



ANAEMIA AND INHOSPITAL MORTALITY IN CHRONIC HEART FAILURE PATIENTS

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ABSTRACT

OBJECTIVE: To determine the association between anaemia and in hospital mortality in patients with chronic heart failure.

MATERIAL AND METHODS: This cross sectional study was conducted at Punjab institute of cardiology, Lahore. 300 patients presenting in emergency department of the hospital with the diagnosis of heart failure (NYHA class III-IV) were included in the study. Patients were randomly divided into two groups. Group I included anaemic patients according to the protocol (Hb less than 10g/dl). Group II patients were non anaemic with normal Hb levels. Both groups received standard medical therapy (ACEI, β -blockers, diuretics) for heart failure. We observed the complications, in hospital mortality and outcome in these patients. Patients were followed up for three days in respective wards of the hospital regarding the complications and outcome.

RESULTS: In Group I, 68(45%) patients expired in the hospital While in Group II 41(27.5%) expired. Total no. of patients who died were 109(36.3%). In Group I 83(55.0%) patients were discharged while in group 2 108(72.5%) patients were discharged from hospital. Total no. of patients discharged from the hospital were 191(63.7%).

CONCLUSION: Anaemia increases the mortality and morbidity in heart failure patients.

KEY WORDS: Anaemia, in hospital mortality and heart failure.

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INTRODUCTION

Anaemia is a common co morbid condition in patients with heart failure and is associated with worse long-term outcomes¹. Prevalence of anaemia depends on the severity of chronic heart failure but may be as high as 50% in selected patients².

Although the cause of anaemia in heart failure is unclear, the weight of evidence suggests that neurohumoral and proinflammatory cytokine activation in heart failure favors the development of anaemia of chronic disease and depresses bone marrow function³. Similarly the mechanisms by which anaemia worsens heart failure may be related to increased workload.

Accumulating evidences suggests that anaemia

may be an independent risk factor for mortality among patients with heart failure. Additionally clinical studies among small number of heart failure patients suggest that anaemia is associated with increased hospitalization, mortality and morbidity in NYHA class III-IV heart failure patients⁴.

Anaemia or low Hb have consistently been shown to be independently associated with increased risk of mortality and hospitalizations for HF in acute and chronic HF with LV dysfunction. Anaemia increased the relative risk of death in these studies by 20% to 50%. A similar relationship has also been shown in patients with HF with preserved LV function³. Anaemia is frequently observed in patients with chronic heart failure. Prevalence of anaemia depends both on the severity of CHF and diagnostic criteria used to define it, but it may be as high as 50% in selected patients. Several studies in different patient populations found an association of anaemia with impaired cardiac function, more healthcare utilization, and morbidity².

Anaemia has recently been recognized as an important co morbid condition and a potentially novel therapeutic target in patients with heart failure (HF). Anaemia is common in HF patients, with prevalence ranging from 4% to 55% depending on the population studied⁵. Multiple potential mechanisms of action exist between anaemia and

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MA: Collected the data, did statistics and wrote the article. KEA: Helped him in this regard.

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the clinical syndrome of HF, including hemodilution, activation of inflammation, renal insufficiency, and malnutrition. A growing body of evidence from observational database and clinical trials suggest that anaemia is an independent risk factor for adverse outcomes in patients with HF⁵. However preliminary data suggest that treatment of anaemia may result in significant symptomatic improvement in HF⁶.

The magnitude of in hospital mortality in anaemic patients is 46.8% and 29.5% in non anaemic patients with chronic heart failure². This study will enable us to prevent morbidity and mortality in patients of heart failure by correcting Hb level. This study has been designed to evaluate the effect of low Hb level among patients with NYHA class III-IV heart failure. The rationale of this study is to evaluate the association between anaemia and heart failure.

MATERIAL AND METHODS:

This study was conducted at Punjab Institute of Cardiology, Lahore, from 05th of May,2013 to Nov 03,2014.

A total of 300 patients presenting in emergency department of the hospital with the diagnosis of heart failure were enrolled in the study after an informed consent. Patients between 25 to 70 years of age including both genders presenting in the emergency department with NYHA class III-IV heart failure were divided in group I(anaemic i.e., Hb < 10g/dl) and group II(non anaemic with normal Hb level). The patients with altered mental status due to some metabolic cause, with H/o malignancy, chronic renal failure (creatinine>1.5mg/dl) and diabetes mellitus(Random Blood Sugar >200mg/dl) were excluded from the study.

All Patients were followed during their hospital stay.

STATISTICAL ANALYSIS:

Data was analyzed using SPSS version 10. quantitative variable like age was presented as mean ± standard deviation. Qualitative variable like gender was presented as frequency and percentage. Efficacy in both groups was compared by using Chi-Square test. P value < 0.05 was taken as significant.

RESULTS:

Mean age of the patients was 58.3±10.7 years. Out of 300 patients 195 (65%) were male and 105 (35%) were female. They were divided into two groups I and II by randomization, group I containing 151 and group II 149 patients. In Group I the mean age was 58.7±10.6 years.

Out of 151 patients 98(64.9%) were male and 53(35.1%) were female. In Group II the mean

Table 1. Baseline Characteristics

Characteristics	Group I (n=151)	Group II(n=149)	Total (n=300)
Age mean years	58.7±10.6	57.9±10.8	58.3±10.7
Gender	Male	98(64.9%)	195(65.0%)
	Female	53(35.1%)	105(35%)
Dyspnea	151(100%)	149(100%)	300(100%)
Fatigue	28(18.5%)	25(16.8%)	53(17.7%)
Orthopnea	40(26.5%)	48(32.2%)	88(29.3%)
NYHA class	3.52±0.50	3.34±0.47	3.43±0.49
Heart rate	90.75±17.90	90.95±19.51	90.85±18.69
Systolic B.P	138.01±34.47	143.54±32.89	140.74±33.76
Diastolic B.P	83.31±17.81	88.54±18.57	85.88±18.34

Table 2. Signs of Heart Failure

Characteristics	Group I	Group II	Total
Edema	150(99.3%)	146(98.0%)	296(98.7%)
Rales-Bi lateral	151(100%)	148(99.3%)	299(99.7%)
Hepatomegaly	3(2.0%)	2(1.3%)	5(1.7%)
Ascites	151(100%)	149(100%)	300(100%)
J.V.P raised	15(9.9%)	23(15.4%)	38(12.7%)

Table 3. Laboratory Data

Lab/ECHO Findings	Group I	Group II	Total
R.B.S	156.60±22.0	149.90±29.44	153.27±26.14
HB	8.30±1.10	13.68±1.47	10.97±2.99
S/Creatinine	1.07±0.86	1.00±0.26	1.03±0.64
S/Na	140.52±9.78	141.52±6.58	141.02±8.35
S/K ⁺	4.07±0.57	4.11±0.59	4.09±0.58
E.F	27.12±2.61	27.55±2.88	27.33±2.75

Table 4. Outcome of the Patients with Heart Failure

Characteristics	Group I	Group II	Total
Death	68(45.0%)	41(27.5%)	109(36.3%)
Acute pulmonary edema	1(0.7%)	1(0.7%)	2(0.7%)
A/fib	1(0.7%)	1(0.7%)	2(0.7%)
Discharge	83(55.0%)	108(72.5%)	191(63.7%)

age was 57.9±10.8 years. Out of 149 patients 97 (65.1%) were male and 52 (34.9%) were female. All patients either in group I or II had dyspnea. overall orthopnea was seen in 88(29.3%) patients. In group I, 40 (26.5%) patients were having orthopnea while in group II, 48(32.2%) patients were having orthopnea. Overall patients having fatigue were 53(17.7%) In group I it was 28(18.5%) while in group II it was 25(16.8%). Mean heart rate of the patients was 90.85±18.69. In group I it was 90.75±17.90 while in group 2 it was 90.95±19.51. Mean systolic and diastolic B.P of the patients were (140.74±33.76mmhg) and (85.88±18.34mmhg) respectively. In group I systolic B.P was 138.01±34.47 while diastolic B.P was 83.31±17.81. In group II systolic B.P was 143.54±32.89 and diastolic B.P was 88.54±18.57. (table 1)



Following signs of heart failure were seen in these patients. Patients having pedal edema was 296(98.7%). In group I it was 150(99.3%) and in group II it was 146(98.0%). Rales and ascites were present in almost all of the patients. while patients having hepatomegaly in group I was 3(2%) and in group II it was 2(1.3%) and patients having hepatomegaly were 5(1.7%). Patients having raised JVP were 38(12.7%) while in group I it was 15(9.9%) and in group II it was 23(15.4%). (table 2)

Laboratory data(table 3) of the patients showed mean random blood sugar in group I was 156.60 ± 22 and in Group II it was 149.90 ± 29.44 while mean BSR was 153.27 ± 26.14 . Mean Hb of the patients was 10.97 ± 2.99 g/dl. In group I it was 8.30 ± 1.10 g/dl and in group II 13.68 ± 1.47 g/dl. Mean serum creatinine of the population was 1.03 ± 0.64 mg/dl. While mean serum creatinine of Group I was 1.07 ± 0.86 mg/dl and Group II it was 1 ± 0.26 mg/dl. Serum sodium and potassium in Group I was 140.52 ± 9.78 mmol/l and 4.07 ± 0.57 mmol/l while in Group II it was 141.52 ± 6.58 mmol/l and 4.11 ± 0.59 mmol/l and mean was 141.02 ± 8.35 mmol/l and 4.09 ± 0.58 mmol/l. Mean ejection fraction of the patient was 27.33 ± 2.75 . In Group I it was 27.12 ± 2.61 while in Group II it was 27.55 ± 2.88 .

The precipitants of heart failure were infection, poor compliance of the patients and drugs. Infection occurred in 31(10.3%) patients, Poor compliance was seen in 254(84.7%) patients, Drugs causing heart failure were present in 15(5.0%) patients. 14(4.7%) patients were alcoholics and 2(0.7%) patients were pregnant.

The number of patients died in group I was 45% and 27.5% in group II while mean was 36.3%. overall percentage of patients having pulmonary edema and atrial fibrillation was 0.7%. The number of patients discharged in both groups was 63.7%(table 4)

DISCUSSION:

Anaemia is a common co morbid condition in patients with heart failure and is associated with worse long-term outcomes¹. Prevalence of anaemia depends on the severity of chronic heart failure but may be as high as 50% in selected patients².

The results of this study are also supported by Horwich et al, in 2002, they compared the impact of in hospital mortality in anaemic and non anaemic chronic heart failure patients⁷. Anaemia is associated with worst symptoms, greater impairment of functional capacity and significant increase in

mortality in patients with advanced heart failure. In the anaemic patient heart failure death accounted for 46.8% while in non anaemic group it accounted for 29.5%². However, most of the previous trials comparing anaemic and non anaemic patients, have shown increased in hospital mortality in anaemic patients ranging from 20 to 50%³.

In 2003 Mozaffarian et al showed that anaemia predicts mortality in severe heart failure patients⁸. Among patients with severe HF, a significant independent association was observed between anaemia and total mortality, with progressively higher mortality with increasing severity of anaemia. The magnitude of the increased risk is striking, with a 52% higher risk of death in the low Hb group compared to normal Hb group. This increased risk is more than twice the risk associated with diabetes, smoking, a decade of age, or a 10% difference in EF in this population.

In 2008 Groenveld et al did a systematic review and meta analysis showing anaemia and mortality in heart failure patients. This was the first meta-analysis to address the relationship between anaemia and mortality in patients with CHF². In their analysis, which examined more than 150,000 subjects, anaemia was frequently observed in over one-third of CHF patients. Presence of anaemia in CHF patients is associated with an increased mortality risk in patients with systolic as well as diastolic heart failure. The adverse effect we found is substantial and significant. When assessing the mortality risk by using multivariate analyses, anaemia remains an independent risk factor for mortality in CHF patients.

In prior studies, it was observed that CHF is often accompanied by anaemia. A wide range of anaemia prevalence in CHF has been reported as high as 50%². The WHO criteria was used in the majority of studies. Results of this meta-analysis clearly indicate the need for standardized definitions of anaemia in CHF patients. The definition of anaemia appeared to be a major source of heterogeneity. However, despite different definitions of anaemia in the present meta-analysis, the association with mortality was robust, using different analysis strategies².

In 2008, Inder S. Anand³ et al have shown that anaemia have consistently been shown to be independently associated with increased risk of mortality and hospitalizations for chronic HF with LV dysfunction. Anaemia increased the risk of death in these studies by 20% to 50%. New-onset anaemia and a decrease in Hb over time are also



associated with increased mortality.

Prior epidemiologic studies that have included Hb in their analyses provide supportive evidence for the significant relationship between anaemia, HF and prognosis. Anaemia was associated with an increased risk of death or HF rehospitalization in California patients hospitalized for HF between 1983 and 1999⁷.

In 2007 Tang et al⁹ observed in their study that anaemia in patients with chronic heart failure has been under recognized and under evaluated in clinical practice. Meanwhile, careful follow-up in patients with sequential evaluation of their Hb levels showed that a relatively large cohort (up to 43% of patients with anaemia detected in a single time point at baseline) may proceed with resolution of their Hb to their non anemic levels over time. Particularly reassuring was the fact that these patients with so-called transient anaemia may show equivalent long-term outcomes when compared with those without anaemia.

Although many heart failure studies have shown that anaemia was associated with worse prognosis¹⁰⁻¹⁴. Few have explored the impact of longitudinal changes in anaemia status as well as the consequences of these changes on clinical outcomes. These findings complement prior observations from Val-HeFT (Valsartanin Heart Failure Trial) and COMET (Carvedilol or Metoprolol Evaluation Trial), showing that patients with the largest decrease in Hb levels face the worse in hospitalization, morbidity, and mortality¹⁵. Furthermore, prior studies showed that patients with normal Hb levels have survival rates significantly better than those of patients with low Hb^{16,17}. Because only a minority of patients received treatment for anaemia, it is

conceivable that anaemia in a substantial number of patients may have resolved after standard heart failure management, particularly with better control of fluid status (leading to less dilutional anaemia) and neurohormonal antagonism. But in our set up patients are more prone to non compliance to drugs and diet, so we have fairly a high ratio of anaemic patients mortality in chronic heart failure.

The results of the study are similar to the previous studies of Anand et al and Mozaffarian et al who demonstrated higher mortality in anaemic groups as compared to non anaemics^{3,8}.

Although current study describes a remarkable association between anaemia and HF mortality, the pathophysiologic relationship between Hb and HF progression requires further study. Hemoglobin may be a marker of poor prognosis in HF or, conversely, it may play a causative role in HF progression. Several potential explanations for the association between low Hb and poor prognosis deserve exploration.

CONCLUSION:

Current study indicates that anaemia is a significant independent risk factor for death among patients with severe HF, particularly death due to progressive pump failure. If this association is causal, normalization of Hct in this population would be expected to reduce mortality by approximately 40-50% based on the magnitude of risk observed in our study. These results support the need for further investigation of the etiologies, prevention, and treatment of anaemia in HF, including appropriately powered randomized clinical trials to determine whether prevention or treatment of anaemia reduces mortality in severe HF.



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