Original Article

Severe Anaemia as A Predictor of Mortality in Heart Failure Patients

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Abstract

Introduction: Anaemia at the time of diagnosis of heart failure is said to be an independent factor for mortality during the following years. In this study, the effect of severe anaemia at the time of diagnosis, in the outcome of heart failure in the form of in hospital mortality is studied.

Methods: One hundred eighty-four heart failure patients admitted in Manamohan Cardiothoraccic Vascular and Transplant Centre between September 2011 to March 2012, age above 15 years were enrolled in the study. Baseline investigations and hemoglobin was done and the patients were followed up till discharge or in hospital mortality.

Results: Among the 184 heart failure patients 115(62.5%) had anaemia. When evaluated in a bivariate model, the odds ratio of death for patients with mild anaemia compared with patients with no anaemia was 3.9(0.6-22.6, p value 0.124) for moderate anaemia 4.5 (0.9-23.07, p value 0.064) and for severe anaemia 46.06 (8.6-246.05, p value 0.000), respectively. On multivariate analysis severe anaemia 919 (5.6-149762.9, p value 0.009) was still found to be a significant predictor of mortality.

Conclusion: Severe anaemia at the time of diagnosis of heart failure is an independent predictor of in hospital mortality.

Key word: Anemya, heartfailure patient, mortality

Introduction

Anaemia is common in patients with heart failure (HF) and is found in 4-55% of the patients [1-4]. Many studies have demonstrated anaemia to be a risk factor in patients with heart failure[5, 6]. Anaemia at the time of diagnosis of heart failure is an independent factor for mortality during the following years but loses its influence on mortality over time[7]. Of note, anemia is not only prevalent in the congestive heart failure (CHF) population, but several studies in different patient populations found an association with anemia, impaired cardiac function, more health care utilization, and morbidity[8,9–14].

Although most studies have documented higher mortality rates in anemic CHF patients[8,15–20], some studies report the absence of an adverse effect of anemia on mortality in CHF [(4,21,22)].

Elucidating the contribution of anemia to mortality may lead to a more accurate risk profiling in CHF patients, especially since several treatment options for anemia exist including erythropoietin (EPO) and iron therapy [23, 24]. Ultimately, this may lead to more effective therapeutic strategies from a risk-benefit perspective in heart failure patients.

In this study, the effect of severe anaemia in the outcome of heart failure in the form of mortality was evaluated.

Methods

Patient population

One hundred eighty four heart failure patients admitted in MCVTC between September 2011 to March 2012, age above 15 years who were diagnosed clinically by Framingham

criteria were enrolled in the study. The initial screening consisted of a clinical history, a physical examination, and baseline investigations at the time of diagnosis. Echocardiogram was also done during the hospital stay. Baseline investigations include- Complete Blood Count (CBC), Renal Function Test (RFT), Lliver Function Test (LFT), Prothrombin Time (PT), Electrocardiogram (ECG), Chest X-ray PA view. The patients were daily followed up till discharge or death during the hospital stay.

Patients were excluded if they have had an myocardial infarction (MI) within seven days before screening, If they had a heart rate of less than 50 beats per min during waking hours, sinoatrial block or second- or third- degree atrioventricular block that was not treated with a pacemaker, a corrected QT interval exceeding 460 msec (500 msec in patients with bundle-branch block), a systolic BP of >180 and diastolic blood pressure of more than 110 mm Hg, a systolic blood pressure of less than 80 mm Hg, a serum potassium level of less than 3.6 mmol/L or more than 5.5 mmol per liter, recent use of class I or III antiarrhythmic drugs, a calculated creatinine clearance rate of less than 15 ml per min[9], serious liver dysfunction, acute myocarditis, planned cardiac surgery or angioplasty, severe valvular lesion, cardiac surgery within the preceding four weeks, and the presence of an implantable cardioverter–defibrillator.

Definition of anaemia

Anaemia was defined by the cut-off values defined by the World Health Organisation (WHO): haemoglobin (Hgb) level lower than 120 g/L in women and 130 g/L in men. Mild anaemia, corresponding for the first subgroup in each gender, was defined as hgb. lower than 120 g/L in women, and lower than 130 g/L in men. Moderate anaemia was defined as hgb. lower than 110 g/L in women, and lower than 120 g/L in men. And severe anaemia was defined as hgb < 80gm/l for both women and in men[25].

Ethics

All patients gave their written, informed consent before enrolment. The study received ethical approval from Institutional Review Board of the Institute of Medicine, Tribhuvan University.

Statistical analysis

The data were collected and tabulated. Continuous variables are presented as medians with 5th and 95th percentiles, and discrete variables as percentages. Baseline characteristics were compared using the continuity adjusted Chi-square test for discrete variables and analysis of continuous variables. Multivariable analysis was performed with Biniary logistic Regression. P value <0.05 was considered significant. All calculations were made using SPSS 20 software.

Results

Prevalence of anaemia

Among the 184 heart failure patients 115(62.5%) had anaemia. Among male 54(56%) were anaemic whereas among females 61(69.31%) were anaemic. Females were more anaemic than males. When categorizing anaemia according to severity 38 had mild anaemia, 58 had moderate anaemia and 28 had severe anaemia. Among those who were mild anaemic 27 were male and 11 are female whereas 40 among moderate anaemia were female and 18 were male. Similarly among those who have severe anaemia 10 were male whereas 9 were female. The baseline characteristics of the patients are given in table 1. Anaemia was associated with increasing age, female sex, decreasing creatinine clearance, use of b-blockers, ACEI/ARB, low LVEF, presence of arrhythmia and associated comorbidity like pneumonia.

Table 1 Baseline characteristics of heart failure patients.

	No anaemia (N= 69)	Mild anaemia (N= 38)	Moderate anaemia (N= 58)	Severe anaemia (N= 19)	P value
Age(Median)	58	72	59	68	0.000
Sex(male)	41	27	18	10	0.001
Creat Clearance	79	57	67	73	0.000
B-blockers	59	38	54	19	0.025
ACEI/ARB	55	34	40	11	0.025
Aldosterone antagonist	40	23	23	11	0.118
LVEF	44	40	33	33	0.01
Arrhythmia	25	19	35	17	0.00
Statin	12	5	6	6	0.158
Pneumonia	16	7	21	12	0.002

Mortality analysis

When evaluated in a bivariate model, the odds ratio of death for patients with mild anaemia compared with patients with no anaemia was 3.941(0.687-22.608, p value 0.124) for moderate anaemia 4.598 (0.916-23.075, p value .064) and for severe anaemia 46.062 (8.623-246.054, p value 0.000), respectively.

To investigate whether the increased mortality in patients with anaemia reflected a higher prevalence of concomitant risk factors, a multivariable analysis, including age, gender, creatinine clearance, presence of arrhythmia, ejection fraction, presence of pneumonia, use of beta-blockers, ACEI, statins and aldosterone antagonist as covariates, was performed. Severe anaemia was still found to be a significant predictor of mortality.

Table 2 Multivariate analysis of mortality with anaemia

Category of anaemia	P value	Odds ratio
No anaemia	Reference	-
Mild anaemia	0.559	3.2(0.64-159.47)
Moderate anaemia	0.778	0.59(0.16-21)
Severe anaemia	0.009	919(5.6-149762.937)

Discussion

In our study, anaemia was frequently observed, found in over almost two-third of HF patients which is higher than reports of other studies[1-4]. It could be due to poor nutritional status. It also emphasizes that a large part of the patient population with HF has anaemia as a possible factor of co-morbidity.

Both the short term and long term studies including a recent meta-analysis[2] (6 months to 5 years) have established anaemia as independent predictor of mortality HR 1.46 (1.26-1.69) p<0.001). It has been found in different studies that mortality risk increased with the severity of the anaemia[7].

This study is a prospective study of admitted patients with heart failure during one hospital stay and do not involve patients follow up over time. This study also shows anaemia as an independent predictor of mortality on bivariate analysis. Furthermore on assessing the importance of severity of anaemia on multivariate analysis, severe anaemia was found to be independent predictor of mortality. However, mild and moderate anaemia didn't show statistical significance. It could be due to small sample size, short term data and no long term follow up.

In this study patients had no signs of cancer at the time of inclusion leading to the argument that anaemia in the included patients was caused by chronic disease e.g. kidney disease. This is illustrated in our study by the fact that the more severe the anaemia the lower the creatinine clearance.

Anaemia is a novel therapeutic target in the treatment of HF patients though it still remains controversial whether to treat anaemia in patients with heart failure. The focus is on treatment with intravenous iron treatment and erythropoiesis-stimulating proteins to increase haemoglobin levels. There are several promising randomized trials investigating treatment with erythropoietin or darbepoitin with or without intravenous iron therapy versus placebo[26-30]. In relation to these trials there has recently been raised concern about the possibility of increased risk of thromboembolic events when raising haemoglobin levels.

Conclusion

Among the 184 heart failure patient 155 (62.5%) had anaemia. Hence, severe anaemia at the time of diagnosis of heart failure is an independent predictor mortality in hospitalised patient.

Acknowledgements

Conflict of interests: None

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