

## FREQUENCY OF ANEMIA AND CLINICAL OUTCOME IN PATIENTS WITH CONGESTIVE HEART FAILURE

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### Contribution

MFI & AS conceived the idea, planned the study and drafted the manuscript. IK & AS collected data, did statical analysis and critically reviewed manuscript. All authors contributed significantly to the submitted manuscript.

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### ABSTRACT

**Objective:** To determine the frequency of anemia and its short term clinical outcome among patients with congestive heart failure.

**Methodology:** This cross sectional study was conducted at Cardiology Department Lady Reading Hospital Peshawar. The study duration was six months from January 2014 to January 2016. Patients of either gender with age more than 14 years presenting with congestive heart failure were included in the study. Sample size was calculated using WHO sample calculator. Non probability consecutive sampling technique was used for sample collection.

**Results:** A total of 159 patients were included in the study, mean age was  $68 \pm 1.28$  years. About 57% patients were males. Our study showed that the frequency of anemia was 46(29%) in patients presenting with congestive heart failure of them, in hospital mortality was 7%, and 81 % patients were re hospitalized.

**Conclusion:** Anemia in congestive heart failure acts as a bad prognostic factor resulting in increased rate of mortality and re hospitalization.

**Key Words:** Anemia, Short term clinical outcome, Congestive heart failure.

## INTRODUCTION

Cardiovascular disease has a major impact on global health. According to the World Health Organization, an estimated 17.1 million people died of cardiovascular diseases worldwide in 2004, representing 29% of all deaths; approximately 23.6 million people are expected to die from these diseases in 2030. Congestive Heart failure (HF) is a complex syndrome, resulting from impaired ability of heart to pump, to support a physiological circulation. Congestive heart failure affects about 2% of the western population, with prevalence increasing sharply from 1% in 40 years olds to 10% above age 75 and it is the most common cause of hospitalization in patients over 65 years of age.

Patients with chronic heart failure (CHF) suffer from a marked impairment of health-related quality of life (HRQoL) compared with the normal population and patients with other chronic conditions. Among the factors associated with a reduced HRQoL, dyspnea and fatigue are major symptoms of CHF that persist in many patients despite optimal drug and device management.

Anemia is a common co-morbidity in older adults with heart failure and a preserved ejection fraction (HFPEF) and is associated with worse outcomes. Anemia accompanies chronic heart failure (CHF) in up to 55% of patients. Although the reports of prevalence of anemia vary widely, it is unequivocal that anemia is prevalent in patients with heart failure regardless of the clinical setting. The prevalence of anemia was reported to be 37.2% in a recent meta-analysis of a total of 153,180 patients with heart failure across 34 published studies over a seven-year period (2001–2007). In CHF patients, even mild anemia is associated with worsening of symptoms, increased New York Heart Association (NYHA) class, and impaired functional capacity, quality of life, and survival.<sup>7</sup>

The mechanisms underlying anemia in CHF patients are multi-factorial it can be due to absolute or relative iron and/or erythropoietin deficiency due to chronic inflammation or chronic renal failure is present. Iron plays a vital role in energy-dependent physiological processes such as erythropoiesis and oxidative phosphorylation, and iron deficiency (ID) may be a frequent and significant comorbidity in CHF. Beyond anemia, ID is a determinant of fatigue and impaired exercise capacity in otherwise healthy populations.<sup>5</sup> Nanas et al. found that 73% of patients with advanced heart failure and anemia had depleted iron stores on bone marrow aspiration and Iron deficiency anemia is associated with decreased survival in CHF patients.<sup>11,12</sup> A systematic review of >150 000 patients has shown that patients with CHF and anemia have an increased risk for death; 48% of anemic patients died within 6 months from the time of diagnosis of CHF compared with 29.5% of non-anemic patients.<sup>9</sup>

The present study is designed to determine the frequency of anemia and its three months clinical outcome after treatment in patients with CHF. CHF is not uncommon in our population and carries immense degree of burden on hospital and patient resources due to repeated admissions and chronicity of the illness. Anemia is a frequent association of CHF and carries bad prognosis if left undiagnosed and untreated. This study will provide us with a local data about the frequency and clinical outcome of anemia in patients with CHF. The results of this study will be shared with other locally available cardiologists and physicians and future recommendations may be decided either for conducting more research or practice modifications.

## METHODOLOGY

This cross sectional study was conducted in Cardiology Unit, Lady Reading Hospital Peshawar from January 2014 to 2015. Sample size was calculated; using 11.7% of mortality rate in anemic patients with CHF, calculated with WHO sample size calculator, with 95% confidence interval and 5% margin of error. Non-probability consecutive sampling technique was used. Patients of either gender aged 14 years and above with congestive heart failure of  $\geq 6$  months duration, presenting to Cardiology Unit, Lady Reading Hospital Peshawar were included.

Patients with chronic obstructive pulmonary disease diagnosed by history and FEV<sub>1</sub> of less than 70%, chronic renal failure on dialysis. Chronic liver disease diagnosed by history and medical records, history of intake of any type of multivitamin or iron therapy in the last three months and history of blood transfusions in the last three months or bleeding of any amount in the last three months were excluded from the study.

The study was conducted after approval from hospitals ethical and research committee. All patients of congestive heart failure were included in the study through OPD A&E department ward. The purpose and benefits of the study was explained to all patients and a written informed consent was obtained.

All patients were subjected to detailed history and clinical examination, followed by complete routine clinical examination. Baseline investigations were done which were included complete blood picture to detect anemia. The treatment of anemia was decided in collaboration of physician. All the patients were started on standard treatment of CHF as per hospital protocol and were followed for 7 days to detect in hospital death. All the patients were discharged on standard treatment of CHF if indicated and were followed through telephone or visit in person for 3 months to detect mortality and re admission.

All the above mentioned information including name, age and gender Hemoglobin (Hb) level, re admission and death

was recorded in a pre-designed proforma.

The collected data was stored and analyzed in SPSS version 16 for windows. Mean  $\pm$  SD was calculated for numerical variables like age, gender, Hb level and duration of CHF at presentation. Frequencies and percentages was calculated for categorical variables like gender, anemia and three months clinical outcomes (in hospital mortality, 3 months mortality re admissions). Anemia and three months clinical outcome was stratified among age and gender and duration of CHF to see the effect modifications. All results were presented in the form of tables and graphs.

## RESULTS

This study was conducted at Cardiology Department, Lady Reading Hospital, Peshawar in which 159 patients were observed for the frequency of anemia and clinical outcome and the results were analyzed. About 91 (57%) patients were

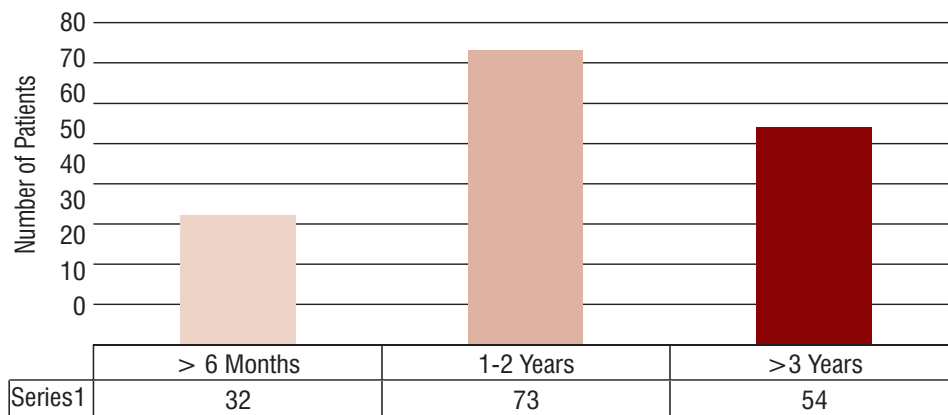
male, 29(18%) patients were in age range 20-40 years, 66(42%) patients were in age range 41-60 years, 48(30%) patients were in age range 61-80 years, and 16 (10%) patients were in age range more than 80 years. Mean age was  $68 \pm 1.2$  years.

Of them 32(20%) patients had CHF for more than 6 months, 73(46%) patients had CHF for 1-2 years, 54(34%) patients had CHF for >3 years. Mean duration was  $1 \pm 2.77$  years (Figure 1).

About 46(29%) patients had Hb Level <11 gm/dl while 113(71%) patients had Hb level more than 11 gm/dl. Mean Hb was  $12 \pm 1.91$  gm/dl (Figure 2).

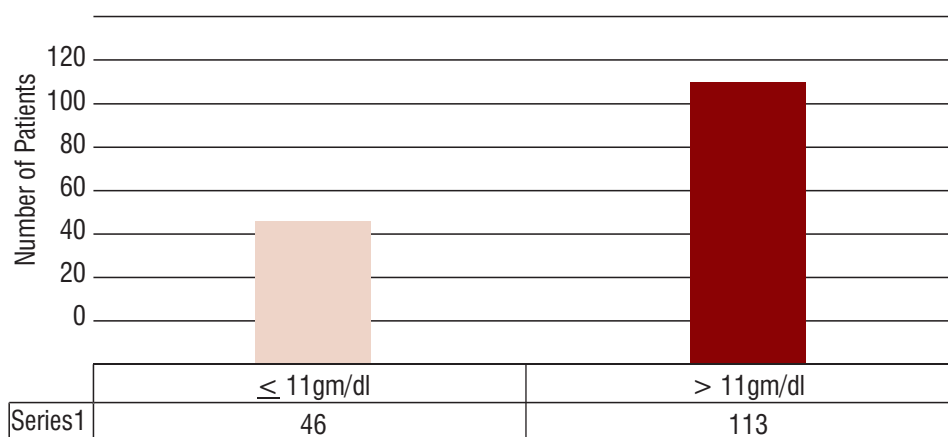
Clinical outcome among 46 anemic patients was analyzed as 3(7%) patients died in hospital, 37(81%) patients were re hospitalized while 6 (12%) patients died at 3 months follow up. Stratification of clinical outcome with age, gender and duration of CHF is given in Table 1.

**Figure 1: Duration of Congestive Heart Failure (n=159)**



Mean duration was 1 years with SD  $\pm 2.77$

**Figure 2: Serum Hemoglobin Level in Patients (n=159)**



Mean Hb was 12 gm/dl with SD  $\pm 1.91$

**Table 1: Stratification of Clinical Outcome in Study Population ( n=46)**

Variable	Hospital Mortality	Re-hospitalized	Mortality
<b>Gender</b>			
Male	02	21	03
Female	01	16	03
p-value = 0.003			
<b>Age distribution:</b>			
20-40 years	00	10	0
41- 60 years	01	14	03
61-80 years	01	12	01
>80 years	03	02	01
p-value = 0.002			
<b>Distribution of CHF</b>			
>6 months	00	06	01
1-2 years	01	20	11
>3 years	01	03	02
p- value = 0.003			

## DISCUSSION

There is ample evidence that suggests anemia is an independent risk factor for worse outcomes in patients with heart failure (CHF) and ischemia heart disease including myocardial infarction, and anemia is a common comorbidity in CHF. Non-anemic patients compared with anemic patients are associated with worse cardiac clinical status, more severe systolic and diastolic dysfunction, a higher beta natriuretic peptide level, rapidly decreasing kidney functions, low physical activity and high dependence, and increased financial burden.

In a systematic review and meta-analysis published in 2008, after a minimal follow-up of 6 months, 46.8% of anemic patients died compared with 29.5% of non-anemic patients irrespective to the cause of CHF. A decrease in 1-g/dL in hemoglobin was independently associated with significantly increased mortality risk.

Our study shows that mean age was 68 years with SD  $\pm 1.28$ . Fifty seven percent patients were male and 43% patients were female. More over the frequency of anemia was 46(29%) in patients presenting with congestive heart failure in which 7% patients had in hospital mortality, 81% patients were re hospitalized while 6 (12%) patients died during 3 months period.

In CHARM Program in the United States and Canada 2653 pateints were randomized and associations between hemoglobin and outcomes were studied. Anemia was more common in heart failure regardless to impaired LV systolic functions. Low levels of hemoglobin was associated with higher LVEF yet was an independent predictor of adverse mortality and morbidity outcomes.

Anemia in CHF mainly is caused by a combination of renal

failure and CHF-induced increased cytokine production resulting in the reduction of erythropoietin (EPO) production, bone marrow resistance to EPO stimulation, reduced intestinal absorption of iron and reduced release of iron from iron stores which is cytokine-induced causes iron deficiency anemia. The use of ACE/ARBs may inhibit the bone marrow response to EPO. In CHF there is hemodilution that causes low hemoglobin level.

Pilot studies have found that in a large number of HF patients it's safe to raise hemoglobin with erythropoietin-stimulating therapies and there is a suggestion that raising hemoglobin in anemic HF patients may lead to improved outcomes. Studies have shown that in anemic patients with reduced ejection fraction of 40% or less, when treated , have shown improvement in NYHA, less dependence of intravenous diuretics, reduced length of stay at the hospital, and improvement in renal functions were all significantly greater in the control group than in the treated group.

The Study of Anemia in Heart Failure Trial (STAMINA-HeFT) is a large multicenter, randomized, double-blind, placebo-controlled trial, demonstrated that even with increase of only 1.0 g/dL or more in hemoglobin resulted in reduction of all-cause mortality or heart failure-related hospitalization. A pragmatic approach to the care of patients with HF needs definitive anemia treatment goals that are dynamic and disease specific, rather than those that adopt a more simplistic hemoglobin-specific approach.

## CONCLUSION

Our study results are very much similar to international studies in anemia prevalence in CHF patients . Therefore it should be considered as bad prognostic factor and should be treated vigorously so as to decrease morbidity and mortality.

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