



EFFECT OF ORAL IRON SUPPLEMENT IN POST MI PATIENTS DISCHARGED WITH MILD TO MODERATE PERSISTENT HOSPITAL ACQUIRED ANEMIA.

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ABSTRACT

Objectives: Evaluation of the outcomes of iron supplement in the patients hospital acquired anemia (HAA) in Acute myocardial infarction patients who survived their initial hospitalization at discharge. **Material and methods:** Prospective, randomized, comparative, open label, parallel study done on 40 patients who were divided into two groups of 20 patients each and were randomized to receive treatment either with oral iron therapy 100mg BD (Group 1)

for 6 months and in Group 2 standard treatment of Post MI was given. Calculating Physical component score did efficacy assessment and mental component score using SF12 form. Observing for the side effects due to iron therapy also did safety assessment. **Results:** There was statistically significant increase in Hgb concentration at 1 month onwards after taking iron therapy and it subsequently kept on increasing till 6 months. Also the physical component score and mental component score was significantly increased at 3 and 6 months $p < .005$ **Conclusion:** Iron therapy significantly improved Hgb concentration and SF12. Physical component score and mental component score were also significantly increased.

KEYWORDS: Hospital Acquired anemia, Short form 12, Hemoglobin, oral iron.

INTRODUCTION

Hospital Acquired Anemia (HAA) is defined as anemia that develops during hospitalization in patients who have a normal admission Hgb level.^[1] Both chronic anemia, which is present at the time of admission to the hospital and hospital-acquired anemia (HAA), which is a new-onset anemia that develops during admission with AMI are associated with greater mortality and poorer health status in patients with AMI.^[2,3]

The risk factors, for HAA development, which can be modifiable, are unrecognized iron deficiency, periprocedural phlebotomy, bleeding episodes. The nonmodifiable^[4] risk factors are age, gender, underlining comorbidities like renal disease, Heart failure, acute inflammation from myocardial necrosis and hemodilution. The longer the duration of stay in hospital accounts for more chances of developing HAA.^[5] Patients who received thrombolytic also had greater phlebotomy volumes over the first 24 hours of hospitalization. The conclusion is higher phlebotomy volumes were more likely contributors to the larger hemoglobin declines in the thrombolysis group. Others can be reinfusion kit arterial line replacement.^[6,7] Erythropoietin resistance and down regulation of iron metabolism also cause anemia by immunity activation.^[8]

Chronic anemia, at the time of admission to the hospital and HAA develops during hospitalization in patients with normal hemoglobin level at admission, are associated with greater mortality and worse health status in patients with acute myocardial infarction (AMI).^[9-13] The origin of anemia is mostly multifactorial. However, cause of anemia is understood to be due to malnutrition, iron deficiency, bone marrow depression, certain medication and diagnostic phlebotomy.^[14-17] Renal dysfunction is a known marker with an adverse prognosis in patients with acute myocardial infarction,^[18] especially in those who have hospital-acquired anemia.. Furthermore, anemia is associated with changes in left ventricular anatomy in patients with chronic kidney disease and ventricular diastolic and/or systolic dysfunction and a consequent increased risk of death.^[19] In Indian population, concentration of Hgb 8-11 g/dl in females and 9-11 g/dl in males in considered as mild to moderate cases of HAA. This classification has been previously shown to be more accurate than World Health Organization (WHO).^[20] The prevalence of HAA ranges from 6.4% to 45%.^[21-23] Only a very few studies have been done on the short term and long term effects of anemia in ST-segment elevation myocardial infarction (STEMI) and non ST-segment elevation myocardial infarction (NSTEMI).^[24] The complications of HAA including heart

failure, recurrent ischemia, re-infarction, cardiogenic shock, stroke, major bleed, and death can occur even after discharge from the hospital. Hospital-acquired anemia and post-myocardial infarction have poor short term and long-term prognosis.^[25-27]

The aim of this study was to know whether oral iron supplements provided better clinical outcome including normalization of HAA, increased Hemoglobin concentration, improved status of health and increased survival of health

MATERIAL AND METHODS

Proposed study was a prospective, controlled and open label comparative clinical study conducted with the collaboration of Departments of Pharmacology, Cardiology and Pathology, Pt. B.D. Sharma, Post Graduate Institute of Medical Sciences, Rohtak. Patients were screened in accordance with the principles of good clinical practices (ICH-GCP) and declaration of Helsinki. Written informed consent was taken from all the eligible patients that were enrolled following inclusion and exclusion criteria of the study. After getting approval from institutional review board screening of 100 post AMI patients presenting in cardiology OPD with history of acute myocardial infarction admitted in ICCU with normal hemoglobin concentration developed HAA in hospital and survived at discharge with persistent HAA. out of 100 post MI patients, 40 patients with mild to moderate persistent HAA were enrolled for the study following inclusion and exclusion criteria.

The patients were enrolled for the study by following inclusion criteria.

1. Patient of either sex aged > 18 yrs.
2. Patients of acute myocardial infarction admitted in cardiology ward with normal hemoglobin levels and later on developed hospital acquired anemia (HAA) during hospitalization (decline of hemoglobin concentration by 2-4 g/dl)
3. AMI patients with mild to moderate HAA (male hemoglobin concentration less than 9-10g/dl and female hemoglobin concentration less than 8-10g/dl) with microcytic hypochromic anemia at discharge from the hospital.
4. Post-MI patients willing to give written informed consent for the study.

The patients were excluded from the study by following exclusion criteria.

1. AMI patients with the presence of anemia at admission and developed severe grade of HAA in hospital requiring urgent management.
2. Patients developed macrocytic hyper chromic anemia in hospital

3. Pre-existing procedure of drug eluting coronary stent implantation.
4. Patients needed an emergency surgery for any reason of MI.
5. Patients with Severe ventricular dysfunction.
6. Patients having active peptic ulcer or upper gastrointestinal bleeding prior 3months and presence of occult blood in stool or gross hematuria.
7. Active bacterial endocarditis or other active infection
8. History of bleeding diathesis.
9. Patients of end stage renal disease.
10. Pregnancy, lactation or parturition within last 90 days

They were divided randomly into two groups; each group had 20 patients. **Group 1** received 100mg ferrous sulfate (iron) two times a day orally after meal daily for 6 months. **Group 2:** received placebo along with standard medication of post-MI the post-MI patients with mild to moderate HAA received standard treatment of post MI in addition .The patients were instructed to do follow up at 1,3 and 6 months of discharge from hospital. Clinical examination, status of health, laboratory investigation and safety profile of iron supplement were done on each visit.

Primary End Points

- Assessment of Hospital- Acquired Anemia (levels of hemoglobin)
- Peripheral blood film or Reticulocyte count
- Health status
- Post MI survival rate / mortality

Secondary End Point

1. Mean Corpuscular Volume (MCV)
2. Mean Corpuscular Hemoglobin (MCH)
3. Mean Corpuscular Hemoglobin Concentration (MCHC)
4. Packed cell volume (PCV)
5. Hematocrit count

Health status were assessed using short-term form -12, Physical component summary score and mental component summary score (SF-12 PCS and MCS).^[29] The SF-12 is multipurpose short form survey with 12 questions. It measures general health domains, physical functioning subdomains, bodily pain subdomains, vitality subdomains, emotional subdomain,

mental health subdomain and social functioning subdomain The questions were combined, scored, and weighted to create two scales that provide glimpses into mental and physical functioning and overall health-related-quality of life

Patient having major toxicity to oral iron therapy necessitating discontinuation of iron therapy were withdrawn from study and appropriate treatment given.

Both descriptive and analytical statistics was used in the study as was appropriate Collected data were entered in the MS Excel spread sheet, coded appropriately and later cleaned for any possible typing errors. Analysis was carried out using SPSS (Statistical Package for Social Studies). The data were pooled and presented as the mean $\pm$ standard error of mean.. All tests were performed at a 5% level significance, thus an association was significant if the value was less than 0.05 (p value < 0.05)

RESULTS

A total of 80 patients of post myocardial infarction patients with anemia were screened for the study. Out of these 27 patients were excluded as they did not match the predefined inclusion criteria i.e. 8 patients had SBP>160 mm of Hg and DBP >100 mm of Hg, 3 patients had uncorrected primary valvular disease, 7 patients had severe renal disease, 5 patients had unstable angina and 4 patients underwent recent cardiac surgery. Only 40 patients completed the study and the rest were lost to follow up (Flow chart – 1) .The results of the present study on the impact of oral iron therapy in the changes in Hgb concentration, status of health were analysed statistically and are discussed.

The baseline characteristics of the study population are shown in Table 1. All post-MI patients included for the study had following demographic patterns.

TABLE 1: STUDY POPULATION CHARACTERISTICS.

Demographic parameters	GROUP I (n=20)	GROUP II (n=)
Age (years)	57.45 $\pm$ 11.830	55.95 $\pm$ 14.214
Male:Female	16/4	16/4
SBP:DBP	131.70 $\pm$ 2.084/86.20 $\pm$ 1.472	133.60 $\pm$ 1.690/85.90 $\pm$ 1.031

Age is expressed as Mean $\pm$ S.D

1. Hemoglobin Concentrations

Hemoglobin (Hgb)

On intragroup analysis, as shown in table 2 and figure 1, there was significant increase in Hgb values after 3 and 6 months ($p < .001$) of oral iron treatment in group I. On the other hand there was decrease in Hgb values after 1, 3 and 6 month of treatment in group II as compared to the pre-treatment period. So there was improvement of Hgb values in group I, whereas there was decline in Hgb values in group II. At 1 month in both groups the changes were not significant compared to pretreatment condition.

Intergroup analysis of Hgb values showed statistical significant difference after 3 and 6 months of treatment i.e. there was greater improvement of Hgb values in group I as compared to group II after 3 and 6 months of treatment. $P < .001$.

TABLE 2

Group	Pre-treatment	After treatment		
		1 month	3 month	6 month
1	9.730±.237	10.410±.23	11.125±.196	11.880±.142
2	10.005±.218	9.870±.199	9.775±.219	9.805±.217

PHYSICAL COMPONENT SCORE (PCS) OF SF- 12

On intragroup analysis, as shown in table 3 and figure 2 there was significant increase in PCS scores after 1,3 and 6 months of oral iron treatment in group I and group II, as compared to the pre-treatment period. In group 2 from 3 month to 6 month the changes were not significant. So there was improvement in physical quality of life in both the groups. **Intergroup analysis**, of PCS scores showed statistical significant difference ($p < 0.001$) after 1,3 and 6 months of treatment i.e. there was greater improvement in quality of life in group I as compared to group II after 1 month, 3 and 6 months of treatment.

TABLE 3: Effect of oral iron administration on physical component score (pcs) of sf- 12 in patients of acute myocardial infarction with hospital acquired anaemia.

Group	Pre-treatment	After treatment		
		1 month	3 month	6 month
1	35.750±.530	45.505±.572	55.055±.554	57.235±.358
2	36.320±.469	39.540±.917	44.875±.730	44.455±.825

MENTAL COMPONENT SCORE (MCS) OF SF- 12

On intragroup analysis, as shown in table 4 and figure 3 there was significant increase in MCS scores after 1,3 and 6 months of oral iron treatment in group I and in group II, as

compared to the pre-treatment period there was a significant decrease in the MCS score $p < 0.012$.

Intergroup analysis of MCS scores showed statistical significant difference ($p < 0.001$) after 1, 3 and 6 months of treatment i.e. there was greater improvement in mental status of patients in group I as compared to group II after 1 month, 3 and 6 months of treatment.

TABLE 4: Effect Of Oral Iron Administration On Mental Component Score (Mcs) Of Sf- 12 In Patients Of Acute Myocardial Infarction With Hospital Acquired Anaemia.

Group	Pre-treatment	After treatment		
		1 month	3 month	6 month
1	40.525±1.243	52.390±.484	56.400±.503	58.335±.495
2	44.555±.495	46.255±.708	46.060±.654	41.870±1.443

FLOW CHART-1

ENROLMENT OF STUDY POPULATION

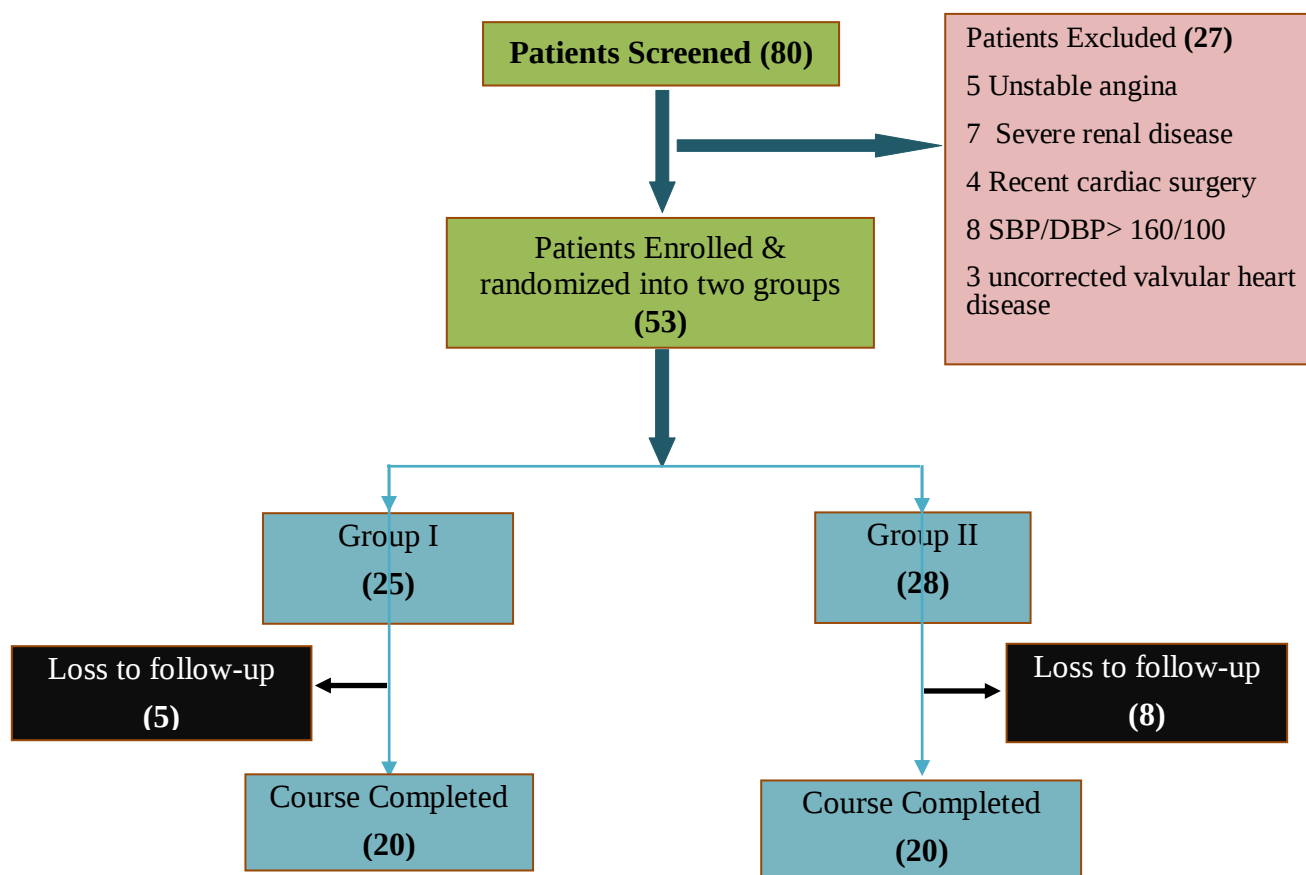


Figure 1 Effect of oral iron administration on hemoglobin (hgb) of sf- 12 in patients of acute myocardial infarction with hospital acquired anaemia.

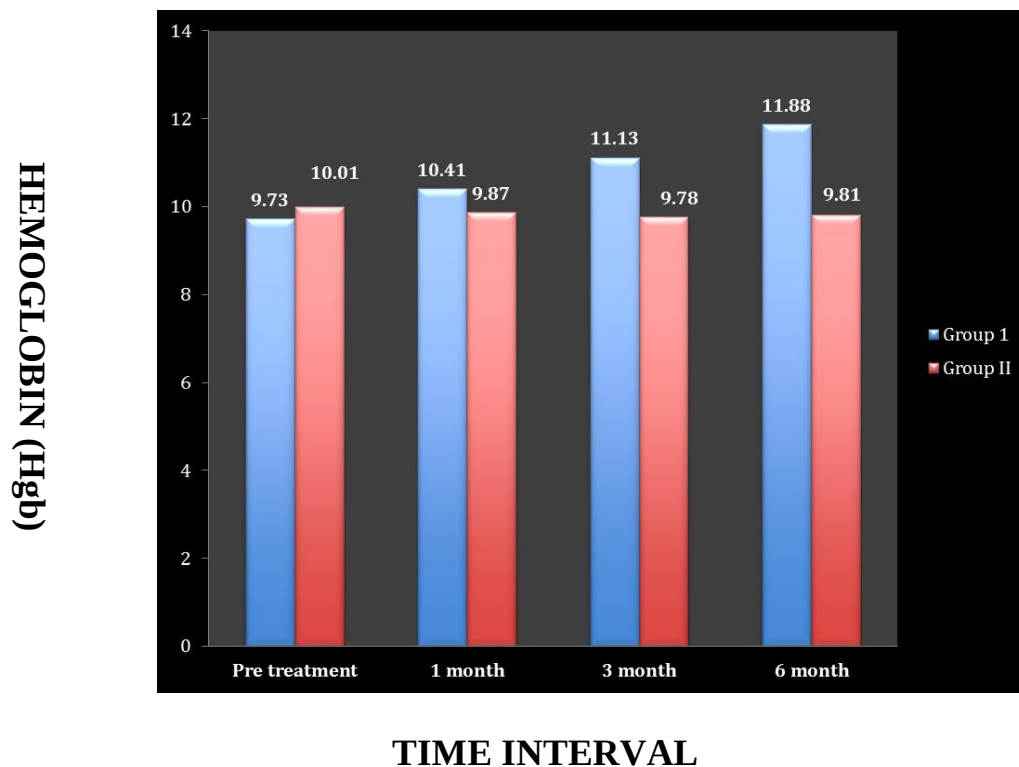


Figure 2 - Effect Of Oral Iron Administration On Physical Component Score (Pcs) Of Sf- 12 In Patients Of Acute Myocardial Infarction With Hospital Acquired Anaemia

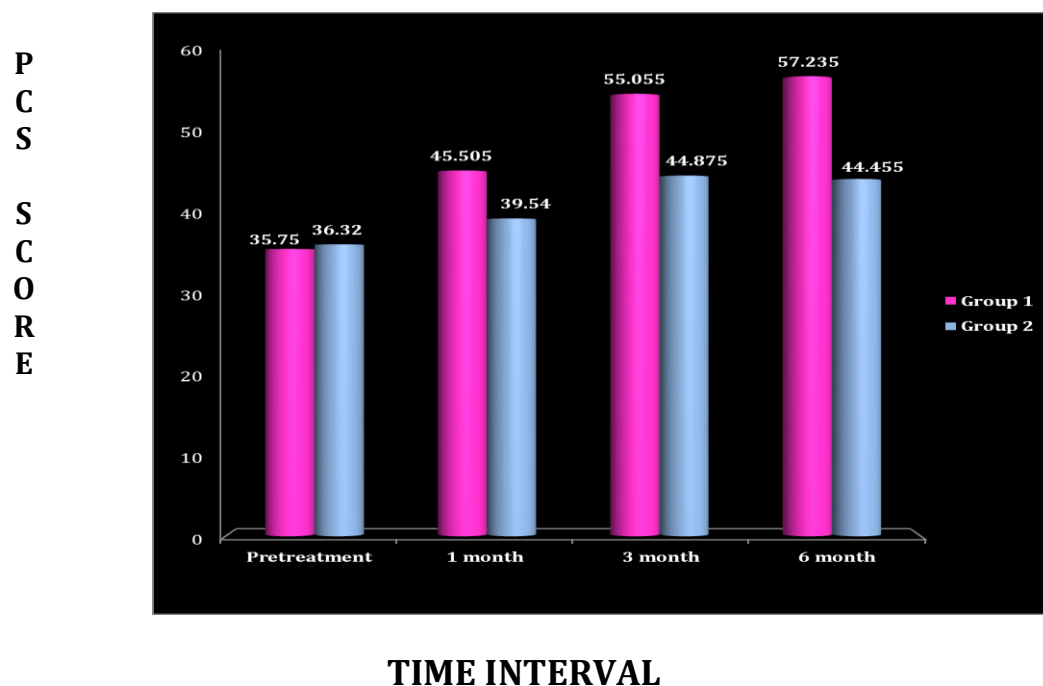
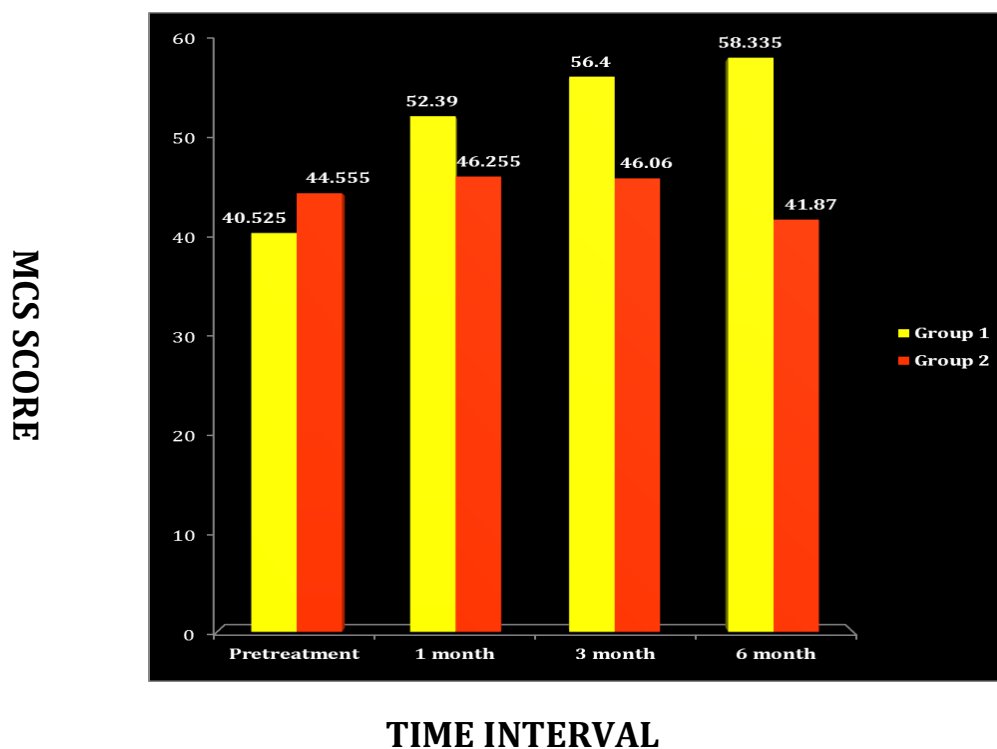


Figure 3: Effect Of Oral Iron Administration On Mental Component Score (Mcs) Of Sf- 12 In Patients Of Acute Myocardial Infarction With Hospital Acquired Anaemia.



DISCUSSION

Our study observed that persistent HAA in post-MI patients at OPD follow-up if not supplemented with iron alone or in combination with folic acid and vitamin B₁₂ the clinical outcomes remained worse leading to increased re-hospitalization coupled with decreased survival and poorer health status, whereas with iron therapy after 6months, there was normalization of persistent HAA by increasing hemoglobin concentration. This led post-MI patients to have better survival with marked improvement in health status.

Our AMI patients had history of normal hemoglobin concentration at admission in cardiology unit and later on developed hospital acquired anemia Survival of patients was at stake as Hgb concentration kept falling.it was interesting to note that patients after 6 months of oral iron supplements Hgb concentration and normalization of persistent HSS. Favorable responses of oral iron supplements started at 3 months. The study showed no appreciable effect during 1 months of iron supplement. Estimation of Hemoglobin concentration within 24 hr at discharge is required in all post MI patients who had developed HAA in hospital. Post MI patients with persistent HAA are crucial during first one month of post hospital period in relation to the episodes of morbidity, mortality and poorer status of health.In our study oral iron supplement was given to half of the patients enrolled and remaining patients were not given iron supplement. Hemoglobin concentration was statistically increased to normal, anemia was corrected and HAA was normalized after 3 and 6 months of iron supplement.

Beneficial effect of iron supplements to post MI patients was due to increasing hemoglobin concentration and thus removing HAA. The clinical outcomes of correcting microcytic and hypochromic anemia and normalizing HAA with iron supplement facilitated post mi patients to have improved status of health, increased no of survival, zero rehospitalisation, declined morbidity and mortality.

The main novel findings of the present study was that in post-MI patients with persistent HAA where baseline hemoglobin are low and a further fall in hemoglobin during follow-up appear to be independently associated with adverse outcome. In the present study, the prevalence of anemia at baseline ($< 12\text{g/dl}$ in women, $< 13\text{g/dl}$ in men) was 28%. From measurements of iron metabolism, it appeared that at baseline, increased risk of a cardiovascular event may be happening.

A unique and novel of the present study is that the development of anemia during follow-up after discharge for AMI is also independently related to increased mortality. Another unique feature of the present study was that we have assessed iron related hematinics in a subgroup of patients. During follow-up, iron deficiency appeared to be the main determinant associated with lower hemoglobin concentrations.

Our observation in present study that oral iron supplement given to post MI patients for period of 3 and 6 months achieve marked increase in in hemoglobin concentration. The increased Hgb concentration transformed persistent HAA to be normal. The study also revealed better survival, improved status of health,

Further clinical study evolving more numbers of the post-MI patients at multicenter investigations is required to support normalization of HAA due to correction of anemia with oral iron therapy, and boosting of hemoglobin concentrations, to make better quality of life, and reduced the incidence of persistent HAA.

CONCLUSION

Iron therapy significantly improved Hgb concentration Starting from 1 month and it kept on increasing till 6 months associated with better outcomes and SF12 including Physical component score and mental component score were also significantly increased which helped improving in quality of life.

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