age and duration. Hospital acquired anemia (HAA) was stratified among age and gender to see effect modification. Results were presented as tables and charts. Post stratification chi-square test was applied. $P \leqslant 0.05$ was taken as significant.

RESULTS

A total of 246 patients with acute myocardial infarction (AMI) were included in the study. Of these patients

137(55.69%) were males. Mean age was 57.9±11 years. Mean body weight was 73.8±6.9 Kg. Of the total, 58(27.57%) were hypertensive where as diabetes mellitus was found in 48(19.5%) of study population. Chronic kidney disease was found in 9(3.65%) of patients while 34 (13.82%) were smoker. Dyslipedemia was found in 27(10.97%). Hospital acquired anemia (HAA) (hemoglobin< 12g/dl in female and <13g/dl in male) on 5th admission day was found in 50(20.32%) patients. Of them 15 (30%) patients were having acute anterior wall MI, 05 (10%) patients had acute anterior and inferior wall MI, 10 (20%) patients had isolated inferior wall MI, 06(12%) patients with acute inferior wall MI also had right ventricular extension, 06 (12%) patients with acute acute inferioroposterior wall MI, 04(8%) patients got inferolateral wall MI while 04 (8%) patients had acute inferior wall MI with posterior and lateral wall extension. Mean baseline hemoglobin was 14.3±1.2g/dl in males and 13.42±1.31 g/dl in females. Mean follow up hemoglobin was 11.4±1.72g/dl and 10.3 ±1.67g/dl in males and females respectively. In patients found to have HAA, 23(46 %) were female and 27(54%) were male.

DISCUSSION

We found that almost one fifth of patients who had normal hemoglobin at admission developed anemia by hospital discharge in our study. Although inpatient bleeding was a strong independent predictor of HAA, most patients with HAA did not have a documented bleeding event during hospitalization, suggesting that HAA is not simply a surrogate for in-hospital bleeding events. Importantly, moderate-severe HAA was associated with increased long-term 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.[1,3]

Table 1: Baseline Characteristics of Study Population

Baseline characteristics	Total number	Percentages
Age±SD	57.9±11 years	
Male	137	55.69%
Female	109	44.30%
Weight(Kg)	73.8±6.9 Kg	
Hypertension	58	27.57%
Diabetes Mellitus	48	19.5%
Chronic kidney disease	9	3.65%
Smoker	34	13.82%
Dyslipedemia	27	10.97%
Streptokinase given	198	80.5%

Several studies about the prognostic value of anemia associated with evident bleeding or with large falls in levels. In a recent study of patients who had suffered myocardial infarction, showed that for each 1 g/dl fall in admission hemoglobin level, the risk of all-cause mortality of heart failure after 2 years increased proportionally and independently.

On the other hand, it has been reported that the admission hemoglobin level is an independent predictor in patients with ACS. Thus, in a large study of elderly patients and myocardial infarction, 30-day mortality was associated with lower admission hematocrit level.[4]

It has been observed in a study by Salisbury et al. that significant variability occur in incidence of HAA across hospital sites.[3] Prior studies have established the short and long-term prognostic significance of chronic anemia, and more recent reports have examined the association between changes in Hb during hospitalization and outcomes.[5-8,9] Aronson et al, found that decline in Hb during AMI hospitalization was independently associated with mortality.[10] Their analyses included both patients with baseline anemia and new onset anemia during hospitalization. It is unclear from these studies whether the relationship between inpatient Hb decline and survival is present among those with normal baseline Hb. A study by Selisbury et al, extends these insights by defining a population with acute anemia, a potentially preventable condition, and observing that moderate-severe HAA is associated with an increased risk of mortality of similar magnitude to those with chronic anemia. Our findings also support observations by Sattur et al, in a single-center study showed that incident anemia in PCI patients was independently associated with long-term mortality.[11] In our study PCI were performed in about 42% of patients. The anemia threshold used in that study (Hgb ≤10 g/dL) was relatively low, potentially leading to overestimation of the association between anemia 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, multicenter cohort, focusing on patients with AMI and using standard definitions of anemia. Moreover, our analyses provided new data about the variability of HAA. Our findings have important clinical implications. Several of the correlates of HAA are also associated with chronic anemia and bleeding in AMI patients (such as age, female sex, acute heart failure, and chronic kidney disease) and probably identify a high-risk population with poor hematopoietic reserve.[6,10,12,13] 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, 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.[12-14,15-18] Salisbury et al, found strong association between moderate-severe HAA and 12-month mortality, even after adjustment for the presence and severity of bleeding, indicating that HAA is distinct from bleeding and is clinically important. Although the major causes of HAA among those without documented bleeding remains unclear, it may be related to subclinical blood loss (such as frequent phlebotomy), undetected minor per procedural bleeding (nuisance bleeding). However, we adjusted the discharge hemoglobin values for in hospital blood transfusion to minimize this issue. It is also possible that frequent scheduled phlebotomy was associated with HAA, however this data was not included in registry. Our definition of chronic anemia was any anemia present at admission, which could have captured sub-acute cases in addition to those with long term anemia. Finally, these observational data do not allow us to draw conclusions about causal relationships between HAA and mortality, and it remains unclear whether HAA is a marker for or a mediator of poor outcomes. HAA is common in AMI patients who are treated medically or with percutaneous coronary intervention. Development of moderate-severe HAA is associated with higher mortality and worse health status in the first year after AMI, independent of documented in-hospital bleeding.[1,3] Better understanding of whether prevention of HAA is feasible and can improve patient outcomes is needed.

In our study, 1 in 5 patients who did not have baseline anemia (and did not undergo coronary bypass surgery) developed moderate to severe HAA. Several factors contribute to development of HAA. Some of these are not modifiable (age, sex, chronic kidney disease, acute inflammation from AMI), but two of these are clearly under the control of health care providers: prevention of peri procedural bleeding and minimization of phlebotomy.[19,20] Alternative anticoagulants such as bivalirudin, closure devices, and radial access for coronary angiography all reduce the incidence of periprocedural bleeding.[15,17,18,21] However, no clear bleeding event is identified in patients with HAA.[11,19] Phlebotomy has been suggested as a cause of in-hospital hemoglobin level declines in patients with AMI.[22] Our findings have important clinical implications. Diagnostic blood loss remained relatively constant throughout the course of hospital stay after the first 2 days of hospitalization and was particularly high among patients with long stay. Since most diagnostic evaluation and therapeutic interventions often occur early during AMI hospitalization, it is likely that much of the blood taken later during hospitalization represents routine, laboratory investigations that could lead to ongoing blood loss. Our findings are likely generalizable to other populations of seriously ill medical patients. In this regard, further studies that establish whether minimizing DBL can prevent HAA and improve patient outcomes could have broad implications for hospitalized patients.

LIMITATIONS

Several limitations of our study should be considered. First, we were unable to assess the impact of hemodilution from intravenous fluids or fluid retention; however, since large hemoglobin level declines were required to develop HAA, hemodilution is an unlikely culprit for HAA in our patient population. Second, hemoglobin assessments were not performed at regular intervals because the Health Facts database reflects routine clinical practice. Although there was variability in the number and timing of hemoglobin assessments, these data are generalizable to real-world clinical practices in which these tests are obtained at the discretion of the treating physician. Third, we used a single threshold for moderate to severe HAA of hemoglobin levels lower than 11 g/dL. Ideally, age, sex, and race specific thresholds would be used to define moderate to severe HAA; however, there are no reports in the literature that describe different thresholds for anemia severity by sex, race, or age. In addition, using the WHO anemia definition (which is not race specific) did not change our results.[18] Finally, patients with HAA had greater disease severity and more comorbidities than patients who did not, as indicated by their demographics, comorbidities, and in-hospital complications. Given the retrospective nature of these analyses, residual and unmeasured confounding cannot be excluded, and no causal inference can be drawn from these observational data. Randomized trials are needed to test the hypothesis that reducing phlebotomy prevents HAA and improves patient's outcomes.

CONCLUSION

Blood loss from phlebotomy is substantial in patients with AMI, varies across hospitals, and is independently associated with the development of HAA. Studies are needed to test whether strategies that limit both the number of blood draws and the volume of blood removed for diagnostic testing can prevent HAA and improve clinical outcomes in patients with AMI.

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