

Pattern of Anemia in Patients with Heart Failure in Ischemic Heart Disease

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ABSTRACT

Background: Anemia is common health problem encountered in patients with heart failure which in turn is one of the common presenting feature of ischemic heart disease. This study aims to study the patterns and types of anemia in patients admitted with heart failure in ischemic heart disease.

Methods: A cross sectional hospital based study for one year in eligible patients as ischemic heart disease in clinical heart failure. Blood parameters especially RBC indices, biochemical parameters including iron profile, serum ferritin, vitamin B12, folic acid were studied.

Results: Out of 77 patients with mean age 67 ± 7 years, anemia was common in female (63.6%) and elderly (66.2%). Other most common precipitants of heart failure in anemia were recent MI (<1 month) 55.8% and renal disease (55.8%), hypertension (49.4%) and diabetes (42.9%). Most common pattern of anemia according to RBC indices were normocytic (60.3%), hypochromic (79.3%), normocytic hypochromic anemia (48.2%) Iron deficiency was found in 25 (33.7%) of which absolute iron deficiency was in 12 (16.2%) and relative iron deficiency 13 (17.5%). Anemia of chronic disease were in 24 (32.4%), vitamin B12 deficiency 15 (20.2%) and Folic acid deficiency in 2 (2.7%).

Conclusion: In heart failure with ischemic heart disease patient, anemia is common precipitating factor. Normocytic and hypochromic pattern are the commonest pattern. Iron deficiency is the commonest. Timely detection and management of iron deficiency may prevent heart failure even in ischemic heart disease.

Keywords: anemia; heart failure; iron deficiency; ischemia heart disease

INTRODUCTION

Anemia is common health problem encountered in daily practice. The prevalence of anaemia in heart failure was 42%.¹ The anemia prevalence in patients with MI was about 23 to 40.4%.^{2,3} Heart failure has been described in 70% of ischemic heart disease patients.⁴ According to WHO anemia is considered if haemoglobin less than 13gm/dl in female and 12 gm/dl in male. Anemia has been classified as mild anemia (hemoglobin 9.0–10.9 gm/dL), moderate anemia (hemoglobin 7.0–8.9 gm/dL), and severe anemia (hemoglobin less than 7.0 gm/dL).^{5,6} NYHA functional classification is still in use for defining clinical assessment of severity of heart disease especially heart failure.^{7,8} This study aims to study the patterns and types of anemia in patients admitted with heart failure in ischemic heart disease.

METHOD

This was a cross sectional study done in Gautam Buddha Community Heart Hospital for one year after

approval from the institutional review committee (IRC-Reference no 2079/080-78). Sample size was 77 calculated with the formula $n = Z^2 \times p \times (1-p) / e^2$ where n = required sample size, $Z = 1.96$ at 95% Confidence Interval, p = prevalence of anemia in patient with heart failure in reference population and e = margin of error, 10% in this study. Eligible patients were anemic patients of ischemic heart disease in NYHA II-IV heart failure. Anemic patients considered were of moderate to severe anemia (<10gm/dl). Patients with present or past history of positive cardiac biomarkers (Trop I positive) or presence of existing regional motion abnormalities in echocardiography were considered eligible. Definitions used for RBC indices were according to size by using Mean Corpuscular Volume (MCV) as microcytic (<80 fL), normocytic (80-99fL), macrocytic (≥ 100 fL) and according to haemoglobin concentration using MCHC, hypochromic (<32 gm/dl) and normochromia (≥ 32 gm/dl).^{9,10} Iron deficiency considered were absolute

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iron deficiency (Serum Ferritin <100 ug/ml) and relative iron deficiency (Serum Ferritin 100-300 ug/ml and Transferrin Saturation <20%).^{11,12} Anemia of chronic disease considered when anemia with history of any chronic disease with Serum Ferritin >300 ug/ml, and normal Vitamin B12 and normal Folate level.^{11,12} Vitamin B12 Deficiency is considered as < 150 pg/ml and Serum Folate as <3 ng/ml.^{13,14} RBC indices were calculated according to automatic hematology analyzer DYMIND UN73. Iron profile calculated using Abbott Architect i 2000 SR analyzer. Data was tabulated in Excel and later analysed in SPSS. Categorical values were expressed as frequency and percentage while continuous variables were presented as means.

RESULTS

Seventy-seven patients were studied. There were 49 (63.6%) females and 28(36.4%) males. Mean age was 67.7±13 years. Fifty one (66.2%) patients were of age ≥ 65 years of which 35 were female. Common factors precipitating heart failure in patients were enlisted in (Table 1).

Factors	Frequency (%)
Female Gender	49(63.6)
Elderly (>65 years)	51(66.2)
Recent MI(<1 month)	43(55.8)
Renal Disease	43(55.8)
Acute	20(25.1)
Chronic	23(29.9)
Hypertension	38(49.4)
Diabetes Mellitus	33(42.9)
Present Smoking/Tobacco	15(19.5)
Hypothyroidism	15(19.5)
COPD	13(17)
Valvular heart disease	12(15.6)
GI bleeding	10(13)
Atrial fibrillation	7(9.1)
Dyslipidemia(Increase LDL)	6(6.5)

Hematological parameters were included in Table 2. Biochemical parameters included were Blood Urea 64.8±44.4, Serum Creatinine 2.3±2.2 mg/dl, Serum Sodium 135.8±5.4, serum Potassium 4.1±0.6, Routine Blood Sugar 168.6±91.5, Total cholesterol 153.3±42.1

mg/dl, LDL 74±33.3, Triglyceride 130.4±88.4 mg/dl. Iron profile, Vitamin B12 and Serum Folate studied were enlisted in Table 3.

Hematological Parameters	Mean	SD
Hemoglobin (gm/dl)	8.6	1.4
WBC (/ cum)	9632	5974
Platelete Count(/cum)	185959	78063
MCV(fL)	86.7	10.3
MCHC(gm/dl)	30.8	1.62
MCH(pg/RBC)	27.7	8.7
RDW(%)	16.91	2.6
RDW(fL)	51.4	6.9

Biochemical Parameters (n=74)	Mean	SD
Serum Iron (ugm/dl)	36.4	32
TIBC (ugm/dl)	206.6	107
Serum Ferritin (ugm/l)	296.9	230.8
Transferrin saturation (%)	24	28.4
Serum Vitamin B12 (pg/ml)	398.2	470
Serum Folate (ng/ml)	11.6	7.5

Pattern of anemia studied according to RBC Indices were enlisted in Table 4.

Types of anemia	Frequency (%)
According to MCV (fL)	
Microcytic (<80)	17(29.3)
Normocytic (80-99)	35(60.3)
Macrocytic (≥100)	6(1)
According to MCHC (gm/dl)	
Hypochromic (<32)	46(79.3)
Normochromic (≥32)	12(20.7)
Mixed pattern(according to MCV and MCHC)	
Normocytic Normochromic	7(12)
Microcytic Hypochromic	13(22.4)
Nomocytic Hypochromic	28(48.2)
Microcytic Normochromic	4(6.8)
Macrocytic	6 (1)

Types of anemia as given in peripheral blood smear by pathologists were enlisted in Table 5.

Table 5. Pattern of anemia according to pathologist report. (n=58)	
Types of Anemia according to Peripheral Blood Smear (n=58)	Frequency (%)
Nomocytic Normochromic	46(79)
Microcytic Hypochromic	12(21)

Types of anemia recorded in heart failure patients according to biochemical indices in Table 6.

Table 6. Types of anemia in ischemic heart failure patients.	
Types of anemia	Frequency (%)
Absolute Iron deficiency anemia	
Serum Ferritin <100 ug/ml	12(16.2)
Relative Iron deficiency anemia	
Serum Ferritin <300ug/ml + Transferrin Saturation <20%	13(17.5)
Anemia of chronic disease	
Serum Ferritin >300 ug/ml, normal B12 and Folate	24(32.4)
Vitamin B12 deficiency anemia	
<150 pg/ml	15(20.2)
Folic acid deficiency (ng/ml)	

DISCUSSION

As 66 % of patients were elderly ≥ 65 years with overall mean age 67.7 years, the age of study population was similar to other studies in heart failure.¹⁵ The higher prevalence of ischemic heart disease in elderly female, malnutrition, decrease iron intake, the higher prevalence of UGI bleeding and higher comorbidities in female had been described for anemia and heart failure.^{16,17} Renal diseases and Recent CAD (<1 month) were the common disease precipitating heart failure. Long standing diabetes and hypertension can cause chronic renal injury which cause anemia in late stage.¹⁸ Hypotension, use of diuretics, contrast and multiple medicines may have precipitated acute renal injury which in turn may have precipitated heart failure. Acute on chronic renal disease were also noticed causing chronic heart failure.¹⁹ Recent coronary artery disease have precipitated heart failure in anemic patients. Use of high dose anti-plateletes can cause upper GI bleeding.²⁰ The bleeding of haemorrhoids and other causes of lower GI bleeding were also common after

use of high dose of antiplateletes.²¹ Existing LV Systolic dysfunction, valvular regurgitation, existing or old regional wall abnormalities, mechanical complications of ischemia and arrhythmia may have precipitated heart failure.²² Factors precipitating heart failure according to Bhandari et al. were anemia (84%), elderly (53.65%) hypertension (31.7%), diabetes (32.9%) and atrial fibrillation (36.5%) but no gender differences in prevalence of heart failure.²³ Bista et al reported causes for anemia as age >65 years, (58.4%), female (55.3%), diabetes (43%), hypertension (35.3%), COPD (23.07), coronary artery disease (47.6), atrial fibrillation (3%) and heart failure with reduced ejection fraction (90%).¹⁵ Normocytic and hypochromic anemia were most common according to RBC indices. In renal disease and other chronic diseases, normocytic normochromic anemia were common.²⁴ In absolute iron deficiency anemia, microcytic hypochromia has been described.²⁵ In peripheral blood study normocytic normochromic anemia were recorded. Mishra et al. had reported 47% microcytic hypochromic anemia, 22% macrocytic anemia and 22% normochromic anemia.²⁶ In study by Singh et al 60% had microcytic hypochromic, dimorphic (20.8%), normochromic anemia (14.8%) and macrocytic normochromic (2.85%).²⁷ Our study population were elderly with multiple comorbidities compared with the population studied by Mishra et al and Singh et al. Use of RBC indices have varying sensitivity and specificity. Red blood indices include Mean Corpuscle volume (MCV), Mean Corpuscular hemoglobin concentration (MCHC) and Mean Corpuscular Hemoglobin (MCH) are major RBC indices. Normal values defined for MCV is 87 ± 7 fL, MCH 29 ± 2 pg/cell, MCHC 34 ± 2 gm/dl and RDW $13 \pm 1.5\%$. Sensitivity of MCV, MCHC and MCH for normocytic normochromic anemia as 78%, 100% and 67%, Microcytic hypochromic anemia as 78%, 14% and 80% and macrocytic anemia as 100%, 10% and 100%.^{26,27} In study by Joosten et al. in geriatric hospitalized population, 30-45% patients had anemia of chronic disease, 15 to 30% iron deficiency anemia and 5 to 10% as Vitamin B12 and Folate deficiency.²⁸ In study by Mishra et al. the

prevalence of iron deficiency was 35%.²⁶ In study by Bhandari et al. iron deficiency was in 54% of which 34% was absolute and 20% had relative iron deficiency.²⁴ Prevalence of iron deficiency by Bista et al. in heart failure was 77 % (absolute iron deficiency in 22 % and relative iron deficiency 55%).¹⁵ Iron deficiency was noted in 37.5% patients. Even patients are normocytic, in patients with heart failure with anemia, Iron profile should be routinely done to look for iron deficiency. Management accordingly can improve result. Vitamin B12 deficiency has been higher prevalence in North India.²⁹ In patients with heart failure with anemia in ischemic heart disease, low vitamin B12 in 25% of study population raise need of further study.

Differences in pattern of anemia by RBC indices and Pathological reports were observed. Laboratory reports should be carefully interpreted depending upon the symptoms of patients. Pathological blood film reports as subjective may have varied according to expertise. Cross verification could have prevented such differences in our study. Anemia considered in

study was less than 10gm/l. While WHO considered anemia in less than 11 gm/dl in female and 12gm/dl in male. Including all anemic patients according to WHO criteria will have given more clear picture of the burden. False increase in acute phase reactants especially serum ferritin in different inflammatory conditions makes it difficult to distinguish iron deficiency anemia with anemia of chronic disease. Use of serum transferrin receptor or serum transferrin receptor index can help in the purpose.³⁰

CONCLUSION

In heart failure with ischemic heart disease patient, anemia is common precipitating factor. Normocytic and hypochromic pattern are the commonest. Iron deficiency is the commonest cause. Timely detection and treatment of iron deficiency may prevent heart failure. Unnecessary iron supplementation for any cause of anemia should be avoided.

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REFERENCE

- Ikama MS, Nsitou BM, Kocko I, Mongo NS, Kimbally-Kaky G, Nkoua JL. Prevalence of anaemia among patients with heart failure at the Brazzaville University Hospital. *Cardiovasc J Afr.* 2015 May-Jun;26(3):140-2. [DOI] [PubMed]
- da Silveira AD, Ribeiro RA, Rossini AP, et al. Association of anemia with clinical outcomes in stable coronary artery disease. *Coron Artery Dis.* 2008;19(1):21-26. [DOI]
- McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. *N Engl J Med.* 1971 Dec 23;285(26):1441-6. [DOI]
- Cleland JG, McGowan J. Heart failure due to ischaemic heart disease: epidemiology, pathophysiology and progression. *J CardiovascPharmacol.* 1999;33Suppl 3:S17-S29. [DOI]
- Nutritional anaemias. Report of a WHO scientific group. Geneva, World Health Organization, 1968. (WHO Technical Report Series, No. 405). [Link]
- Preventing and controlling anaemia through primary health care: a guide for health administrators and programme managers. Geneva, World Health Organization, 1989. [Link]
- The Criteria Committee of the New York Heart Association Nomenclature and criteria for diagnosis of diseases of the heart and blood vessels. Boston: Little Brown, 1964 [DOI].
- Raphael C, Briscoe C, Davies J, Ian Whinnett Z, Manisty C, Sutton R, Mayet J, Francis DP. Limitations of the New York Heart Association functional classification system and self-reported walking distances in chronic heart failure. *Heart.* 2007 Apr;93(4):476-82. [DOI] [PMID] [PMCID]
- Tkaczyszyn M, Comín-Colet J, Voors AA, van Veldhuisen DJ, Enjuanes C, Moliner-

- Borja P, Rozentryt P, Poloński L, Banasiak W, Ponikowski P, van der Meer P, Jankowska EA. Iron deficiency and red cell indices in patients with heart failure. *Eur J Heart Fail.* 2018 Jan;20(1):114-122. [DOI] [PMID]
10. Sarma PR. Red Cell Indices. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical Methods: The History, Physical, and Laboratory Examinations.* 3rd edition. Boston: Butterworths; 1990. Chapter 152. [Link]
 11. Poggiali E, Migone De Amicis M, Motta I. Anemia of chronic disease: a unique defect of iron recycling for many different chronic diseases. *Eur J Intern Med.* 2014 Jan;25(1):12-7. [DOI]
 12. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021 Sep 21;42(36):3599-3726. [DOI]
 13. Madu AJ, Ughasoro MD. Anaemia of Chronic Disease: An In-Depth Review. *Med PrincPract.* 2017;26(1):1-9. [DOI] [PMID]
 14. Andrès E, Loukili NH, Noel E, Kaltenbach G, Abdelgheni MB, Perrin AE, Noblet-Dick M, Maloisel F, Schlienger JL, Blicklé JF. Vitamin B12 (cobalamin) deficiency in elderly patients. *CMAJ.* 2004 Aug 3;171(3):251-9. [DOI]
 15. WHO. Serum and red blood cell folate concentrations for assessing folate status in populations. *Vitamin and Mineral Nutrition Information System.* Geneva: World Health Organization. 2015 [Link]
 16. Bista M, Mehta RK, Parajuli SB et al. Prevalence of anemia and associated factors among patients with heart failure at Birat Medical College Teaching Hospital. *Nepalese Heart Journal.* 2023; 20(1); 43–48. [DOI]
 17. Lanier JB, Park JJ, Callahan RC. Anemia in Older Adults. *Am Fam Physician.* 2018;98(7):437-442. [PubMed]
 18. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics--2014 update: a report from the American Heart Association. *Circulation.* 2014;129(3):e28-e292. [DOI]
 19. Poudyal A, Karki KB, Shrestha N, et al. Prevalence and risk factors associated with chronic kidney disease in Nepal: evidence from a nationally representative population-based cross-sectional study. *BMJ Open* 2022;12:e057509. [DOI]
 20. Xanthopoulos A, Papamichail A, Briasoulis A, Loritis K, Bourazana A, Magouliotis DE, Sarafidis P, Stefanidis I, Skoularigis J, Triposkiadis F. Heart Failure in Patients with Chronic Kidney Disease. *J Clin Med.* 2023 Sep 21;12(18):6105. [DOI]
 21. Huang KW, Luo JC, Leu HB, et al. Risk factors for upper gastrointestinal bleeding in coronary artery disease patients receiving both aspirin and clopidogrel. *J Chin Med Assoc.* 2013;76(1):9-14. [DOI]
 22. Casado Arroyo R, Polo-Tomas M, Roncalés MP, Scheiman J, Lanas A. Lower GI bleeding is more common than upper among patients on dual antiplatelet therapy: long-term follow-up of a cohort of patients commonly using PPI co-therapy. *Heart.* 2012;98(9):718-723. [DOI]
 23. Gheorghide M, Sopko G, De Luca L, Velazquez EJ, Parker JD, Binkley PF, Sadowski Z, Golba KS, Prior DL, Rouleau JL, Bonow RO. Navigating the crossroads of coronary artery disease and heart failure. *Circulation.* 2006 Sep 12;114(11):1202-13. [DOI]
 24. Bhandari A, Shah P, Pandey NK, Nepal R, Sherchand O. Anaemia among Patients of Heart Failure in a Tertiary Care Centre of Nepal: A Descriptive Cross-sectional Study. *JNMA J Nepal Med Assoc.* 2021 Sep 15;59(241):833-838. [DOI]
 25. Bhatta S, Aryal, G., & Kafle, R. (2011). Anemia in chronic kidney disease patients in predialysis and postdialysis stages. *Journal of Pathology of Nepal,* 1(1), 26–29. [DOI]
 26. Kafle, S., & Lakhey, M. (2016). Etiological study of microcytic hypochromic anemia. *Journal of*

- Pathology of Nepal, 6(12), 994–997. [DOI]
27. Mishra, S. K., Marasini, S., Gupta, B. K., Agrawal, K. K., & Gautam, N. (2018). Prevalence of Iron Deficiency Anemia in Anemic Patients: A Hospital Based Study. *Journal of Universal College of Medical Sciences*, 6(2), 41–45. [DOI]
28. Singh M, Kafle S. U., Shaukin S, et al. (2020). Study of peripheral blood smear findings in patients of anemia and to compare it with automated hematology analyzer generated red cell parameters. *Birat Journal of Health Sciences*. 2020; 5(3):1231–1235. [DOI]
29. Joosten E, Pelemans W, Hiele M, Noyen J, Verhaeghe R, Boogaerts MA. Prevalence and causes of anaemia in a geriatric hospitalized population. *Gerontology*. 1992; 38(1-2):111-7.
- [DOI] [PMID]
30. Singla R, Garg A, Surana V, Aggarwal S, Gupta G, Singla S. Vitamin B12 Deficiency is Endemic in Indian Population: A Perspective from North India. *Indian J EndocrinolMetab*. 2019 Mar-Apr;23(2):211-214. [DOI]
31. Skikne, B.S., Punnonen, K., Caldron, P.H., Bennett, M.T., Rehu, M., Gasior, G.H., Chamberlin, J.S., Sullivan, L.A., Bray, K.R. and Southwick, P.C. (2011), Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia: A prospective multicenter evaluation of soluble transferrin receptor and the sTfR/log ferritin index†. *Am. J. Hematol.*, 86: 923-927. [DOI]

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